Dossier zur Nutzenbewertung gemäß § 35a SGB V

Isatuximab (SARCLISA®)

Sanofi-Aventis Deutschland GmbH

Anhang 4-G

Isatuximab in Kombination mit Pomalidomid und Dexamethason zur Behandlung des rezidivierten und refraktären Multiplen Myeloms bei Erwachsenen, die mindestens zwei vorausgegangene Therapien, darunter Lenalidomid und einen Proteasom-Inhibitor, erhalten haben und unter der letzten Therapie eine Krankheitsprogression zeigten.

Stand: 07.05.2021

Studie ICARIA-MM (EFC14335)

Endpunkt **Seite**

1. Datenschnitt (11 OCT 2018)

2. Datenschnitt (01 OCT 2020)

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16.2.6.2.1 Overall survival
16.2.6.2.1.2 Subgroup analyses by age (IRT)
16.2.6.2.1.2.1 Overall survival according to age (IRT) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	24 (34.3)	17 (31.5)	17 (31.5)	18 (26.5)	15 (51.7)	8 (25.0)	0.3429
Number (%) of patients censored	46 (65.7)	37 (68.5)	37 (68.5)	50 (73.5)	14 (48.3)	24 (75.0)	
Kaplan-Meier estimates of OS in months							
25% quantile (95% CI)	7.39 (4.468 to 11.565)	8.44 (4.830 to NC)	10.09 (4.600 to 14.489)	10.71 (6.867 to NC)	4.76 (1.248 to 7.294)	10.38 (3.351 to NC)	
Median (95% CI)	NC (11.565 to NC)	NC (14.259 to NC)	14.49 (14.357 to NC)	NC (14.456 to NC)	10.25 (4.895 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.489 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6185		0.3853		0.0329	
Hazard ratio (95% CI) vs Pd	-	0.85 (0.46 to 1.59)		0.75 (0.38 to 1.45)		0.40 (0.17 to 0.96)	
P-value	-	0.6189		0.3869		0.0391	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_os_age_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.3 Subgroup analyses by nb of prior lines (IRT)
16.2.6.2.1.3.1 Overall survival according to nb of prior lines (IRT) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	34 (33.7)	28 (27.5)	22 (42.3)	15 (28.8)	0.5859
Number (%) of patients censored	67 (66.3)	74 (72.5)	30 (57.7)	37 (71.2)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	7.82 (4.567 to 11.565)	10.09 (5.947 to NC)	5.16 (4.468 to 9.068)	10.64 (4.895 to NC)	
Median (95% CI)	NC (13.897 to NC)	NC (14.423 to NC)	14.49 (8.509 to NC)	NC (14.456 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.489 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2581		0.1193	
Hazard ratio (95% CI) vs Pd	-	0.75 (0.45 to 1.24)		0.60 (0.31 to 1.15)	
P-value	-	0.2599		0.1234	
OS probability (95% CI)[a]					
2 Months	0.941 (0.873 to 0.973)	0.980 (0.923 to 0.995)	0.942 (0.830 to 0.981)	0.962 (0.855 to 0.990)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.4 Subgroup analyses by gender
16.2.6.2.1.4.1 Overall survival according to gender - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	21 (30.0)	24 (27.0)	35 (42.2)	19 (29.2)	0.3922
Number (%) of patients censored	49 (70.0)	65 (73.0)	48 (57.8)	46 (70.8)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	10.02 (4.567 to 14.357)	9.59 (4.895 to NC)	6.05 (4.140 to 7.951)	10.64 (6.341 to 14.456)	
Median (95% CI)	NC (14.357 to NC)	NC (NC to NC)	14.49 (11.236 to NC)	NC (14.259 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6184		0.0569	
Hazard ratio (95% CI) vs Pd	-	0.86 (0.48 to 1.55)		0.58 (0.33 to 1.02)	
P-value	-	0.6188		0.0599	
OS probability (95% CI)[a]					
2 Months	0.943 (0.855 to 0.978)	0.966 (0.899 to 0.989)	0.939 (0.860 to 0.974)	0.984 (0.894 to 0.998)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.5 Subgroup analyses by race
16.2.6.2.1.5.1 Overall survival according to race - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	49 (38.9)	31 (26.3)	2 (10.5)	4 (16.7)	0.2936
Number (%) of patients censored	77 (61.1)	87 (73.7)	17 (89.5)	20 (83.3)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	6.24 (4.567 to 9.068)	10.71 (8.312 to NC)	NC (6.472 to NC)	NC (1.478 to NC)	
Median (95% CI)	14.49 (12.879 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0203		0.5496	
Hazard ratio (95% CI) vs Pd	-	0.59 (0.38 to 0.93)		1.67 (0.31 to 9.12)	
P-value	-	0.0218		0.5539	
OS probability (95% CI)[a]					
2 Months	0.936 (0.876 to 0.968)	0.991 (0.941 to 0.999)	1.000 (1.000 to 1.000)	0.958 (0.739 to 0.994)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.6 Subgroup analyses by ethnic origin
16.2.6.2.1.6.1 Overall survival according to ethnic origin - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	2 (66.7)	0 (0.0)	48 (35.8)	35 (26.9)	0.9768
Number (%) of patients censored	1 (33.3)	4 (100.0)	86 (64.2)	95 (73.1)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	0.36 (0.361 to NC)	NC (NC to NC)	7.39 (5.125 to 10.251)	10.64 (8.312 to NC)	
Median (95% CI)	4.04 (0.361 to NC)	NC (NC to NC)	14.49 (13.897 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (0.361 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0701		0.0750	
Hazard ratio (95% CI) vs Pd	-			0.67 (0.44 to 1.04)	
P-value	-	0.9986		0.0769	
OS probability (95% CI)[a]					
2 Months	0.667 (0.054 to 0.945)	1.000 (1.000 to 1.000)	0.947 (0.893 to 0.975)	0.984 (0.939 to 0.996)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_os_ethn_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.7 Subgroup analyses by geographical region
16.2.6.2.1.7.1 Overall survival according to geographical region - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[b]**
Number (%) of deaths	27 (35.5)	18 (32.7)	8 (40.0)	8 (28.6)	0 (0.0)	2 (28.6)	1 (6.7)	2 (9.5)	20 (54.1)	13 (30.2)	0.6319
Number (%) of patients censored	49 (64.5)	37 (67.3)	12 (60.0)	20 (71.4)	5 (100.0)	5 (71.4)	14 (93.3)	19 (90.5)	17 (45.9)	30 (69.8)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	7.29 (4.041 to 11.236)	8.28 (4.337 to 14.259)	6.83 (0.230 to 13.897)	9.13 (4.468 to NC)	NC (NC to NC)	8.80 (5.947 to NC)	NC (8.509 to NC)	NC (1.478 to NC)	4.76 (2.070 to 6.242)	10.71 (4.895 to NC)	
Median (95% CI)	NC (14.357 to NC)	NC (14.259 to NC)	13.90 (5.027 to NC)	NC (11.368 to NC)	NC (NC to NC)	NC (5.947 to NC)	NC (NC to NC)	NC (NC to NC)	11.56 (5.158 to NC)	NC (14.423 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.897 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.489 to NC)	NC (NC to NC)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.7 Subgroup analyses by geographical region
16.2.6.2.1.7.1 Overall survival according to geographical region - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[b]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.6713		0.5233		0.2137		0.7570		0.0166	
Hazard ratio (95% CI) vs Pd	-	0.88 (0.48 to 1.60)		0.73 (0.27 to 1.95)				1.46 (0.13 to 16.07)		0.43 (0.22 to 0.88)	
P-value	-	0.6715		0.5250		0.9978		0.7584		0.0198	
OS probability (95% CI)[a]											
2 Months	0.934 (0.848 to 0.972)	0.964 (0.862 to 0.991)	0.950 (0.695 to 0.993)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.952 (0.707 to 0.993)	0.919 (0.769 to 0.973)	0.976 (0.843 to 0.997)	
4 Months	0.853 (0.750 to 0.916)	0.890 (0.771 to 0.949)	0.950 (0.695 to 0.993)	0.964 (0.772 to 0.995)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.905 (0.670 to 0.975)	0.865 (0.705 to 0.941)	0.952 (0.823 to 0.988)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.8 Subgroup analyses by regulatory region
16.2.6.2.1.8.1 Overall survival according to regulatory region - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	35 (36.1)	23 (29.9)	21 (37.5)	20 (26.0)	0.6995
Number (%) of patients censored	62 (63.9)	54 (70.1)	35 (62.5)	57 (74.0)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	6.60 (4.567 to 10.382)	10.38 (5.782 to NC)	7.16 (4.468 to 12.879)	11.37 (7.688 to NC)	
Median (95% CI)	14.49 (14.357 to NC)	NC (14.259 to NC)	NC (11.565 to NC)	NC (14.456 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2765		0.1443	
Hazard ratio (95% CI) vs Pd	-	0.75 (0.44 to 1.27)		0.64 (0.34 to 1.17)	
P-value	-	0.2782		0.1477	
OS probability (95% CI)[a]					
2 Months	0.938 (0.867 to 0.972)	0.974 (0.900 to 0.993)	0.946 (0.843 to 0.982)	0.974 (0.899 to 0.993)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.9 Subgroup analyses by baseline ECOG PS
16.2.6.2.1.9.1 Overall survival according to baseline ECOG PS - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	49 (35.8)	36 (26.1)	7 (43.8)	7 (43.8)	0.4476
Number (%) of patients censored	88 (64.2)	102 (73.9)	9 (56.3)	9 (56.3)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	7.39 (5.027 to 10.382)	11.37 (8.444 to 14.456)	4.47 (0.690 to 8.509)	3.35 (0.361 to NC)	
Median (95% CI)	NC (13.897 to NC)	NC (14.456 to NC)	NC (4.468 to NC)	NC (3.351 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0455		0.8709	
Hazard ratio (95% CI) vs Pd	-	0.65 (0.42 to 0.99)		1.09 (0.38 to 3.11)	
P-value	-	0.0472		0.8708	
OS probability (95% CI)[a]					
2 Months	0.941 (0.886 to 0.970)	0.985 (0.943 to 0.996)	0.938 (0.632 to 0.991)	0.875 (0.586 to 0.967)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.10 Subgroup analyses by ISS staging
16.2.6.2.1.10.1 Overall survival according to ISS staging - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	8 (15.7)	11 (17.2)	18 (32.1)	16 (30.2)	29 (67.4)	16 (47.1)	0.2426
Number (%) of patients censored	43 (84.3)	53 (82.8)	38 (67.9)	37 (69.8)	14 (32.6)	18 (52.9)	
Kaplan-Meier estimates of OS in months							
25% quantile (95% CI)	NC (10.382 to NC)	NC (9.133 to NC)	9.07 (4.895 to 14.489)	10.38 (5.881 to 14.456)	2.83 (1.248 to 4.468)	4.83 (3.055 to 9.593)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.236 to NC)	NC (14.259 to NC)	5.16 (4.140 to 12.879)	14.42 (6.341 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.489 to NC)	NC (NC to NC)	14.36 (8.641 to NC)	NC (14.423 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6963		0.5559		0.0307	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.48 to 2.98)		0.82 (0.42 to 1.60)		0.51 (0.28 to 0.95)	
P-value	-	0.6967		0.5563		0.0337	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_os_seiss_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.11 Subgroup analyses by R-ISS stage
16.2.6.2.1.11.1 Overall survival according to R-ISS stage - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	1 (3.2)	5 (12.8)	36 (36.7)	28 (28.3)	19 (79.2)	10 (62.5)	0.2087
Number (%) of patients censored	30 (96.8)	34 (87.2)	62 (63.3)	71 (71.7)	5 (20.8)	6 (37.5)	
Kaplan-Meier estimates of OS in months							
25% quantile (95% CI)	NC (NC to NC)	NC (10.645 to NC)	7.72 (5.158 to 11.236)	10.38 (7.688 to 14.456)	1.97 (0.230 to 2.891)	3.43 (0.361 to 6.341)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	14.49 (12.879 to NC)	NC (14.423 to NC)	4.04 (2.004 to 6.374)	6.69 (3.351 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	10.25 (4.140 to NC)	NC (6.341 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1602		0.1540		0.1678	
Hazard ratio (95% CI) vs Pd	-	4.12 (0.48 to 35.31)		0.70 (0.43 to 1.15)		0.59 (0.27 to 1.26)	
P-value	-	0.1958		0.1562		0.1728	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_os_seriss_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.2.1.12.1 Overall survival according to cytogenetic abnormality (del17p) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	10 (43.5)	8 (57.1)	35 (36.8)	29 (24.6)	0.1344
Number (%) of patients censored	13 (56.5)	6 (42.9)	60 (63.2)	89 (75.4)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	3.75 (0.230 to 4.140)	3.52 (0.361 to 6.341)	7.82 (5.125 to 11.236)	14.26 (8.805 to NC)	
Median (95% CI)	NC (3.745 to NC)	6.34 (3.351 to NC)	14.49 (13.897 to NC)	NC (14.456 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (6.341 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6899		0.0314	
Hazard ratio (95% CI) vs Pd	-	1.21 (0.48 to 3.07)		0.59 (0.36 to 0.96)	
P-value	-	0.6903		0.0335	
OS probability (95% CI)[a]					
2 Months	0.865 (0.638 to 0.955)	0.857 (0.539 to 0.962)	0.958 (0.892 to 0.984)	0.991 (0.941 to 0.999)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_os_cyto_de_i_t_x.rtf (20APR2021 10:48)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.13 Subgroup analyses by cytogenetic abnormality
16.2.6.2.1.13.1 Overall survival according to cytogenetic abnormality - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	14 (38.9)	11 (45.8)	29 (37.2)	26 (25.2)	0.1651
Number (%) of patients censored	22 (61.1)	13 (54.2)	49 (62.8)	77 (74.8)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	4.04 (2.004 to 10.251)	4.47 (0.361 to 9.133)	7.95 (5.158 to 11.565)	14.26 (8.444 to NC)	
Median (95% CI)	NC (4.764 to NC)	10.71 (4.895 to NC)	14.36 (13.897 to NC)	NC (14.456 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.489 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7767		0.0453	
Hazard ratio (95% CI) vs Pd	-	1.12 (0.51 to 2.47)		0.58 (0.34 to 0.99)	
P-value	-	0.7768		0.0478	
OS probability (95% CI)[a]					
2 Months	0.915 (0.759 to 0.972)	0.875 (0.661 to 0.958)	0.949 (0.869 to 0.980)	1.000 (1.000 to 1.000)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_os_care_de_i_t_x.rtf (20APR2021 10:48)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.14 Subgroup analyses by previous autologous stem-cell
16.2.6.2.1.14.1 Overall survival according to previous autologous stem-cell - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	30 (33.3)	26 (31.3)	26 (41.3)	17 (23.9)	0.0984
Number (%) of patients censored	60 (66.7)	57 (68.7)	37 (58.7)	54 (76.1)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	9.07 (4.600 to 13.897)	9.13 (5.782 to 14.259)	5.16 (2.595 to 8.509)	14.42 (5.947 to NC)	
Median (95% CI)	NC (13.897 to NC)	NC (14.259 to NC)	NC (8.509 to NC)	NC (14.456 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7690		0.0149	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.55 to 1.56)		0.47 (0.26 to 0.88)	
P-value	-	0.7695		0.0173	
OS probability (95% CI)[a]					
2 Months	0.966 (0.899 to 0.989)	0.963 (0.891 to 0.988)	0.905 (0.800 to 0.956)	0.986 (0.904 to 0.998)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_os_auto_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.15 Subgroup analyses by previous allogenic transplantation
16.2.6.2.1.15.1 Overall survival according to previous allogenic transplantation - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	0 (0.0)	0 (0.0)	56 (37.1)	43 (28.3)	0.9997
Number (%) of patients censored	2 (100.0)	2 (100.0)	95 (62.9)	109 (71.7)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	6.60 (4.895 to 10.021)	10.38 (7.031 to 14.456)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.897 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0629	
Hazard ratio (95% CI) vs Pd	-			0.69 (0.46 to 1.02)	
P-value	-			0.0644	
OS probability (95% CI)[a]					
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.940 (0.888 to 0.968)	0.974 (0.931 to 0.990)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_os_allt_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.16 Subgroup analyses by MM type at SE
16.2.6.2.1.16.1 Overall survival according to MM type at SE - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	39 (38.6)	29 (27.9)	12 (29.3)	7 (21.2)	0.8894
Number (%) of patients censored	62 (61.4)	75 (72.1)	29 (70.7)	26 (78.8)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	6.37 (4.764 to 10.251)	10.71 (7.688 to 14.456)	8.51 (2.595 to NC)	NC (3.351 to NC)	
Median (95% CI)	14.49 (11.565 to NC)	NC (14.423 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0728		0.3515	
Hazard ratio (95% CI) vs Pd	-	0.65 (0.40 to 1.05)		0.64 (0.25 to 1.64)	
P-value	-	0.0753		0.3554	
OS probability (95% CI)[a]					
2 Months	0.950 (0.884 to 0.979)	0.990 (0.933 to 0.999)	0.927 (0.790 to 0.976)	0.939 (0.779 to 0.984)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_os_semm_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.6.2.1.17.1 Overall survival according to MM type at initial diagnosis - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	39 (39.0)	29 (28.4)	17 (32.7)	14 (27.5)	0.7542
Number (%) of patients censored	61 (61.0)	73 (71.6)	35 (67.3)	37 (72.5)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	6.37 (4.600 to 10.251)	10.71 (7.688 to 14.456)	7.39 (2.595 to NC)	10.09 (4.862 to NC)	
Median (95% CI)	14.49 (11.565 to NC)	NC (14.423 to NC)	NC (14.357 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0766		0.4769	
Hazard ratio (95% CI) vs Pd	-	0.65 (0.40 to 1.05)		0.77 (0.38 to 1.57)	
P-value	-	0.0792		0.4788	
OS probability (95% CI)[a]					
2 Months	0.950 (0.883 to 0.979)	0.990 (0.932 to 0.999)	0.923 (0.808 to 0.970)	0.941 (0.829 to 0.981)	

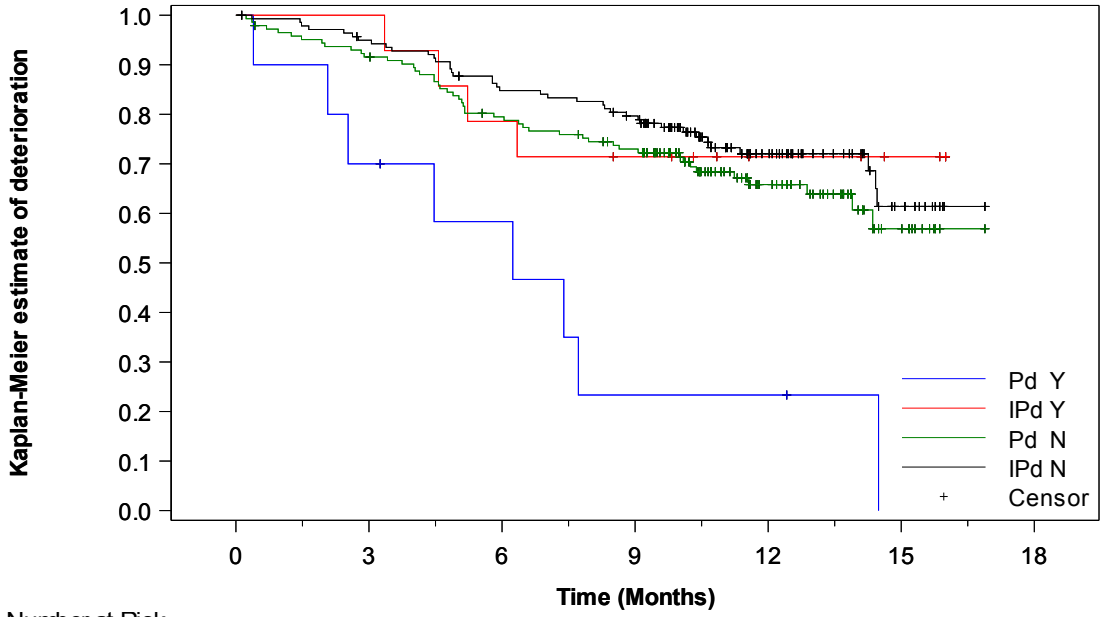
Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_os_dghc_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.18 Subgroup analyses by existing plasmacytoma
16.2.6.2.1.18.1 Overall survival according to existing plasmacytoma - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	8 (80.0)	4 (28.6)	48 (33.6)	39 (27.9)	0.0378
Number (%) of patients censored	2 (20.0)	10 (71.4)	95 (66.4)	101 (72.1)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	2.53 (0.394 to 6.242)	6.34 (3.351 to NC)	7.95 (5.092 to 11.236)	10.64 (8.279 to 14.456)	
Median (95% CI)	6.24 (0.394 to 14.489)	NC (5.224 to NC)	NC (13.897 to NC)	NC (14.456 to NC)	
75% quantile (95% CI)	7.72 (4.468 to 14.489)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0060		0.2235	
Hazard ratio (95% CI) vs Pd	-	0.21 (0.06 to 0.71)		0.77 (0.50 to 1.17)	
P-value	-	0.0122		0.2248	
OS probability (95% CI)[a]					
2 Months	0.900 (0.473 to 0.985)	1.000 (1.000 to 1.000)	0.944 (0.891 to 0.971)	0.971 (0.925 to 0.989)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_os_mri_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.18 Subgroup analyses by existing plasmacytoma
16.2.6.2.1.18.2 Overall survival according to existing plasmacytoma - Kaplan-Meier curve- ITT population



Number at Risk

Pd Y	10	7	5	2	2	0	0
IPd Y	14	14	11	9	5	3	0
Pd N	143	130	111	99	44	11	0
IPd N	140	131	116	107	46	12	0

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.19 Subgroup analyses by baseline creatinine clearance
16.2.6.2.1.19.1 Overall survival according to baseline creatinine clearance - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	24 (25.0)	15 (17.2)	27 (55.1)	20 (36.4)	0.7780
Number (%) of patients censored	72 (75.0)	72 (82.8)	22 (44.9)	35 (63.6)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	10.09 (6.045 to NC)	NC (10.645 to NC)	5.13 (2.004 to 7.294)	8.31 (4.830 to 14.423)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	11.56 (6.604 to 14.489)	NC (10.710 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	14.49 (14.357 to 14.489)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1464		0.0328	
Hazard ratio (95% CI) vs Pd	-	0.62 (0.33 to 1.19)		0.53 (0.30 to 0.96)	
P-value	-	0.1501		0.0357	
OS probability (95% CI)[a]					
2 Months	0.969 (0.906 to 0.990)	0.988 (0.920 to 0.998)	0.898 (0.772 to 0.956)	0.982 (0.878 to 0.997)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_os_crcl_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.2.1.20.1 Overall survival according to previous therapy with anti-CD38 mAB - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	2 (100.0)	0 (0.0)	54 (35.8)	43 (28.3)	0.9826
Number (%) of patients censored	0 (0.0)	2 (100.0)	97 (64.2)	109 (71.7)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	4.04 (4.041 to 6.604)	NC (NC to NC)	7.39 (5.027 to 10.251)	10.38 (7.031 to 14.456)	
Median (95% CI)	5.32 (4.041 to 6.604)	NC (NC to NC)	NC (13.897 to NC)	NC (NC to NC)	
75% quantile (95% CI)	6.60 (4.041 to 6.604)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.1055	
Hazard ratio (95% CI) vs Pd	-			0.72 (0.48 to 1.07)	
P-value	-	0.9991		0.1073	
OS probability (95% CI)[a]					
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.940 (0.888 to 0.968)	0.974 (0.931 to 0.990)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_os_prmab_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.21 Subgroup analyses by refractory to PI status
16.2.6.2.1.21.1 Overall survival according to refractory to PI status - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	43 (37.4)	33 (28.0)	13 (34.2)	10 (27.8)	0.5148
Number (%) of patients censored	72 (62.6)	85 (72.0)	25 (65.8)	26 (72.2)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	6.47 (4.567 to 10.021)	10.64 (7.688 to 14.456)	7.95 (4.008 to NC)	10.09 (2.760 to NC)	
Median (95% CI)	14.36 (12.879 to NC)	NC (14.456 to NC)	NC (10.382 to NC)	NC (10.710 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0467		0.6971	
Hazard ratio (95% CI) vs Pd	-	0.63 (0.40 to 1.00)		0.85 (0.37 to 1.94)	
P-value	-	0.0486		0.6974	
OS probability (95% CI)[a]					
2 Months	0.930 (0.865 to 0.964)	0.983 (0.933 to 0.996)	0.974 (0.828 to 0.996)	0.944 (0.796 to 0.986)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.22 Subgroup analyses by refractory to IMID status
16.2.6.2.1.22.1 Overall survival according to refractory to IMID status - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	54 (37.5)	41 (27.9)	2 (22.2)	2 (28.6)	0.3668
Number (%) of patients censored	90 (62.5)	106 (72.1)	7 (77.8)	5 (71.4)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	6.37 (4.764 to 9.068)	10.64 (7.031 to 14.456)	13.90 (11.236 to NC)	7.69 (6.867 to NC)	
Median (95% CI)	NC (14.357 to NC)	NC (NC to NC)	NC (11.236 to NC)	NC (6.867 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.897 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0416		0.2467	
Hazard ratio (95% CI) vs Pd	-	0.66 (0.44 to 0.99)		3.89 (0.33 to 45.38)	
P-value	-	0.0430		0.2782	
OS probability (95% CI)[a]					
2 Months	0.937 (0.883 to 0.967)	0.973 (0.929 to 0.990)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_os_refr1_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.1 Overall survival
16.2.6.2.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.2.1.23.1 Overall survival according to refractory to refractory to lenalidomide in last previous regimen - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of deaths	31 (35.2)	26 (28.0)	25 (38.5)	17 (27.9)	0.4878
Number (%) of patients censored	57 (64.8)	67 (72.0)	40 (61.5)	44 (72.1)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	7.29 (4.764 to 10.382)	10.64 (5.224 to 14.423)	5.16 (3.745 to 11.236)	10.38 (7.031 to NC)	
Median (95% CI)	NC (14.489 to NC)	NC (14.423 to NC)	14.36 (11.236 to NC)	NC (14.456 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.357 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3335		0.0819	
Hazard ratio (95% CI) vs Pd	-	0.77 (0.46 to 1.30)		0.58 (0.31 to 1.08)	
P-value	-	0.3350		0.0856	
OS probability (95% CI)[a]					
2 Months	0.955 (0.883 to 0.983)	0.967 (0.902 to 0.989)	0.922 (0.823 to 0.967)	0.984 (0.889 to 0.998)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_os_llen_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.2 Subgroup analyses by age (IRT)
16.2.6.1.1.2.1 PFS - Primary analysis based on disease assessment by the IRC according to age (IRT) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	41 (58.6)	26 (48.1)	29 (53.7)	32 (47.1)	19 (65.5)	15 (46.9)	0.5952
Number (%) of patients censored	29 (41.4)	28 (51.9)	25 (46.3)	36 (52.9)	10 (34.5)	17 (53.1)	
Kaplan-Meier estimates of PFS in months							
25% quantile (95% CI)	2.30 (1.478 to 3.055)	3.81 (2.398 to 4.830)	2.89 (2.333 to 5.585)	5.82 (3.285 to 8.246)	1.94 (0.329 to 3.745)	3.09 (2.366 to 8.969)	
Median (95% CI)	5.03 (3.285 to 8.279)	11.53 (4.567 to 14.784)	8.57 (4.567 to 12.057)	11.56 (8.279 to NC)	4.47 (2.595 to 7.754)	11.40 (4.435 to NC)	
75% quantile (95% CI)	NC (8.378 to NC)	14.78 (13.306 to NC)	12.48 (10.251 to NC)	NC (15.211 to NC)	10.05 (5.585 to NC)	NC (12.255 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0916		0.0797		0.0302	
Hazard ratio (95% CI) vs Pd	-	0.66 (0.40 to 1.07)		0.64 (0.38 to 1.06)		0.48 (0.24 to 0.95)	
P-value	-	0.0940		0.0822		0.0339	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_age_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.3 Subgroup analyses by nb of prior lines (IRT)
16.2.6.1.1.3.1 PFS - Primary analysis based on disease assessment by the IRC according to nb of prior lines (IRT) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	57 (56.4)	44 (43.1)	32 (61.5)	29 (55.8)	0.9583
Number (%) of patients censored	44 (43.6)	58 (56.9)	20 (38.5)	23 (44.2)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	2.89 (2.300 to 4.041)	4.14 (2.760 to 8.115)	1.94 (0.986 to 2.825)	4.27 (2.990 to 5.848)	
Median (95% CI)	7.82 (5.027 to 10.086)	12.25 (8.969 to NC)	4.27 (2.563 to 8.575)	9.40 (4.830 to 14.784)	
75% quantile (95% CI)	NC (11.072 to NC)	NC (15.211 to NC)	NC (7.031 to NC)	14.78 (12.715 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0085		0.0381	
Hazard ratio (95% CI) vs Pd	-	0.59 (0.40 to 0.88)		0.59 (0.36 to 0.98)	
P-value	-	0.0093		0.0403	
PFS probability (95% CI)[a]					
2 Months	0.854 (0.762 to 0.913)	0.904 (0.823 to 0.949)	0.697 (0.542 to 0.808)	0.922 (0.804 to 0.970)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_plne_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.4 Subgroup analyses by gender
16.2.6.1.1.4.1 PFS - Primary analysis based on disease assessment by the IRC according to gender - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	41 (58.6)	43 (48.3)	48 (57.8)	30 (46.2)	0.5454
Number (%) of patients censored	29 (41.4)	46 (51.7)	35 (42.2)	35 (53.8)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	2.86 (1.938 to 3.713)	3.84 (2.990 to 6.472)	2.60 (1.478 to 3.154)	4.70 (1.971 to 7.031)	
Median (95% CI)	6.47 (3.745 to 11.072)	11.50 (8.246 to 14.784)	7.39 (3.811 to 8.575)	12.71 (7.031 to 15.211)	
75% quantile (95% CI)	NC (11.072 to NC)	NC (14.784 to NC)	12.48 (9.528 to NC)	NC (13.897 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0624		0.0106	
Hazard ratio (95% CI) vs Pd	-	0.67 (0.43 to 1.02)		0.55 (0.35 to 0.88)	
P-value	-	0.0641		0.0117	
PFS probability (95% CI)[a]					
2 Months	0.813 (0.694 to 0.889)	0.941 (0.864 to 0.975)	0.789 (0.674 to 0.867)	0.866 (0.750 to 0.931)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_sex_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.5 Subgroup analyses by race
16.2.6.1.1.5.1 PFS - Primary analysis based on disease assessment by the IRC according to race - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	74 (58.7)	56 (47.5)	10 (52.6)	10 (41.7)	0.8587
Number (%) of patients censored	52 (41.3)	62 (52.5)	9 (47.4)	14 (58.3)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	2.79 (1.938 to 3.154)	4.57 (3.515 to 7.031)	2.89 (0.986 to 7.819)	5.78 (2.168 to 12.255)	
Median (95% CI)	6.47 (4.468 to 9.528)	11.53 (8.969 to 14.784)	7.85 (1.971 to NC)	12.25 (5.782 to NC)	
75% quantile (95% CI)	NC (10.251 to NC)	NC (14.784 to NC)	NC (7.852 to NC)	NC (12.255 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0023		0.1900	
Hazard ratio (95% CI) vs Pd	-	0.59 (0.41 to 0.83)		0.56 (0.23 to 1.35)	
P-value	-	0.0026		0.1960	
PFS probability (95% CI)[a]					
2 Months	0.814 (0.729 to 0.875)	0.928 (0.861 to 0.963)	0.767 (0.492 to 0.906)	1.000 (1.000 to 1.000)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_race_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.6 Subgroup analyses by ethnic origin
16.2.6.1.1.6.1 PFS - Primary analysis based on disease assessment by the IRC according to ethnic origin - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	2 (66.7)	2 (50.0)	79 (59.0)	59 (45.4)	0.1555
Number (%) of patients censored	1 (33.3)	2 (50.0)	55 (41.0)	71 (54.6)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	0.36 (0.361 to 5.027)	11.56 (11.565 to 13.306)	2.79 (1.971 to 3.154)	4.50 (3.680 to 6.472)	
Median (95% CI)	5.03 (0.361 to 5.027)	13.31 (11.565 to 13.306)	7.03 (4.468 to 8.279)	12.25 (8.542 to NC)	
75% quantile (95% CI)	5.03 (0.361 to 5.027)	13.31 (11.565 to 13.306)	NC (10.086 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0311		0.0007	
Hazard ratio (95% CI) vs Pd	-			0.56 (0.40 to 0.79)	
P-value	-	0.9980		0.0008	
PFS probability (95% CI)[a]					
2 Months	0.667 (0.054 to 0.945)	1.000 (1.000 to 1.000)	0.816 (0.735 to 0.875)	0.943 (0.883 to 0.972)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_ethn_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.7 Subgroup analyses by geographical region
16.2.6.1.1.7.1 PFS - Primary analysis based on disease assessment by the IRC according to geographical region - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[b]**
Number (%) of events	39 (51.3)	24 (43.6)	14 (70.0)	15 (53.6)	2 (40.0)	3 (42.9)	8 (53.3)	8 (38.1)	26 (70.3)	23 (53.5)	0.9308
Number (%) of patients censored	37 (48.7)	31 (56.4)	6 (30.0)	13 (46.4)	3 (60.0)	4 (57.1)	7 (46.7)	13 (61.9)	11 (29.7)	20 (46.5)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	2.79 (1.413 to 3.745)	2.83 (1.938 to 4.435)	2.83 (0.230 to 4.731)	4.47 (2.760 to 7.425)	5.03 (2.595 to NC)	2.37 (1.708 to NC)	3.06 (1.971 to 7.852)	5.82 (2.628 to 12.255)	2.30 (0.986 to 2.858)	4.70 (2.990 to 8.115)	
Median (95% CI)	7.75 (3.811 to 10.251)	11.53 (3.943 to NC)	5.59 (2.825 to 10.382)	12.71 (4.830 to 13.306)	NC (2.595 to NC)	11.56 (1.708 to NC)	7.85 (2.891 to NC)	NC (5.815 to NC)	4.70 (2.595 to 8.378)	11.20 (7.031 to NC)	
75% quantile (95% CI)	NC (10.251 to NC)	NC (13.897 to NC)	10.38 (5.585 to NC)	13.31 (12.715 to NC)	NC (2.595 to NC)	NC (11.565 to NC)	NC (7.852 to NC)	NC (12.255 to NC)	12.48 (7.031 to NC)	NC (14.784 to NC)	
Comparison vs. Pd											

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_greg_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.7 Subgroup analyses by geographical region
16.2.6.1.1.7.1 PFS - Primary analysis based on disease assessment by the IRC according to geographical region - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[b]**
Log-Rank test p-value[a] vs Pd	-	0.1422		0.1720		0.8923		0.1846		0.0233	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.41 to 1.14)		0.60 (0.29 to 1.25)		1.13 (0.19 to 6.85)		0.52 (0.19 to 1.39)		0.53 (0.30 to 0.93)	
P-value	-	0.1446		0.1765		0.8923		0.1922		0.0257	
PFS probability (95% CI)[a]											
2 Months	0.774 (0.648 to 0.860)	0.817 (0.678 to 0.901)	0.844 (0.591 to 0.947)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.857 (0.334 to 0.979)	0.857 (0.539 to 0.962)	1.000 (1.000 to 1.000)	0.771 (0.595 to 0.879)	0.928 (0.793 to 0.976)	
4 Months	0.619 (0.484 to 0.729)	0.645 (0.492 to 0.763)	0.633 (0.381 to 0.806)	0.815 (0.611 to 0.918)	0.800 (0.204 to 0.969)	0.714 (0.258 to 0.920)	0.635 (0.331 to 0.830)	0.895 (0.641 to 0.973)	0.571 (0.393 to 0.715)	0.804 (0.645 to 0.897)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_greg_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.8 Subgroup analyses by regulatory region
16.2.6.1.1.8.1 PFS - Primary analysis based on disease assessment by the IRC according to regulatory region - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	52 (53.6)	36 (46.8)	37 (66.1)	37 (48.1)	0.7207
Number (%) of patients censored	45 (46.4)	41 (53.2)	19 (33.9)	40 (51.9)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	2.60 (1.413 to 3.713)	2.99 (1.971 to 7.031)	2.83 (1.938 to 3.285)	4.70 (3.713 to 7.031)	
Median (95% CI)	7.03 (4.041 to 9.758)	11.50 (7.491 to 14.784)	6.47 (3.285 to 8.575)	12.25 (7.622 to NC)	
75% quantile (95% CI)	NC (10.251 to NC)	NC (13.897 to NC)	12.48 (8.575 to NC)	NC (15.211 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0377		0.0105	
Hazard ratio (95% CI) vs Pd	-	0.64 (0.41 to 0.98)		0.56 (0.35 to 0.88)	
P-value	-	0.0393		0.0116	
PFS probability (95% CI)[a]					
2 Months	0.779 (0.673 to 0.855)	0.831 (0.722 to 0.901)	0.834 (0.705 to 0.910)	0.986 (0.908 to 0.998)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_rreg_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.6.1.1.9.1 PFS - Primary analysis based on disease assessment by the IRC according to baseline ECOG PS - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	80 (58.4)	62 (44.9)	9 (56.3)	11 (68.8)	0.5468
Number (%) of patients censored	57 (41.6)	76 (55.1)	7 (43.8)	5 (31.3)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	2.79 (1.938 to 3.055)	4.50 (3.680 to 7.031)	2.76 (0.066 to 4.041)	2.43 (0.263 to 2.760)	
Median (95% CI)	7.03 (4.698 to 9.528)	11.53 (8.969 to NC)	4.04 (2.595 to 8.575)	5.88 (1.708 to 13.897)	
75% quantile (95% CI)	NC (10.382 to NC)	NC (14.784 to NC)	8.57 (4.041 to NC)	13.90 (2.760 to 15.211)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0011		0.6874	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.41 to 0.81)		0.83 (0.33 to 2.09)	
P-value	-	0.0012		0.6878	
PFS probability (95% CI)[a]					
2 Months	0.795 (0.712 to 0.857)	0.923 (0.861 to 0.958)	0.862 (0.550 to 0.964)	0.794 (0.488 to 0.929)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_ecog_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.10 Subgroup analyses by ISS staging
16.2.6.1.1.10.1 PFS - Primary analysis based on disease assessment by the IRC according to ISS staging - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	28 (54.9)	25 (39.1)	32 (57.1)	23 (43.4)	27 (62.8)	24 (70.6)	0.7901
Number (%) of patients censored	23 (45.1)	39 (60.9)	24 (42.9)	30 (56.6)	16 (37.2)	10 (29.4)	
Kaplan-Meier estimates of PFS in months							
25% quantile (95% CI)	4.73 (2.595 to 7.852)	7.62 (3.713 to 11.203)	2.76 (1.938 to 2.858)	4.44 (2.760 to 5.881)	1.48 (0.361 to 2.858)	2.43 (1.840 to 4.567)	
Median (95% CI)	9.76 (7.754 to 12.485)	13.31 (11.203 to NC)	5.03 (2.858 to 10.053)	11.53 (5.782 to NC)	3.29 (1.971 to 5.585)	6.47 (2.760 to 9.495)	
75% quantile (95% CI)	NC (12.057 to NC)	NC (14.784 to NC)	NC (9.758 to NC)	NC (NC to NC)	7.43 (4.468 to NC)	12.71 (8.542 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1250		0.0237		0.1081	
Hazard ratio (95% CI) vs Pd	-	0.66 (0.38 to 1.13)		0.54 (0.32 to 0.93)		0.63 (0.36 to 1.11)	
P-value	-	0.1277		0.0259		0.1110	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_seiss_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.11 Subgroup analyses by R-ISS stage
16.2.6.1.1.11.1 PFS - Primary analysis based on disease assessment by the IRC according to R-ISS stage - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	17 (54.8)	13 (33.3)	57 (58.2)	47 (47.5)	15 (62.5)	13 (81.3)	0.9871
Number (%) of patients censored	14 (45.2)	26 (66.7)	41 (41.8)	52 (52.5)	9 (37.5)	3 (18.8)	
Kaplan-Meier estimates of PFS in months							
25% quantile (95% CI)	5.65 (2.891 to 8.279)	8.94 (3.844 to 12.255)	2.76 (1.938 to 3.055)	4.27 (3.088 to 5.815)	1.25 (0.066 to 1.971)	1.91 (0.361 to 2.760)	
Median (95% CI)	10.38 (7.754 to NC)	14.78 (11.203 to NC)	6.47 (4.041 to 9.528)	11.50 (7.491 to 15.211)	1.97 (1.248 to 3.285)	2.79 (1.840 to 9.495)	
75% quantile (95% CI)	NC (12.057 to NC)	NC (14.784 to NC)	11.20 (10.053 to NC)	NC (13.306 to NC)	3.29 (2.793 to NC)	9.49 (2.760 to 13.897)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1408		0.0068		0.1966	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.28 to 1.20)		0.59 (0.40 to 0.87)		0.60 (0.28 to 1.31)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_seriss_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.1.1.12.1 PFS - Primary analysis based on disease assessment by the IRC according to cytogenetic abnormality (del17p) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	13 (56.5)	7 (50.0)	60 (63.2)	58 (49.2)	0.6565
Number (%) of patients censored	10 (43.5)	7 (50.0)	35 (36.8)	60 (50.8)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	2.83 (0.230 to 3.745)	2.63 (0.361 to 4.468)	2.60 (1.938 to 3.088)	4.70 (3.088 to 7.031)	
Median (95% CI)	7.39 (2.793 to 11.072)	9.13 (1.807 to NC)	5.59 (3.811 to 8.049)	11.53 (8.279 to 13.897)	
75% quantile (95% CI)	11.07 (7.392 to NC)	NC (4.468 to NC)	NC (9.758 to NC)	NC (13.897 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5655		0.0021	
Hazard ratio (95% CI) vs Pd	-	0.76 (0.30 to 1.92)		0.57 (0.40 to 0.82)	
P-value	-	0.5667		0.0024	
PFS probability (95% CI)[a]					
2 Months	0.832 (0.564 to 0.943)	0.755 (0.416 to 0.914)	0.795 (0.694 to 0.865)	0.929 (0.863 to 0.964)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_cyto_de_i_t_x.rtf (20APR2021 10:48)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.6.1.1.13.1 PFS - Primary analysis based on disease assessment by the IRC according to cytogenetic abnormality - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	22 (61.1)	14 (58.3)	48 (61.5)	50 (48.5)	0.9990
Number (%) of patients censored	14 (38.9)	10 (41.7)	30 (38.5)	53 (51.5)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	2.76 (1.183 to 2.825)	2.63 (0.361 to 5.782)	2.86 (1.938 to 4.271)	4.50 (3.088 to 7.031)	
Median (95% CI)	3.75 (2.793 to 7.885)	7.49 (2.628 to NC)	7.43 (4.468 to 9.758)	11.56 (8.542 to 13.897)	
75% quantile (95% CI)	9.76 (4.731 to NC)	NC (7.491 to NC)	NC (10.251 to NC)	15.21 (13.897 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2137		0.0196	
Hazard ratio (95% CI) vs Pd	-	0.65 (0.33 to 1.28)		0.62 (0.42 to 0.93)	
P-value	-	0.2171		0.0207	
PFS probability (95% CI)[a]					
2 Months	0.753 (0.549 to 0.874)	0.776 (0.543 to 0.900)	0.821 (0.711 to 0.892)	0.939 (0.870 to 0.972)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_care_de_i_t_x.rtf (20APR2021 10:48)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.6.1.1.14.1 PFS - Primary analysis based on disease assessment by the IRC according to previous autologous stem-cell - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	55 (61.1)	40 (48.2)	34 (54.0)	33 (46.5)	0.9403
Number (%) of patients censored	35 (38.9)	43 (51.8)	29 (46.0)	38 (53.5)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	2.79 (1.971 to 3.713)	4.27 (2.825 to 7.425)	2.60 (1.281 to 3.088)	4.44 (2.760 to 5.881)	
Median (95% CI)	7.03 (4.567 to 9.528)	11.50 (8.246 to 14.784)	5.85 (3.088 to 10.382)	11.56 (6.472 to NC)	
75% quantile (95% CI)	12.48 (10.053 to NC)	15.21 (13.897 to NC)	NC (10.382 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0135		0.0465	
Hazard ratio (95% CI) vs Pd	-	0.60 (0.40 to 0.90)		0.62 (0.38 to 1.00)	
P-value	-	0.0145		0.0486	
PFS probability (95% CI)[a]					
2 Months	0.799 (0.693 to 0.872)	0.898 (0.806 to 0.948)	0.803 (0.672 to 0.886)	0.925 (0.830 to 0.968)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_auto_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.6.1.1.15.1 PFS - Primary analysis based on disease assessment by the IRC according to previous allogenic transplantation - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	1 (50.0)	1 (50.0)	88 (58.3)	72 (47.4)	0.5171
Number (%) of patients censored	1 (50.0)	1 (50.0)	63 (41.7)	80 (52.6)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	7.03 (7.031 to NC)	2.99 (2.990 to NC)	2.76 (1.971 to 2.891)	4.27 (3.088 to 5.848)	
Median (95% CI)	NC (7.031 to NC)	NC (2.990 to NC)	5.85 (4.468 to 8.279)	11.53 (8.936 to 13.897)	
75% quantile (95% CI)	NC (7.031 to NC)	NC (2.990 to NC)	NC (10.251 to NC)	NC (14.784 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.0010	
Hazard ratio (95% CI) vs Pd	-	1.41 (0.08 to 23.57)		0.59 (0.43 to 0.81)	
P-value	-	0.8092		0.0011	
PFS probability (95% CI)[a]					
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.798 (0.719 to 0.857)	0.909 (0.848 to 0.946)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_allt_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.16 Subgroup analyses by MM type at SE
16.2.6.1.1.16.1 PFS - Primary analysis based on disease assessment by the IRC according to MM type at SE - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	57 (56.4)	51 (49.0)	26 (63.4)	13 (39.4)	0.3641
Number (%) of patients censored	44 (43.6)	53 (51.0)	15 (36.6)	20 (60.6)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	2.83 (1.971 to 3.811)	4.47 (3.023 to 5.881)	1.97 (1.281 to 2.891)	5.82 (1.446 to 11.400)	
Median (95% CI)	7.75 (4.698 to 9.758)	11.56 (8.279 to 14.784)	5.03 (2.595 to 10.382)	13.90 (8.115 to NC)	
75% quantile (95% CI)	NC (10.086 to NC)	NC (14.784 to NC)	12.06 (7.425 to NC)	NC (13.897 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0360		0.0066	
Hazard ratio (95% CI) vs Pd	-	0.67 (0.46 to 0.98)		0.40 (0.20 to 0.79)	
P-value	-	0.0372		0.0087	
PFS probability (95% CI)[a]					
2 Months	0.832 (0.737 to 0.895)	0.940 (0.871 to 0.973)	0.730 (0.556 to 0.845)	0.870 (0.689 to 0.949)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_semm_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.6.1.1.17.1 PFS - Primary analysis based on disease assessment by the IRC according to MM type at initial diagnosis - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	56 (56.0)	50 (49.0)	32 (61.5)	23 (45.1)	0.3980
Number (%) of patients censored	44 (44.0)	52 (51.0)	20 (38.5)	28 (54.9)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	2.83 (1.938 to 3.811)	4.47 (3.023 to 5.881)	1.97 (1.413 to 2.891)	3.29 (1.971 to 7.031)	
Median (95% CI)	7.75 (4.567 to 9.758)	11.56 (8.279 to 14.784)	4.76 (2.858 to 9.528)	11.40 (6.472 to NC)	
75% quantile (95% CI)	NC (10.251 to NC)	NC (14.784 to NC)	12.06 (8.049 to NC)	NC (13.897 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0389		0.0158	
Hazard ratio (95% CI) vs Pd	-	0.67 (0.46 to 0.98)		0.52 (0.30 to 0.89)	
P-value	-	0.0402		0.0178	
PFS probability (95% CI)[a]					
2 Months	0.830 (0.734 to 0.894)	0.939 (0.868 to 0.972)	0.740 (0.588 to 0.844)	0.846 (0.704 to 0.924)	

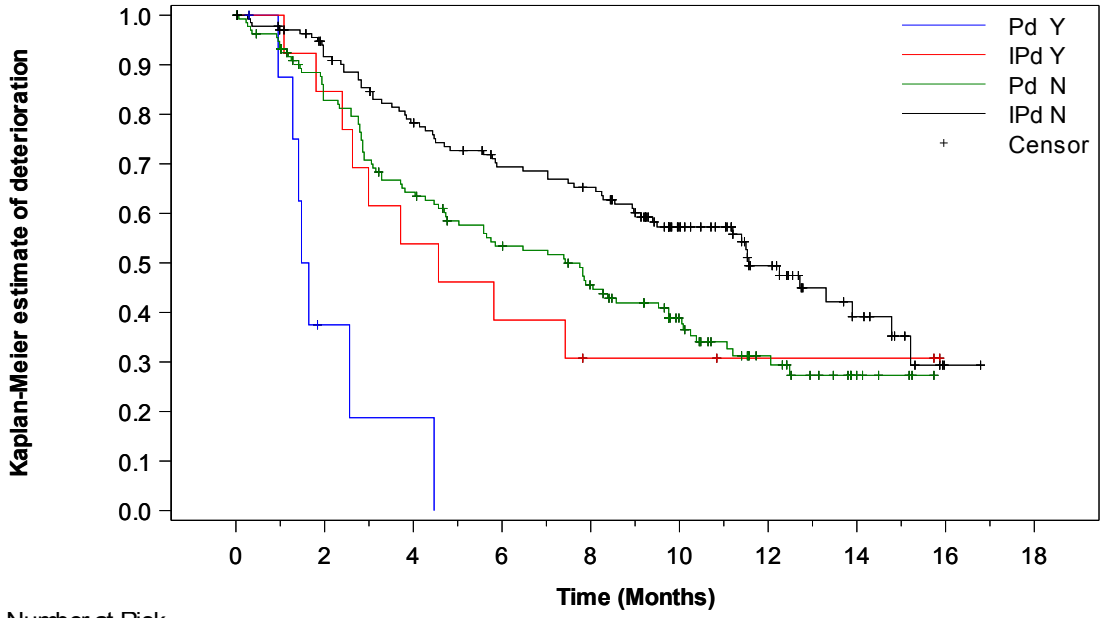
Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_dghc_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.6.1.1.18.1 PFS - Primary analysis based on disease assessment by the IRC according to existing plasmacytoma - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	7 (70.0)	9 (64.3)	82 (57.3)	64 (45.7)	0.0350
Number (%) of patients censored	3 (30.0)	5 (35.7)	61 (42.7)	76 (54.3)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	1.35 (0.953 to 1.643)	2.63 (1.084 to 4.567)	2.83 (2.300 to 3.285)	4.50 (3.285 to 7.031)	
Median (95% CI)	1.56 (0.953 to 4.468)	4.57 (2.398 to NC)	7.43 (4.764 to 9.528)	11.56 (9.396 to 14.784)	
75% quantile (95% CI)	2.56 (1.413 to 4.468)	NC (3.713 to NC)	NC (11.072 to NC)	NC (14.784 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0052		0.0022	
Hazard ratio (95% CI) vs Pd	-	0.22 (0.07 to 0.69)		0.60 (0.43 to 0.84)	
P-value	-	0.0094		0.0024	
PFS probability (95% CI)[a]					
2 Months	0.375 (0.087 to 0.674)	0.846 (0.512 to 0.959)	0.828 (0.751 to 0.883)	0.916 (0.854 to 0.953)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_mri_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.6.1.1.18.2 PFS - Primary analysis based on disease assessment by the IRC according to existing plasmacytoma - Kaplan-Meier curve- ITT population



Number at Risk

Pd Y	10	1	0	0	0	0	0
IPd Y	14	8	5	3	2	2	0
Pd N	143	88	63	44	17	3	0
IPd N	140	109	84	69	28	7	0

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.6.1.1.19.1 PFS - Primary analysis based on disease assessment by the IRC according to baseline creatinine clearance - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	55 (57.3)	36 (41.4)	29 (59.2)	30 (54.5)	0.7575
Number (%) of patients censored	41 (42.7)	51 (58.6)	20 (40.8)	25 (45.5)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	2.89 (1.971 to 4.698)	4.47 (3.713 to 8.246)	2.56 (1.446 to 2.858)	4.83 (2.760 to 7.491)	
Median (95% CI)	7.89 (5.651 to 10.086)	12.71 (8.936 to NC)	3.75 (2.760 to 6.472)	9.49 (7.031 to 13.897)	
75% quantile (95% CI)	NC (10.382 to NC)	NC (15.211 to NC)	NC (5.585 to NC)	14.78 (13.306 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0093		0.0085	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.38 to 0.88)		0.50 (0.30 to 0.85)	
P-value	-	0.0102		0.0098	
PFS probability (95% CI)[a]					
2 Months	0.821 (0.724 to 0.886)	0.939 (0.860 to 0.974)	0.780 (0.619 to 0.879)	0.942 (0.830 to 0.981)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_crcl_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.1.1.20.1 PFS - Primary analysis based on disease assessment by the IRC according to previous therapy with anti-CD38 mAB - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	0 (0.0)	2 (100.0)	89 (58.9)	71 (46.7)	0.9772
Number (%) of patients censored	2 (100.0)	0 (0.0)	62 (41.1)	81 (53.3)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	NC (NC to NC)	3.71 (3.713 to 11.400)	2.76 (1.971 to 3.055)	4.27 (3.023 to 5.848)	
Median (95% CI)	NC (NC to NC)	7.56 (3.713 to 11.400)	6.47 (4.468 to 8.279)	11.56 (8.936 to 14.784)	
75% quantile (95% CI)	NC (NC to NC)	11.40 (3.713 to 11.400)	NC (10.382 to NC)	NC (14.784 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0010	
Hazard ratio (95% CI) vs Pd	-			0.59 (0.43 to 0.81)	
P-value	-			0.0011	
PFS probability (95% CI)[a]					
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.800 (0.722 to 0.858)	0.909 (0.848 to 0.946)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_prmab_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.21 Subgroup analyses by refractory to PI status
16.2.6.1.1.21.1 PFS - Primary analysis based on disease assessment by the IRC according to refractory to PI status - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	67 (58.3)	57 (48.3)	22 (57.9)	16 (44.4)	0.6518
Number (%) of patients censored	48 (41.7)	61 (51.7)	16 (42.1)	20 (55.6)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	2.30 (1.478 to 2.858)	4.14 (3.023 to 5.782)	3.29 (2.595 to 5.848)	7.03 (1.971 to 11.532)	
Median (95% CI)	5.59 (3.713 to 8.049)	11.40 (7.622 to 14.784)	7.85 (4.731 to 12.485)	12.25 (8.115 to NC)	
75% quantile (95% CI)	12.06 (10.053 to NC)	NC (15.211 to NC)	NC (9.528 to NC)	13.90 (12.255 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0022		0.2226	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.40 to 0.82)		0.67 (0.35 to 1.28)	
P-value	-	0.0025		0.2256	
PFS probability (95% CI)[a]					
2 Months	0.751 (0.654 to 0.825)	0.928 (0.860 to 0.963)	0.942 (0.787 to 0.985)	0.855 (0.687 to 0.937)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_refr4_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.22 Subgroup analyses by refractory to IMID status
16.2.6.1.1.22.1 PFS - Primary analysis based on disease assessment by the IRC according to refractory to IMID status - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	85 (59.0)	72 (49.0)	4 (44.4)	1 (14.3)	0.7131
Number (%) of patients censored	59 (41.0)	75 (51.0)	5 (55.6)	6 (85.7)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	2.76 (1.938 to 2.891)	4.14 (3.023 to 5.815)	9.53 (1.906 to NC)	NC (2.168 to NC)	
Median (95% CI)	5.65 (4.041 to 7.885)	11.50 (8.279 to 13.897)	NC (1.906 to NC)	NC (2.168 to NC)	
75% quantile (95% CI)	12.48 (10.086 to NC)	NC (14.784 to NC)	NC (9.758 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0007		0.3046	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.42 to 0.80)		0.33 (0.04 to 3.00)	
P-value	-	0.0008		0.3283	
PFS probability (95% CI)[a]					
2 Months	0.795 (0.713 to 0.855)	0.906 (0.843 to 0.944)	0.889 (0.433 to 0.984)	1.000 (1.000 to 1.000)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_refr1_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.1 Primary efficacy endpoint
16.2.6.1.1 Progression Free Survival
16.2.6.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.1.1.23.1 PFS - Primary analysis based on disease assessment by the IRC according to refractory to refractory to lenalidomide in last previous regimen - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	56 (63.6)	42 (45.2)	33 (50.8)	31 (50.8)	0.2378
Number (%) of patients censored	32 (36.4)	51 (54.8)	32 (49.2)	30 (49.2)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	2.76 (1.938 to 2.891)	5.59 (2.628 to 8.115)	2.83 (1.478 to 4.468)	3.84 (2.990 to 4.830)	
Median (95% CI)	5.65 (3.713 to 7.885)	11.56 (8.936 to 15.211)	7.82 (4.468 to 11.072)	9.40 (4.830 to NC)	
75% quantile (95% CI)	12.06 (8.378 to NC)	NC (13.897 to NC)	NC (11.072 to NC)	NC (14.784 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0007		0.2863	
Hazard ratio (95% CI) vs Pd	-	0.50 (0.34 to 0.76)		0.77 (0.47 to 1.25)	
P-value	-	0.0009		0.2877	
PFS probability (95% CI)[a]					
2 Months	0.819 (0.714 to 0.889)	0.872 (0.781 to 0.927)	0.775 (0.644 to 0.863)	0.966 (0.871 to 0.991)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_llen_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.2 Subgroup analyses by age (IRT)
16.2.6.2.2.2.1 Summary of overall response rate as per IRC according to age (IRT) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**Treat.-by-subgroup[b]**
Best Overall Response							
Stringent complete response	1 (1.4)	0	0	0	0	0	
Complete response	2 (2.9)	3 (5.6)	0	3 (4.4)	0	1 (3.1)	
Very good partial response	3 (4.3)	14 (25.9)	7 (13.0)	19 (27.9)	0	9 (28.1)	
Partial response	18 (25.7)	15 (27.8)	14 (25.9)	22 (32.4)	9 (31.0)	7 (21.9)	
Minimal response	8 (11.4)	1 (1.9)	7 (13.0)	5 (7.4)	2 (6.9)	4 (12.5)	
Stable disease	23 (32.9)	13 (24.1)	12 (22.2)	11 (16.2)	10 (34.5)	9 (28.1)	
Non Progressive Disease	1 (1.4)	1 (1.9)	2 (3.7)	2 (2.9)	0	1 (3.1)	
Progressive disease	5 (7.1)	4 (7.4)	4 (7.4)	1 (1.5)	5 (17.2)	1 (3.1)	
Unconfirmed progressive disease	4 (5.7)	1 (1.9)	0	0	0	0	
Not evaluable	5 (7.1)	2 (3.7)	8 (14.8)	5 (7.4)	3 (10.3)	0	
Overall Response as per IRC (sCR, CR, VGPR or PR)							
Not responders	46 (65.7)	22 (40.7)	33 (61.1)	24 (35.3)	20 (69.0)	15 (46.9)	
95% CI[a]	(0.5340 to 0.7665)	(0.2757 to 0.5497)	(0.4688 to 0.7408)	(0.2408 to 0.4783)	(0.4917 to 0.8472)	(0.2909 to 0.6526)	
Responders	24 (34.3)	32 (59.3)	21 (38.9)	44 (64.7)	9 (31.0)	17 (53.1)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_age_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.2 Subgroup analyses by age (IRT)
16.2.6.2.2.2.1 Summary of overall response rate as per IRC according to age (IRT) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**Treat.-by-subgroup[b]**
95% CI[a]	(0.2335 to 0.4660)	(0.4503 to 0.7243)	(0.2592 to 0.5312)	(0.5217 to 0.7592)	(0.1528 to 0.5083)	(0.3474 to 0.7091)	
Risk ratio 95% CI vs Pd	-	0.62 (0.430 to 0.893)		0.58 (0.392 to 0.851)		0.68 (0.436 to 1.060)	
P-value [b]	-	0.0104		0.0056		0.0881	
P-value heterogeneity[b]	-						0.8626
Odds ratio 95% CI vs Pd	-	0.36 (0.172 to 0.749)		0.35 (0.165 to 0.729)		0.40 (0.138 to 1.139)	
P-value [b]	-	0.0065		0.0054		0.0855	
P-value heterogeneity[b]	-						0.9789
Percent difference 95% CI vs Pd (%)	-	-24.97 (-42.230 to -7.717)		-25.82 (-43.152 to -8.482)		-22.09 (-46.322 to 2.141)	
P-value [b]	-	0.0047		0.0036		0.0738	
P-value heterogeneity[b]	-						0.9695

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_age_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.3 Subgroup analyses by nb of prior lines (IRT)
16.2.6.2.2.3.1 Summary of overall response rate as per IRC according to nb of prior lines (IRT) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	Treat.-by-subgroup[b]
Best Overall Response					
Stringent complete response	1 (1.0)	0	0	0	
Complete response	1 (1.0)	6 (5.9)	1 (1.9)	1 (1.9)	
Very good partial response	9 (8.9)	27 (26.5)	1 (1.9)	15 (28.8)	
Partial response	28 (27.7)	25 (24.5)	13 (25.0)	19 (36.5)	
Minimal response	12 (11.9)	4 (3.9)	5 (9.6)	6 (11.5)	
Stable disease	28 (27.7)	27 (26.5)	17 (32.7)	6 (11.5)	
Non Progressive Disease	2 (2.0)	3 (2.9)	1 (1.9)	1 (1.9)	
Progressive disease	7 (6.9)	4 (3.9)	7 (13.5)	2 (3.8)	
Unconfirmed progressive disease	3 (3.0)	1 (1.0)	1 (1.9)	0	
Not evaluable	10 (9.9)	5 (4.9)	6 (11.5)	2 (3.8)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	62 (61.4)	44 (43.1)	37 (71.2)	17 (32.7)	
95% CI[a]	(0.5118 to 0.7091)	(0.3337 to 0.5332)	(0.5692 to 0.8287)	(0.2033 to 0.4711)	
Responders	39 (38.6)	58 (56.9)	15 (28.8)	35 (67.3)	
95% CI[a]	(0.2909 to 0.4882)	(0.4668 to 0.6663)	(0.1713 to 0.4308)	(0.5289 to 0.7967)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_plne_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.3 Subgroup analyses by nb of prior lines (IRT)
16.2.6.2.2.3.1 Summary of overall response rate as per IRC according to nb of prior lines (IRT) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Pd	-	0.70 (0.535 to 0.923)		0.46 (0.299 to 0.705)	
P-value [b]	-	0.0113		0.0004	
P-value heterogeneity[b]	-				0.1005
Odds ratio 95% CI vs Pd	-	0.48 (0.272 to 0.838)		0.20 (0.085 to 0.455)	
P-value [b]	-	0.0101		0.0002	
P-value heterogeneity[b]	-				0.0853
Percent difference 95% CI vs Pd (%)	-	-18.25 (-31.814 to -4.684)		-38.46 (-56.258 to -20.665)	
P-value [b]	-	0.0085		<.0001	
P-value heterogeneity[b]	-				0.0765

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_plne_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.4 Subgroup analyses by gender
16.2.6.2.2.4.1 Summary of overall response rate as per IRC according to gender - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Stringent complete response	1 (1.4)	0	0	0	
Complete response	1 (1.4)	3 (3.4)	1 (1.2)	4 (6.2)	
Very good partial response	7 (10.0)	24 (27.0)	3 (3.6)	18 (27.7)	
Partial response	19 (27.1)	24 (27.0)	22 (26.5)	20 (30.8)	
Minimal response	9 (12.9)	6 (6.7)	8 (9.6)	4 (6.2)	
Stable disease	18 (25.7)	23 (25.8)	27 (32.5)	10 (15.4)	
Non Progressive Disease	2 (2.9)	3 (3.4)	1 (1.2)	1 (1.5)	
Progressive disease	6 (8.6)	1 (1.1)	8 (9.6)	5 (7.7)	
Unconfirmed progressive disease	0	0	4 (4.8)	1 (1.5)	
Not evaluable	7 (10.0)	5 (5.6)	9 (10.8)	2 (3.1)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	42 (60.0)	38 (42.7)	57 (68.7)	23 (35.4)	
95% CI[a]	(0.4759 to 0.7153)	(0.3226 to 0.5363)	(0.5756 to 0.7841)	(0.2392 to 0.4823)	
Responders	28 (40.0)	51 (57.3)	26 (31.3)	42 (64.6)	
95% CI[a]	(0.2847 to 0.5241)	(0.4637 to 0.6774)	(0.2159 to 0.4244)	(0.5177 to 0.7608)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_sex_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.4 Subgroup analyses by gender
16.2.6.2.2.4.1 Summary of overall response rate as per IRC according to gender - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Pd	-	0.71 (0.523 to 0.969)		0.52 (0.359 to 0.739)	
P-value [b]	-	0.0309		0.0003	
P-value heterogeneity[b]	-				0.1818
Odds ratio 95% CI vs Pd	-	0.50 (0.262 to 0.941)		0.25 (0.125 to 0.498)	
P-value [b]	-	0.0320		<.0001	
P-value heterogeneity[b]	-				0.1517
Percent difference 95% CI vs Pd (%)	-	-17.30 (-32.770 to -1.837)		-33.29 (-48.671 to -17.909)	
P-value [b]	-	0.0285		<.0001	
P-value heterogeneity[b]	-				0.1503

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_sex_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.5 Subgroup analyses by race
16.2.6.2.2.5.1 Summary of overall response rate as per IRC according to race - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Stringent complete response	0	0	1 (5.3)	0	
Complete response	2 (1.6)	5 (4.2)	0	2 (8.3)	
Very good partial response	9 (7.1)	30 (25.4)	1 (5.3)	11 (45.8)	
Partial response	32 (25.4)	39 (33.1)	8 (42.1)	3 (12.5)	
Minimal response	15 (11.9)	10 (8.5)	1 (5.3)	0	
Stable disease	40 (31.7)	22 (18.6)	5 (26.3)	6 (25.0)	
Non Progressive Disease	3 (2.4)	4 (3.4)	0	0	
Progressive disease	10 (7.9)	4 (3.4)	2 (10.5)	0	
Unconfirmed progressive disease	3 (2.4)	1 (0.8)	1 (5.3)	0	
Not evaluable	12 (9.5)	3 (2.5)	0	2 (8.3)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	83 (65.9)	44 (37.3)	9 (47.4)	8 (33.3)	
95% CI[a]	(0.5690 to 0.7408)	(0.2856 to 0.4667)	(0.2445 to 0.7114)	(0.1563 to 0.5532)	
Responders	43 (34.1)	74 (62.7)	10 (52.6)	16 (66.7)	
95% CI[a]	(0.2592 to 0.4310)	(0.5333 to 0.7144)	(0.2886 to 0.7555)	(0.4468 to 0.8437)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_race_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.5 Subgroup analyses by race
16.2.6.2.2.5.1 Summary of overall response rate as per IRC according to race - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Pd	-	0.57 (0.434 to 0.739)		0.70 (0.335 to 1.477)	
P-value [b]	-	<.0001		0.3515	
P-value heterogeneity[b]	-				0.5870
Odds ratio 95% CI vs Pd	-	0.31 (0.182 to 0.522)		0.56 (0.160 to 1.925)	
P-value [b]	-	<.0001		0.3527	
P-value heterogeneity[b]	-				0.3905
Percent difference 95% CI vs Pd (%)	-	-28.58 (-40.664 to -16.506)		-14.04 (-43.482 to 15.412)	
P-value [b]	-	<.0001		0.3490	
P-value heterogeneity[b]	-				0.3690

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_race_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.6 Subgroup analyses by ethnic origin
16.2.6.2.2.6.1 Summary of overall response rate as per IRC according to ethnic origin - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	IPd (N=4)	Pd (N=134)	IPd (N=130)	Treat.-by-subgroup[b]
Best Overall Response					
Stringent complete response	0	0	1 (0.7)	0	
Complete response	0	0	2 (1.5)	7 (5.4)	
Very good partial response	0	1 (25.0)	9 (6.7)	38 (29.2)	
Partial response	0	2 (50.0)	37 (27.6)	37 (28.5)	
Minimal response	1 (33.3)	0	14 (10.4)	10 (7.7)	
Stable disease	1 (33.3)	0	43 (32.1)	26 (20.0)	
Non Progressive Disease	0	1 (25.0)	3 (2.2)	3 (2.3)	
Progressive disease	0	0	11 (8.2)	3 (2.3)	
Unconfirmed progressive disease	0	0	4 (3.0)	1 (0.8)	
Not evaluable	1 (33.3)	0	10 (7.5)	5 (3.8)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	3 (100.0)	1 (25.0)	85 (63.4)	48 (36.9)	
95% CI[a]	(0.2924 to 1.0000)	(0.0063 to 0.8059)	(0.5468 to 0.7158)	(0.2863 to 0.4583)	
Responders	0	3 (75.0)	49 (36.6)	82 (63.1)	
95% CI[a]	-	(0.1941 to 0.9937)	(0.2842 to 0.4532)	(0.5417 to 0.7137)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_ethn_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.6 Subgroup analyses by ethnic origin
16.2.6.2.2.6.1 Summary of overall response rate as per IRC according to ethnic origin - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Pd	-	0.37 (0.283 to 0.476)		0.58 (0.446 to 0.750)	
P-value [b]	-	<.0001		<.0001	
P-value heterogeneity[b]	-				<.0001
Odds ratio 95% CI vs Pd	-	0.00 (0.000 to .)		0.34 (0.204 to 0.558)	
P-value [b]	-	0.9771		<.0001	
P-value heterogeneity[b]	-				0.9788
Peto Odds ratio 95% CI vs Pd	-	0.07 (0.000 to 1.190)		0.35 (0.210 to 0.560)	
P-value [b]	-	0.0662		<.0001	
P-value heterogeneity	-				0.2793
Percent difference 95% CI vs Pd (%)	-	-75.00 (-86.686 to -63.314)		-26.51 (-38.195 to -14.824)	
P-value [b]	-	<.0001		<.0001	
P-value heterogeneity[b]	-				<.0001

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_ethn_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.7 Subgroup analyses by geographical region
16.2.6.2.2.7.1 Summary of overall response rate as per IRC according to geographical region - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	Treat.-by-subgroup p[b]
Best Overall Response											
Stringent complete response	0	0	0	0	0	0	1 (6.7)	0	0	0	
Complete response	0	0	0	1 (3.6)	0	2 (28.6)	0	2 (9.5)	2 (5.4)	2 (4.7)	
Very good partial response	4 (5.3)	10 (18.2)	2 (10.0)	11 (39.3)	1 (20.0)	1 (14.3)	1 (6.7)	11 (52.4)	2 (5.4)	9 (20.9)	
Partial response	21 (27.6)	14 (25.5)	5 (25.0)	10 (35.7)	2 (40.0)	2 (28.6)	7 (46.7)	2 (9.5)	6 (16.2)	16 (37.2)	
Minimal response	7 (9.2)	5 (9.1)	4 (20.0)	4 (14.3)	1 (20.0)	0	1 (6.7)	0	4 (10.8)	1 (2.3)	
Stable disease	20 (26.3)	17 (30.9)	8 (40.0)	2 (7.1)	0	1 (14.3)	5 (33.3)	4 (19.0)	12 (32.4)	9 (20.9)	
Non Progressive Disease	2 (2.6)	1 (1.8)	0	0	0	0	0	0	1 (2.7)	3 (7.0)	
Progressive disease	8 (10.5)	4 (7.3)	0	0	1 (20.0)	1 (14.3)	0	0	5 (13.5)	1 (2.3)	
Unconfirmed progressive disease	2 (2.6)	1 (1.8)	0	0	0	0	0	0	2 (5.4)	0	
Not evaluable	12 (15.8)	3 (5.5)	1 (5.0)	0	0	0	0	2 (9.5)	3 (8.1)	2 (4.7)	
Overall Response as per IRC (sCR, CR, VGPR or PR)											
Not responders	51 (67.1)	31 (56.4)	13 (65.0)	6 (21.4)	2 (40.0)	2 (28.6)	6 (40.0)	6 (28.6)	27 (73.0)	16 (37.2)	
95% CI[a]	(0.5537 to 0.7746)	(0.4232 to 0.6970)	(0.4078 to 0.8461)	(0.0830 to 0.4095)	(0.0527 to 0.8534)	(0.0367 to 0.7096)	(0.1634 to 0.6771)	(0.1128 to 0.5218)	(0.5588 to 0.8621)	(0.2298 to 0.5327)	
Responders	25 (32.9)	24 (43.6)	7 (35.0)	22 (78.6)	3 (60.0)	5 (71.4)	9 (60.0)	15 (71.4)	10 (27.0)	27 (62.8)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_greg_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.7 Subgroup analyses by geographical region
16.2.6.2.2.7.1 Summary of overall response rate as per IRC according to geographical region - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**Treat.-by-subgroup[b]**
95% CI[a]	(0.2254 to 0.4463)	(0.3030 to 0.5768)	(0.1539 to 0.5922)	(0.5905 to 0.9170)	(0.1466 to 0.9473)	(0.2904 to 0.9633)	(0.3229 to 0.8366)	(0.4782 to 0.8872)	(0.1379 to 0.4412)	(0.4673 to 0.7702)	
Risk ratio 95% CI vs Pd	-	0.84 (0.634 to 1.114)		0.33 (0.151 to 0.721)		0.71 (0.145 to 3.521)		0.71 (0.284 to 1.794)		0.51 (0.329 to 0.789)	
P-value [b]	-	0.2244		0.0056		0.6784		0.4728		0.0026	
P-value heterogeneity[b]	-										0.1292
Odds ratio 95% CI vs Pd	-	0.63 (0.308 to 1.300)		0.15 (0.040 to 0.535)		0.60 (0.052 to 6.863)		0.60 (0.147 to 2.450)		0.22 (0.084 to 0.572)	
P-value [b]	-	0.2120		0.0038		0.6802		0.4755		0.0020	
P-value heterogeneity[b]	-										0.2137
Percent difference 95% CI vs Pd (%)	-	-10.74 (-27.644 to 6.160)		-43.57 (-69.522 to -17.621)		-11.43 (-66.093 to 43.236)		-11.43 (-42.989 to 20.132)		-35.76 (-56.181 to -15.346)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_greg_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.7 Subgroup analyses by geographical region
16.2.6.2.2.7.1 Summary of overall response rate as per IRC according to geographical region - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	Treat.-by-subgroup[b]
P-value [b]	-	0.2120		0.0011		0.6810		0.4766		0.0006	
P-value heterogeneity[b]	-										0.1572

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_greg_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.8 Subgroup analyses by regulatory region
16.2.6.2.2.8.1 Summary of overall response rate as per IRC according to regulatory region - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	IPd (N=77)	Pd (N=56)	IPd (N=77)	Treat.-by-subgroup[b]
Best Overall Response					
Stringent complete response	0	0	1 (1.8)	0	
Complete response	1 (1.0)	2 (2.6)	1 (1.8)	5 (6.5)	
Very good partial response	6 (6.2)	15 (19.5)	4 (7.1)	27 (35.1)	
Partial response	25 (25.8)	22 (28.6)	16 (28.6)	22 (28.6)	
Minimal response	10 (10.3)	6 (7.8)	7 (12.5)	4 (5.2)	
Stable disease	23 (23.7)	21 (27.3)	22 (39.3)	12 (15.6)	
Non Progressive Disease	2 (2.1)	1 (1.3)	1 (1.8)	3 (3.9)	
Progressive disease	13 (13.4)	6 (7.8)	1 (1.8)	0	
Unconfirmed progressive disease	3 (3.1)	1 (1.3)	1 (1.8)	0	
Not evaluable	14 (14.4)	3 (3.9)	2 (3.6)	4 (5.2)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	65 (67.0)	38 (49.4)	34 (60.7)	23 (29.9)	
95% CI[a]	(0.5673 to 0.7622)	(0.3776 to 0.6100)	(0.4675 to 0.7350)	(0.1997 to 0.4138)	
Responders	32 (33.0)	39 (50.6)	22 (39.3)	54 (70.1)	
95% CI[a]	(0.2378 to 0.4327)	(0.3900 to 0.6224)	(0.2650 to 0.5325)	(0.5862 to 0.8003)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_rreg_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.8 Subgroup analyses by regulatory region
16.2.6.2.2.8.1 Summary of overall response rate as per IRC according to regulatory region - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Pd	-	0.74 (0.564 to 0.962)		0.49 (0.329 to 0.737)	
P-value [b]	-	0.0249		0.0006	
P-value heterogeneity[b]	-				0.1019
Odds ratio 95% CI vs Pd	-	0.48 (0.259 to 0.890)		0.28 (0.133 to 0.571)	
P-value [b]	-	0.0200		0.0006	
P-value heterogeneity[b]	-				0.2543
Percent difference 95% CI vs Pd (%)	-	-17.66 (-32.287 to -3.032)		-30.84 (-47.284 to -14.404)	
P-value [b]	-	0.0181		0.0003	
P-value heterogeneity[b]	-				0.2393

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_rreg_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.9 Subgroup analyses by baseline ECOG PS
16.2.6.2.2.9.1 Summary of overall response rate as per IRC according to baseline ECOG PS - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Stringent complete response	1 (0.7)	0	0	0	
Complete response	2 (1.5)	7 (5.1)	0	0	
Very good partial response	10 (7.3)	38 (27.5)	0	4 (25.0)	
Partial response	37 (27.0)	43 (31.2)	4 (25.0)	1 (6.3)	
Minimal response	16 (11.7)	8 (5.8)	1 (6.3)	2 (12.5)	
Stable disease	39 (28.5)	29 (21.0)	6 (37.5)	4 (25.0)	
Non Progressive Disease	2 (1.5)	3 (2.2)	1 (6.3)	1 (6.3)	
Progressive disease	12 (8.8)	4 (2.9)	2 (12.5)	2 (12.5)	
Unconfirmed progressive disease	4 (2.9)	1 (0.7)	0	0	
Not evaluable	14 (10.2)	5 (3.6)	2 (12.5)	2 (12.5)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	87 (63.5)	50 (36.2)	12 (75.0)	11 (68.8)	
95% CI[a]	(0.5485 to 0.7156)	(0.2823 to 0.4484)	(0.4762 to 0.9273)	(0.4134 to 0.8898)	
Responders	50 (36.5)	88 (63.8)	4 (25.0)	5 (31.3)	
95% CI[a]	(0.2844 to 0.4515)	(0.5516 to 0.7177)	(0.0727 to 0.5238)	(0.1102 to 0.5866)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_ecog_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.9 Subgroup analyses by baseline ECOG PS
16.2.6.2.2.9.1 Summary of overall response rate as per IRC according to baseline ECOG PS - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Pd	-	0.57 (0.442 to 0.737)		0.92 (0.592 to 1.419)	
P-value [b]	-	<.0001		0.6953	
P-value heterogeneity[b]	-				0.0663
Odds ratio 95% CI vs Pd	-	0.33 (0.199 to 0.535)		0.73 (0.155 to 3.472)	
P-value [b]	-	<.0001		0.6949	
P-value heterogeneity[b]	-				0.3298
Percent difference 95% CI vs Pd (%)	-	-27.27 (-38.688 to -15.855)		-6.25 (-37.455 to 24.955)	
P-value [b]	-	<.0001		0.6938	
P-value heterogeneity[b]	-				0.2141

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_ecog_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.10 Subgroup analyses by ISS staging
16.2.6.2.2.10.1 Summary of overall response rate as per IRC according to ISS staging - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**Treat.-by-subgroup[b]**
Best Overall Response							
Stringent complete response	1 (2.0)	0	0	0	0	0	
Complete response	2 (3.9)	3 (4.7)	0	4 (7.5)	0	0	
Very good partial response	3 (5.9)	24 (37.5)	4 (7.1)	11 (20.8)	3 (7.0)	6 (17.6)	
Partial response	17 (33.3)	15 (23.4)	16 (28.6)	19 (35.8)	7 (16.3)	9 (26.5)	
Minimal response	8 (15.7)	2 (3.1)	7 (12.5)	6 (11.3)	2 (4.7)	2 (5.9)	
Stable disease	10 (19.6)	13 (20.3)	19 (33.9)	7 (13.2)	16 (37.2)	12 (35.3)	
Non Progressive Disease	3 (5.9)	1 (1.6)	0	1 (1.9)	0	2 (5.9)	
Progressive disease	4 (7.8)	3 (4.7)	6 (10.7)	2 (3.8)	3 (7.0)	1 (2.9)	
Unconfirmed progressive disease	1 (2.0)	0	0	1 (1.9)	3 (7.0)	0	
Not evaluable	2 (3.9)	3 (4.7)	4 (7.1)	2 (3.8)	9 (20.9)	2 (5.9)	
Overall Response as per IRC (sCR, CR, VGPR or PR)							
Not responders	28 (54.9)	22 (34.4)	36 (64.3)	19 (35.8)	33 (76.7)	19 (55.9)	
95% CI[a]	(0.4034 to 0.6887)	(0.2295 to 0.4730)	(0.5036 to 0.7664)	(0.2314 to 0.5020)	(0.6137 to 0.8824)	(0.3789 to 0.7281)	
Responders	23 (45.1)	42 (65.6)	20 (35.7)	34 (64.2)	10 (23.3)	15 (44.1)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_seiss_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.10 Subgroup analyses by ISS staging
16.2.6.2.2.10.1 Summary of overall response rate as per IRC according to ISS staging - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**Treat.-by-subgroup[b]**
95% CI[a]	(0.3113 to 0.5966)	(0.5270 to 0.7705)	(0.2336 to 0.4964)	(0.4980 to 0.7686)	(0.1176 to 0.3863)	(0.2719 to 0.6211)	
Risk ratio 95% CI vs Pd	-	0.63 (0.411 to 0.955)		0.56 (0.370 to 0.841)		0.73 (0.517 to 1.025)	
P-value [b]	-	0.0297		0.0055		0.0693	
P-value heterogeneity[b]	-						0.6101
Odds ratio 95% CI vs Pd	-	0.43 (0.202 to 0.918)		0.31 (0.141 to 0.682)		0.38 (0.144 to 1.026)	
P-value [b]	-	0.0294		0.0037		0.0563	
P-value heterogeneity[b]	-						0.8390
Percent difference 95% CI vs Pd (%)	-	-20.53 (-38.542 to -2.511)		-28.44 (-46.516 to -10.357)		-20.86 (-41.876 to 0.153)	
P-value [b]	-	0.0257		0.0022		0.0517	
P-value heterogeneity[b]	-						0.7965

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_seiss_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.11 Subgroup analyses by R-ISS stage
16.2.6.2.2.11.1 Summary of overall response rate as per IRC according to R-ISS stage - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**Treat.-by-subgroup[b]**
Best Overall Response							
Stringent complete response	1 (3.2)	0	0	0	0	0	
Complete response	2 (6.5)	2 (5.1)	0	5 (5.1)	0	0	
Very good partial response	2 (6.5)	12 (30.8)	8 (8.2)	28 (28.3)	0	2 (12.5)	
Partial response	11 (35.5)	14 (35.9)	28 (28.6)	27 (27.3)	2 (8.3)	3 (18.8)	
Minimal response	5 (16.1)	0	11 (11.2)	9 (9.1)	1 (4.2)	1 (6.3)	
Stable disease	5 (16.1)	8 (20.5)	30 (30.6)	19 (19.2)	10 (41.7)	6 (37.5)	
Non Progressive Disease	3 (9.7)	1 (2.6)	0	2 (2.0)	0	1 (6.3)	
Progressive disease	2 (6.5)	1 (2.6)	9 (9.2)	4 (4.0)	3 (12.5)	1 (6.3)	
Unconfirmed progressive disease	0	0	2 (2.0)	1 (1.0)	2 (8.3)	0	
Not evaluable	0	1 (2.6)	10 (10.2)	4 (4.0)	6 (25.0)	2 (12.5)	
Overall Response as per IRC (sCR, CR, VGPR or PR)							
Not responders	15 (48.4)	11 (28.2)	62 (63.3)	39 (39.4)	22 (91.7)	11 (68.8)	
95% CI[a]	(0.3015 to 0.6694)	(0.1500 to 0.4487)	(0.5293 to 0.7278)	(0.2972 to 0.4972)	(0.7300 to 0.9897)	(0.4134 to 0.8898)	
Responders	16 (51.6)	28 (71.8)	36 (36.7)	60 (60.6)	2 (8.3)	5 (31.3)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_seriss_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.11 Subgroup analyses by R-ISS stage
16.2.6.2.2.11.1 Summary of overall response rate as per IRC according to R-ISS stage - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**Treat.-by-subgroup[b]**
95% CI[a]	(0.3306 to 0.6985)	(0.5513 to 0.8500)	(0.2722 to 0.4707)	(0.5028 to 0.7028)	(0.0103 to 0.2700)	(0.1102 to 0.5866)	
Risk ratio 95% CI vs Pd	-	0.58 (0.313 to 1.085)		0.62 (0.467 to 0.831)		0.75 (0.527 to 1.068)	
P-value [b]	-	0.0884		0.0014		0.1099	
P-value heterogeneity[b]	-						0.6640
Odds ratio 95% CI vs Pd	-	0.42 (0.155 to 1.134)		0.38 (0.212 to 0.673)		0.20 (0.033 to 1.210)	
P-value [b]	-	0.0865		0.0010		0.0794	
P-value heterogeneity[b]	-						0.7721
Percent difference 95% CI vs Pd (%)	-	-20.18 (-42.833 to 2.469)		-23.87 (-37.481 to -10.262)		-22.92 (-48.279 to 2.446)	
P-value [b]	-	0.0806		0.0006		0.0764	
P-value heterogeneity[b]	-						0.9630

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_seriss_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.2.2.12.1 Summary of overall response rate as per IRC according to cytogenetic abnormality (del17p) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Complete response	0	0	1 (1.1)	4 (3.4)	
Very good partial response	1 (4.3)	4 (28.6)	6 (6.3)	34 (28.8)	
Partial response	4 (17.4)	3 (21.4)	28 (29.5)	37 (31.4)	
Minimal response	2 (8.7)	0	11 (11.6)	9 (7.6)	
Stable disease	10 (43.5)	4 (28.6)	28 (29.5)	23 (19.5)	
Non Progressive Disease	0	0	1 (1.1)	3 (2.5)	
Progressive disease	0	1 (7.1)	9 (9.5)	4 (3.4)	
Unconfirmed progressive disease	2 (8.7)	0	2 (2.1)	0	
Not evaluable	4 (17.4)	2 (14.3)	9 (9.5)	4 (3.4)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	18 (78.3)	7 (50.0)	60 (63.2)	43 (36.4)	
95% CI[a]	(0.5630 to 0.9254)	(0.2304 to 0.7696)	(0.5264 to 0.7283)	(0.2778 to 0.4580)	
Responders	5 (21.7)	7 (50.0)	35 (36.8)	75 (63.6)	
95% CI[a]	(0.0746 to 0.4370)	(0.2304 to 0.7696)	(0.2717 to 0.4736)	(0.5420 to 0.7222)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_cyto_de_i_t_x.rtf (20APR2021 14:47)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.2.2.12.1 Summary of overall response rate as per IRC according to cytogenetic abnormality (del17p) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Pd	-	0.64 (0.362 to 1.129)		0.58 (0.434 to 0.767)	
P-value [b]	-	0.1223		0.0002	
P-value heterogeneity[b]	-				0.7527
Odds ratio 95% CI vs Pd	-	0.28 (0.065 to 1.183)		0.33 (0.190 to 0.588)	
P-value [b]	-	0.0829		0.0002	
P-value heterogeneity[b]	-				0.8143
Percent difference 95% CI vs Pd (%)	-	-28.26 (-59.562 to 3.040)		-26.72 (-39.800 to -13.634)	
P-value [b]	-	0.0766		<.0001	
P-value heterogeneity[b]	-				0.9287

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_cyto_de_i_t_x.rtf (20APR2021 14:47)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.13 Subgroup analyses by cytogenetic abnormality
16.2.6.2.2.13.1 Summary of overall response rate as per IRC according to cytogenetic abnormality - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Complete response	0	0	1 (1.3)	4 (3.9)	
Very good partial response	1 (2.8)	7 (29.2)	6 (7.7)	29 (28.2)	
Partial response	5 (13.9)	5 (20.8)	26 (33.3)	34 (33.0)	
Minimal response	6 (16.7)	1 (4.2)	7 (9.0)	8 (7.8)	
Stable disease	15 (41.7)	7 (29.2)	23 (29.5)	19 (18.4)	
Non Progressive Disease	0	0	1 (1.3)	3 (2.9)	
Progressive disease	2 (5.6)	1 (4.2)	6 (7.7)	4 (3.9)	
Unconfirmed progressive disease	2 (5.6)	0	2 (2.6)	0	
Not evaluable	5 (13.9)	3 (12.5)	6 (7.7)	2 (1.9)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	30 (83.3)	12 (50.0)	45 (57.7)	36 (35.0)	
95% CI[a]	(0.6719 to 0.9363)	(0.2912 to 0.7088)	(0.4598 to 0.6881)	(0.2582 to 0.4498)	
Responders	6 (16.7)	12 (50.0)	33 (42.3)	67 (65.0)	
95% CI[a]	(0.0637 to 0.3281)	(0.2912 to 0.7088)	(0.3119 to 0.5402)	(0.5502 to 0.7418)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_care_de_i_t_x.rtf (20APR2021 14:47)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.13 Subgroup analyses by cytogenetic abnormality
16.2.6.2.2.13.1 Summary of overall response rate as per IRC according to cytogenetic abnormality - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Pd	-	0.60 (0.391 to 0.921)		0.61 (0.437 to 0.840)	
P-value [b]	-	0.0196		0.0028	
P-value heterogeneity[b]	-				0.9718
Odds ratio 95% CI vs Pd	-	0.20 (0.061 to 0.659)		0.39 (0.215 to 0.724)	
P-value [b]	-	0.0084		0.0028	
P-value heterogeneity[b]	-				0.3194
Percent difference 95% CI vs Pd (%)	-	-33.33 (-56.871 to -9.796)		-22.74 (-37.132 to -8.349)	
P-value [b]	-	0.0057		0.0021	
P-value heterogeneity[b]	-				0.4502

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_care_de_i_t_x.rtf (20APR2021 14:47)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.14 Subgroup analyses by previous autologous stem-cell
16.2.6.2.2.14.1 Summary of overall response rate as per IRC according to previous autologous stem-cell - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Stringent complete response	0	0	1 (1.6)	0	
Complete response	1 (1.1)	3 (3.6)	1 (1.6)	4 (5.6)	
Very good partial response	9 (10.0)	21 (25.3)	1 (1.6)	21 (29.6)	
Partial response	22 (24.4)	25 (30.1)	19 (30.2)	19 (26.8)	
Minimal response	11 (12.2)	4 (4.8)	6 (9.5)	6 (8.5)	
Stable disease	26 (28.9)	20 (24.1)	19 (30.2)	13 (18.3)	
Non Progressive Disease	2 (2.2)	2 (2.4)	1 (1.6)	2 (2.8)	
Progressive disease	8 (8.9)	2 (2.4)	6 (9.5)	4 (5.6)	
Unconfirmed progressive disease	4 (4.4)	1 (1.2)	0	0	
Not evaluable	7 (7.8)	5 (6.0)	9 (14.3)	2 (2.8)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	58 (64.4)	34 (41.0)	41 (65.1)	27 (38.0)	
95% CI[a]	(0.5365 to 0.7426)	(0.3028 to 0.5231)	(0.5203 to 0.7666)	(0.2676 to 0.5033)	
Responders	32 (35.6)	49 (59.0)	22 (34.9)	44 (62.0)	
95% CI[a]	(0.2574 to 0.4635)	(0.4769 to 0.6972)	(0.2334 to 0.4797)	(0.4967 to 0.7324)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_auto_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.14 Subgroup analyses by previous autologous stem-cell
16.2.6.2.2.14.1 Summary of overall response rate as per IRC according to previous autologous stem-cell - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Pd	-	0.64 (0.470 to 0.859)		0.58 (0.412 to 0.828)	
P-value [b]	-	0.0034		0.0027	
P-value heterogeneity[b]	-				0.7198
Odds ratio 95% CI vs Pd	-	0.38 (0.207 to 0.710)		0.33 (0.162 to 0.669)	
P-value [b]	-	0.0024		0.0022	
P-value heterogeneity[b]	-				0.7525
Percent difference 95% CI vs Pd (%)	-	-23.48 (-38.021 to -8.940)		-27.05 (-43.429 to -10.674)	
P-value [b]	-	0.0016		0.0013	
P-value heterogeneity[b]	-				0.7486

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_auto_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.15 Subgroup analyses by previous allogenic transplantation
16.2.6.2.2.15.1 Summary of overall response rate as per IRC according to previous allogenic transplantation - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Stringent complete response	0	0	1 (0.7)	0	
Complete response	0	0	2 (1.3)	7 (4.6)	
Very good partial response	0	1 (50.0)	10 (6.6)	41 (27.0)	
Partial response	2 (100.0)	1 (50.0)	39 (25.8)	43 (28.3)	
Minimal response	0	0	17 (11.3)	10 (6.6)	
Stable disease	0	0	45 (29.8)	33 (21.7)	
Non Progressive Disease	0	0	3 (2.0)	4 (2.6)	
Progressive disease	0	0	14 (9.3)	6 (3.9)	
Unconfirmed progressive disease	0	0	4 (2.6)	1 (0.7)	
Not evaluable	0	0	16 (10.6)	7 (4.6)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	0	0	99 (65.6)	61 (40.1)	
95% CI[a]	-	-	(0.5740 to 0.7310)	(0.3227 to 0.4838)	
Responders	2 (100.0)	2 (100.0)	52 (34.4)	91 (59.9)	
95% CI[a]	(0.1581 to 1.0000)	(0.1581 to 1.0000)	(0.2690 to 0.4260)	(0.5162 to 0.6773)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_allt_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.15 Subgroup analyses by previous allogenic transplantation
16.2.6.2.2.15.1 Summary of overall response rate as per IRC according to previous allogenic transplantation - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Pd	-	1.00 (0.000 to .)		0.61 (0.488 to 0.768)	
P-value [b]	-	1.0000		<.0001	
P-value heterogeneity[b]	-				0.9995
Odds ratio 95% CI vs Pd	-	1.00 (0.000 to .)		0.35 (0.220 to 0.563)	
P-value [b]	-	1.0000		<.0001	
P-value heterogeneity[b]	-				0.9991
Percent difference 95% CI vs Pd (%)	-	0.00 (-10.914 to 10.914)		-25.43 (-36.345 to -14.518)	
P-value [b]	-	1.0000		<.0001	
P-value heterogeneity[b]	-				<.0001

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_allt_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.16 Subgroup analyses by MM type at SE
16.2.6.2.2.16.1 Summary of overall response rate as per IRC according to MM type at SE - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Stringent complete response	1 (1.0)	0	0	0	
Complete response	2 (2.0)	2 (1.9)	0	4 (12.1)	
Very good partial response	1 (1.0)	29 (27.9)	8 (19.5)	10 (30.3)	
Partial response	33 (32.7)	34 (32.7)	7 (17.1)	7 (21.2)	
Minimal response	8 (7.9)	8 (7.7)	7 (17.1)	1 (3.0)	
Stable disease	32 (31.7)	23 (22.1)	10 (24.4)	5 (15.2)	
Non Progressive Disease	1 (1.0)	1 (1.0)	0	2 (6.1)	
Progressive disease	10 (9.9)	3 (2.9)	3 (7.3)	2 (6.1)	
Unconfirmed progressive disease	3 (3.0)	1 (1.0)	1 (2.4)	0	
Not evaluable	10 (9.9)	3 (2.9)	5 (12.2)	2 (6.1)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	64 (63.4)	39 (37.5)	26 (63.4)	12 (36.4)	
95% CI[a]	(0.5319 to 0.7273)	(0.2820 to 0.4753)	(0.4694 to 0.7788)	(0.2040 to 0.5488)	
Responders	37 (36.6)	65 (62.5)	15 (36.6)	21 (63.6)	
95% CI[a]	(0.2727 to 0.4681)	(0.5247 to 0.7180)	(0.2212 to 0.5306)	(0.4512 to 0.7960)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_semm_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.16 Subgroup analyses by MM type at SE
16.2.6.2.2.16.1 Summary of overall response rate as per IRC according to MM type at SE - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Pd	-	0.59 (0.443 to 0.791)		0.57 (0.344 to 0.955)	
P-value [b]	-	0.0004		0.0326	
P-value heterogeneity[b]	-				0.7645
Odds ratio 95% CI vs Pd	-	0.35 (0.196 to 0.613)		0.33 (0.127 to 0.858)	
P-value [b]	-	0.0003		0.0231	
P-value heterogeneity[b]	-				0.9929
Percent difference 95% CI vs Pd (%)	-	-25.87 (-39.143 to -12.589)		-27.05 (-49.202 to -4.900)	
P-value [b]	-	0.0002		0.0169	
P-value heterogeneity[b]	-				0.9798

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_semm_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.6.2.2.17.1 Summary of overall response rate as per IRC according to MM type at initial diagnosis - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Stringent complete response	1 (1.0)	0	0	0	
Complete response	2 (2.0)	2 (2.0)	0	5 (9.8)	
Very good partial response	1 (1.0)	28 (27.5)	9 (17.3)	13 (25.5)	
Partial response	33 (33.0)	34 (33.3)	8 (15.4)	10 (19.6)	
Minimal response	8 (8.0)	7 (6.9)	9 (17.3)	3 (5.9)	
Stable disease	31 (31.0)	23 (22.5)	13 (25.0)	10 (19.6)	
Non Progressive Disease	1 (1.0)	1 (1.0)	2 (3.8)	3 (5.9)	
Progressive disease	10 (10.0)	3 (2.9)	4 (7.7)	3 (5.9)	
Unconfirmed progressive disease	3 (3.0)	1 (1.0)	1 (1.9)	0	
Not evaluable	10 (10.0)	3 (2.9)	6 (11.5)	4 (7.8)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	63 (63.0)	38 (37.3)	35 (67.3)	23 (45.1)	
95% CI[a]	(0.5276 to 0.7244)	(0.2788 to 0.4739)	(0.5289 to 0.7967)	(0.3113 to 0.5966)	
Responders	37 (37.0)	64 (62.7)	17 (32.7)	28 (54.9)	
95% CI[a]	(0.2756 to 0.4724)	(0.5261 to 0.7212)	(0.2033 to 0.4711)	(0.4034 to 0.6887)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_dghc_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.6.2.2.17.1 Summary of overall response rate as per IRC according to MM type at initial diagnosis - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Pd	-	0.59 (0.441 to 0.794)		0.67 (0.468 to 0.959)	
P-value [b]	-	0.0005		0.0288	
P-value heterogeneity[b]	-				0.5967
Odds ratio 95% CI vs Pd	-	0.35 (0.197 to 0.619)		0.40 (0.179 to 0.891)	
P-value [b]	-	0.0003		0.0251	
P-value heterogeneity[b]	-				0.7884
Percent difference 95% CI vs Pd (%)	-	-25.75 (-39.125 to -12.365)		-22.21 (-40.968 to -3.451)	
P-value [b]	-	0.0002		0.0205	
P-value heterogeneity[b]	-				0.7629

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_dghc_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.18 Subgroup analyses by existing plasmacytoma
16.2.6.2.2.18.1 Summary of overall response rate as per IRC according to existing plasmacytoma - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Stringent complete response	0	0	1 (0.7)	0	
Complete response	0	0	2 (1.4)	7 (5.0)	
Very good partial response	1 (10.0)	3 (21.4)	9 (6.3)	39 (27.9)	
Partial response	0	4 (28.6)	41 (28.7)	40 (28.6)	
Minimal response	0	0	17 (11.9)	10 (7.1)	
Stable disease	5 (50.0)	4 (28.6)	40 (28.0)	29 (20.7)	
Non Progressive Disease	0	0	3 (2.1)	4 (2.9)	
Progressive disease	2 (20.0)	2 (14.3)	12 (8.4)	4 (2.9)	
Unconfirmed progressive disease	0	0	4 (2.8)	1 (0.7)	
Not evaluable	2 (20.0)	1 (7.1)	14 (9.8)	6 (4.3)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	9 (90.0)	7 (50.0)	90 (62.9)	54 (38.6)	
95% CI[a]	(0.5550 to 0.9975)	(0.2304 to 0.7696)	(0.5447 to 0.7086)	(0.3047 to 0.4716)	
Responders	1 (10.0)	7 (50.0)	53 (37.1)	86 (61.4)	
95% CI[a]	(0.0025 to 0.4450)	(0.2304 to 0.7696)	(0.2914 to 0.4553)	(0.5284 to 0.6953)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_mri_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.18 Subgroup analyses by existing plasmacytoma
16.2.6.2.2.18.1 Summary of overall response rate as per IRC according to existing plasmacytoma - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Pd	-	0.56 (0.316 to 0.978)		0.61 (0.480 to 0.783)	
P-value [b]	-	0.0416		0.0001	
P-value heterogeneity[b]	-				0.7541
Odds ratio 95% CI vs Pd	-	0.11 (0.011 to 1.137)		0.37 (0.228 to 0.599)	
P-value [b]	-	0.0640		<.0001	
P-value heterogeneity[b]	-				0.3200
Percent difference 95% CI vs Pd (%)	-	-40.00 (-72.249 to -7.751)		-24.37 (-35.710 to -13.021)	
P-value [b]	-	0.0152		<.0001	
P-value heterogeneity[b]	-				0.3689

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_mri_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.19 Subgroup analyses by baseline creatinine clearance
16.2.6.2.2.19.1 Summary of overall response rate as per IRC according to baseline creatinine clearance - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	IPd (N=87)	Pd (N=49)	IPd (N=55)	Treat.-by-subgroup[b]
Best Overall Response					
Stringent complete response	1 (1.0)	0	0	0	
Complete response	1 (1.0)	4 (4.6)	1 (2.0)	3 (5.5)	
Very good partial response	9 (9.4)	26 (29.9)	1 (2.0)	15 (27.3)	
Partial response	30 (31.3)	29 (33.3)	10 (20.4)	13 (23.6)	
Minimal response	12 (12.5)	4 (4.6)	4 (8.2)	6 (10.9)	
Stable disease	25 (26.0)	16 (18.4)	20 (40.8)	12 (21.8)	
Non Progressive Disease	3 (3.1)	1 (1.1)	0	3 (5.5)	
Progressive disease	9 (9.4)	4 (4.6)	3 (6.1)	0	
Unconfirmed progressive disease	1 (1.0)	0	3 (6.1)	1 (1.8)	
Not evaluable	5 (5.2)	3 (3.4)	7 (14.3)	2 (3.6)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	55 (57.3)	28 (32.2)	37 (75.5)	24 (43.6)	
95% CI[a]	(0.4678 to 0.6734)	(0.2256 to 0.4306)	(0.6113 to 0.8666)	(0.3030 to 0.5768)	
Responders	41 (42.7)	59 (67.8)	12 (24.5)	31 (56.4)	
95% CI[a]	(0.3266 to 0.5322)	(0.5694 to 0.7744)	(0.1334 to 0.3887)	(0.4232 to 0.6970)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_crcl_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.19 Subgroup analyses by baseline creatinine clearance
16.2.6.2.2.19.1 Summary of overall response rate as per IRC according to baseline creatinine clearance - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Pd	-	0.56 (0.395 to 0.799)		0.58 (0.411 to 0.813)	
P-value [b]	-	0.0014		0.0017	
P-value heterogeneity[b]	-				0.9096
Odds ratio 95% CI vs Pd	-	0.35 (0.193 to 0.649)		0.25 (0.108 to 0.585)	
P-value [b]	-	0.0009		0.0014	
P-value heterogeneity[b]	-				0.5172
Percent difference 95% CI vs Pd (%)	-	-25.11 (-39.106 to -11.109)		-31.87 (-49.748 to -14.000)	
P-value [b]	-	0.0005		0.0005	
P-value heterogeneity[b]	-				0.5579

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_crcl_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.2.2.20.1 Summary of overall response rate as per IRC according to previous therapy with anti-CD38 mAB - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Stringent complete response	0	0	1 (0.7)	0	
Complete response	0	0	2 (1.3)	7 (4.6)	
Very good partial response	0	0	10 (6.6)	42 (27.6)	
Partial response	0	0	41 (27.2)	44 (28.9)	
Minimal response	0	1 (50.0)	17 (11.3)	9 (5.9)	
Stable disease	1 (50.0)	1 (50.0)	44 (29.1)	32 (21.1)	
Non Progressive Disease	0	0	3 (2.0)	4 (2.6)	
Progressive disease	0	0	14 (9.3)	6 (3.9)	
Unconfirmed progressive disease	0	0	4 (2.6)	1 (0.7)	
Not evaluable	1 (50.0)	0	15 (9.9)	7 (4.6)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	2 (100.0)	2 (100.0)	97 (64.2)	59 (38.8)	
95% CI[a]	(0.1581 to 1.0000)	(0.1581 to 1.0000)	(0.5604 to 0.7186)	(0.3103 to 0.4705)	
Responders	0	0	54 (35.8)	93 (61.2)	
95% CI[a]	-	-	(0.2814 to 0.4396)	(0.5295 to 0.6897)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_prmab_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.2.2.20.1 Summary of overall response rate as per IRC according to previous therapy with anti-CD38 mAB - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Pd	-	0.99 (0.786 to 1.249)		0.61 (0.485 to 0.770)	
P-value [b]	-	0.9378		<.0001	
P-value heterogeneity[b]	-				<.0001
Odds ratio 95% CI vs Pd	-	1.00 (0.000 to .)		0.35 (0.221 to 0.564)	
P-value [b]	-	1.0000		<.0001	
P-value heterogeneity[b]	-				0.9991
Percent difference 95% CI vs Pd (%)	-	0.00 (-10.928 to 10.928)		-25.42 (-36.350 to -14.495)	
P-value [b]	-	1.0000		<.0001	
P-value heterogeneity[b]	-				<.0001

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_prmab_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.21 Subgroup analyses by refractory to PI status
16.2.6.2.2.21.1 Summary of overall response rate as per IRC according to refractory to PI status - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Stringent complete response	1 (0.9)	0	0	0	
Complete response	1 (0.9)	5 (4.2)	1 (2.6)	2 (5.6)	
Very good partial response	7 (6.1)	31 (26.3)	3 (7.9)	11 (30.6)	
Partial response	28 (24.3)	35 (29.7)	13 (34.2)	9 (25.0)	
Minimal response	13 (11.3)	9 (7.6)	4 (10.5)	1 (2.8)	
Stable disease	33 (28.7)	25 (21.2)	12 (31.6)	8 (22.2)	
Non Progressive Disease	3 (2.6)	3 (2.5)	0	1 (2.8)	
Progressive disease	13 (11.3)	4 (3.4)	1 (2.6)	2 (5.6)	
Unconfirmed progressive disease	4 (3.5)	1 (0.8)	0	0	
Not evaluable	12 (10.4)	5 (4.2)	4 (10.5)	2 (5.6)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	78 (67.8)	47 (39.8)	21 (55.3)	14 (38.9)	
95% CI[a]	(0.5847 to 0.7623)	(0.3093 to 0.4925)	(0.3830 to 0.7138)	(0.2314 to 0.5654)	
Responders	37 (32.2)	71 (60.2)	17 (44.7)	22 (61.1)	
95% CI[a]	(0.2377 to 0.4153)	(0.5075 to 0.6907)	(0.2862 to 0.6170)	(0.4346 to 0.7686)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_refr4_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.21 Subgroup analyses by refractory to PI status
16.2.6.2.2.21.1 Summary of overall response rate as per IRC according to refractory to PI status - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Pd	-	0.59 (0.455 to 0.759)		0.70 (0.426 to 1.162)	
P-value [b]	-	<.0001		0.1690	
P-value heterogeneity[b]	-				0.5277
Odds ratio 95% CI vs Pd	-	0.31 (0.183 to 0.539)		0.52 (0.203 to 1.306)	
P-value [b]	-	<.0001		0.1615	
P-value heterogeneity[b]	-				0.3656
Percent difference 95% CI vs Pd (%)	-	-28.00 (-40.330 to -15.662)		-16.37 (-38.904 to 6.155)	
P-value [b]	-	<.0001		0.1537	
P-value heterogeneity[b]	-				0.3740

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_refr4_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.22 Subgroup analyses by refractory to IMID status
16.2.6.2.2.22.1 Summary of overall response rate as per IRC according to refractory to IMID status - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Stringent complete response	1 (0.7)	0	0	0	
Complete response	1 (0.7)	7 (4.8)	1 (11.1)	0	
Very good partial response	9 (6.3)	39 (26.5)	1 (11.1)	3 (42.9)	
Partial response	36 (25.0)	42 (28.6)	5 (55.6)	2 (28.6)	
Minimal response	17 (11.8)	10 (6.8)	0	0	
Stable disease	44 (30.6)	32 (21.8)	1 (11.1)	1 (14.3)	
Non Progressive Disease	2 (1.4)	3 (2.0)	1 (11.1)	1 (14.3)	
Progressive disease	14 (9.7)	6 (4.1)	0	0	
Unconfirmed progressive disease	4 (2.8)	1 (0.7)	0	0	
Not evaluable	16 (11.1)	7 (4.8)	0	0	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	97 (67.4)	59 (40.1)	2 (22.2)	2 (28.6)	
95% CI[a]	(0.5906 to 0.7493)	(0.3215 to 0.4853)	(0.0281 to 0.6001)	(0.0367 to 0.7096)	
Responders	47 (32.6)	88 (59.9)	7 (77.8)	5 (71.4)	
95% CI[a]	(0.2507 to 0.4094)	(0.5147 to 0.6785)	(0.3999 to 0.9719)	(0.2904 to 0.9633)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_refr1_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.22 Subgroup analyses by refractory to IMID status
16.2.6.2.2.22.1 Summary of overall response rate as per IRC according to refractory to IMID status - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Pd	-	0.60 (0.474 to 0.749)		1.29 (0.235 to 7.036)	
P-value [b]	-	<.0001		0.7713	
P-value heterogeneity[b]	-				0.3782
Odds ratio 95% CI vs Pd	-	0.32 (0.201 to 0.526)		1.40 (0.143 to 13.692)	
P-value [b]	-	<.0001		0.7717	
P-value heterogeneity[b]	-				0.2184
Percent difference 95% CI vs Pd (%)	-	-27.23 (-38.289 to -16.161)		6.35 (-36.925 to 49.623)	
P-value [b]	-	<.0001		0.7730	
P-value heterogeneity[b]	-				0.1401

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_refr1_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.2.2.23.1 Summary of overall response rate as per IRC according to refractory to refractory to lenalidomide in last previous regimen - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Stringent complete response	0	0	1 (1.5)	0	
Complete response	1 (1.1)	4 (4.3)	1 (1.5)	3 (4.9)	
Very good partial response	3 (3.4)	26 (28.0)	7 (10.8)	16 (26.2)	
Partial response	22 (25.0)	22 (23.7)	19 (29.2)	22 (36.1)	
Minimal response	10 (11.4)	4 (4.3)	7 (10.8)	6 (9.8)	
Stable disease	30 (34.1)	23 (24.7)	15 (23.1)	10 (16.4)	
Non Progressive Disease	2 (2.3)	3 (3.2)	1 (1.5)	1 (1.6)	
Progressive disease	9 (10.2)	5 (5.4)	5 (7.7)	1 (1.6)	
Unconfirmed progressive disease	2 (2.3)	1 (1.1)	2 (3.1)	0	
Not evaluable	9 (10.2)	5 (5.4)	7 (10.8)	2 (3.3)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	62 (70.5)	41 (44.1)	37 (56.9)	20 (32.8)	
95% CI[a]	(0.5978 to 0.7971)	(0.3380 to 0.5476)	(0.4404 to 0.6915)	(0.2131 to 0.4600)	
Responders	26 (29.5)	52 (55.9)	28 (43.1)	41 (67.2)	
95% CI[a]	(0.2029 to 0.4022)	(0.4524 to 0.6620)	(0.3085 to 0.5596)	(0.5400 to 0.7869)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_llen_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.2 Overall response rate as per IRC
16.2.6.2.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.2.2.23.1 Summary of overall response rate as per IRC according to refractory to refractory to lenalidomide in last previous regimen - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Pd	-	0.63 (0.479 to 0.817)		0.58 (0.379 to 0.875)	
P-value [b]	-	0.0006		0.0100	
P-value heterogeneity[b]	-				0.7429
Odds ratio 95% CI vs Pd	-	0.33 (0.178 to 0.613)		0.37 (0.178 to 0.765)	
P-value [b]	-	0.0005		0.0075	
P-value heterogeneity[b]	-				0.8205
Percent difference 95% CI vs Pd (%)	-	-26.37 (-40.305 to -12.432)		-24.14 (-41.047 to -7.225)	
P-value [b]	-	0.0002		0.0053	
P-value heterogeneity[b]	-				0.8413

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response, MR : Minimal response

[a] Estimated using Clopper-Pearson method

[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup and treatment-by subgroup interaction.

NA/NC = Not Applicable / Not Calculable

PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_respfn_llen_de_i_t_x.rtf (12FEB2021 17:15)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.2 Subgroup analyses by age (IRT)
16.2.6.2.3.2.1 Time to progression based on disease assessment by the IRC according to age (IRT) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	38 (54.3)	21 (38.9)	24 (44.4)	28 (41.2)	16 (55.2)	13 (40.6)	0.6474
Number (%) of patients censored	32 (45.7)	33 (61.1)	30 (55.6)	40 (58.8)	13 (44.8)	19 (59.4)	
Kaplan-Meier estimates of TTP in months							
25% quantile (95% CI)	2.76 (1.906 to 3.285)	3.81 (1.971 to 11.499)	3.15 (2.563 to 7.885)	5.88 (3.680 to 8.542)	1.94 (0.329 to 3.811)	4.44 (2.366 to 9.396)	
Median (95% CI)	5.75 (3.285 to 9.758)	13.31 (7.425 to 14.784)	10.25 (6.472 to 12.485)	12.71 (8.542 to NC)	5.59 (1.938 to 9.758)	12.25 (6.472 to NC)	
75% quantile (95% CI)	NC (8.378 to NC)	14.78 (13.306 to NC)	12.48 (10.382 to NC)	NC (15.211 to NC)	10.05 (5.848 to NC)	NC (12.255 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0468		0.1236		0.0385	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.34 to 1.00)		0.65 (0.38 to 1.13)		0.47 (0.22 to 0.98)	
P-value	-	0.0494		0.1264		0.0432	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_age_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.3 Subgroup analyses by nb of prior lines (IRT)
16.2.6.2.3.3.1 Time to progression based on disease assessment by the IRC according to nb of prior lines (IRT) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	49 (48.5)	38 (37.3)	29 (55.8)	24 (46.2)	0.8535
Number (%) of patients censored	52 (51.5)	64 (62.7)	23 (44.2)	28 (53.8)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	2.89 (2.595 to 4.731)	5.78 (2.825 to 8.936)	1.97 (0.986 to 3.055)	4.27 (2.990 to 7.622)	
Median (95% CI)	8.05 (5.749 to 11.203)	13.31 (11.400 to NC)	4.76 (2.825 to 9.758)	11.50 (6.472 to NC)	
75% quantile (95% CI)	NC (11.203 to NC)	NC (15.211 to NC)	NC (7.031 to NC)	NC (12.715 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0103		0.0283	
Hazard ratio (95% CI) vs Pd	-	0.57 (0.37 to 0.88)		0.55 (0.32 to 0.95)	
P-value	-	0.0112		0.0307	
TTP probability (95% CI)[a]					
2 Months	0.868 (0.774 to 0.925)	0.911 (0.830 to 0.955)	0.722 (0.562 to 0.832)	0.940 (0.824 to 0.980)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_plne_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.4 Subgroup analyses by gender
16.2.6.2.3.4.1 Time to progression based on disease assessment by the IRC according to gender - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	35 (50.0)	34 (38.2)	43 (51.8)	28 (43.1)	0.7690
Number (%) of patients censored	35 (50.0)	55 (61.8)	40 (48.2)	37 (56.9)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	2.86 (1.971 to 4.041)	4.14 (3.088 to 8.542)	2.79 (1.643 to 3.285)	5.59 (1.971 to 8.115)	
Median (95% CI)	7.89 (4.041 to 12.057)	11.56 (11.203 to NC)	7.43 (3.811 to 9.758)	13.31 (8.115 to NC)	
75% quantile (95% CI)	NC (11.203 to NC)	NC (14.784 to NC)	12.48 (9.758 to NC)	NC (13.897 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0430		0.0169	
Hazard ratio (95% CI) vs Pd	-	0.62 (0.38 to 0.99)		0.56 (0.35 to 0.91)	
P-value	-	0.0451		0.0184	
TTP probability (95% CI)[a]					
2 Months	0.835 (0.715 to 0.908)	0.963 (0.889 to 0.988)	0.804 (0.685 to 0.881)	0.864 (0.747 to 0.930)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_sex_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.5 Subgroup analyses by race
16.2.6.2.3.5.1 Time to progression based on disease assessment by the IRC according to race - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	64 (50.8)	47 (39.8)	10 (52.6)	10 (41.7)	0.9207
Number (%) of patients censored	62 (49.2)	71 (60.2)	9 (47.4)	14 (58.3)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	2.83 (2.300 to 3.745)	5.85 (3.680 to 8.936)	2.89 (0.986 to 7.819)	5.78 (2.168 to 12.255)	
Median (95% CI)	7.75 (4.764 to 10.053)	12.71 (11.203 to 15.211)	7.85 (1.971 to NC)	12.25 (5.782 to NC)	
75% quantile (95% CI)	NC (12.057 to NC)	NC (15.211 to NC)	NC (7.852 to NC)	NC (12.255 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0024		0.1900	
Hazard ratio (95% CI) vs Pd	-	0.56 (0.38 to 0.82)		0.56 (0.23 to 1.35)	
P-value	-	0.0027		0.1960	
TTP probability (95% CI)[a]					
2 Months	0.839 (0.754 to 0.897)	0.936 (0.870 to 0.969)	0.767 (0.492 to 0.906)	1.000 (1.000 to 1.000)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_race_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.6 Subgroup analyses by ethnic origin
16.2.6.2.3.6.1 Time to progression based on disease assessment by the IRC according to ethnic origin - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	1 (33.3)	2 (50.0)	71 (53.0)	50 (38.5)	0.5453
Number (%) of patients censored	2 (66.7)	2 (50.0)	63 (47.0)	80 (61.5)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	5.03 (NC to NC)	11.56 (11.565 to 13.306)	2.83 (2.300 to 3.285)	5.78 (3.713 to 7.622)	
Median (95% CI)	5.03 (NC to NC)	13.31 (11.565 to 13.306)	7.43 (4.731 to 9.528)	13.90 (9.495 to NC)	
75% quantile (95% CI)	5.03 (NC to NC)	13.31 (11.565 to 13.306)	NC (11.072 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0455		0.0004	
Hazard ratio (95% CI) vs Pd	-			0.52 (0.37 to 0.75)	
P-value	-	0.9986		0.0005	
TTP probability (95% CI)[a]					
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.834 (0.753 to 0.891)	0.950 (0.891 to 0.977)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_ethn_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.7 Subgroup analyses by geographical region
16.2.6.2.3.7.1 Time to progression based on disease assessment by the IRC according to geographical region - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[b]**
Number (%) of events	35 (46.1)	21 (38.2)	12 (60.0)	11 (39.3)	2 (40.0)	3 (42.9)	8 (53.3)	8 (38.1)	21 (56.8)	19 (44.2)	0.9349
Number (%) of patients censored	41 (53.9)	34 (61.8)	8 (40.0)	17 (60.7)	3 (60.0)	4 (57.1)	7 (46.7)	13 (61.9)	16 (43.2)	24 (55.8)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	2.83 (1.413 to 4.041)	3.09 (1.938 to 5.881)	3.09 (1.906 to 5.585)	6.47 (2.825 to 12.715)	5.03 (2.595 to NC)	2.37 (1.708 to NC)	3.06 (1.971 to 7.852)	5.82 (2.628 to 12.255)	2.33 (0.986 to 2.858)	7.03 (2.990 to 9.396)	
Median (95% CI)	8.05 (4.041 to 11.072)	11.53 (4.435 to NC)	6.47 (2.825 to 10.382)	12.71 (6.472 to NC)	NC (2.595 to NC)	11.56 (1.708 to NC)	7.85 (2.891 to NC)	NC (5.815 to NC)	5.65 (2.793 to 12.485)	11.50 (8.115 to NC)	
75% quantile (95% CI)	NC (11.072 to NC)	NC (13.897 to NC)	10.38 (6.472 to NC)	13.31 (12.715 to NC)	NC (2.595 to NC)	NC (11.565 to NC)	NC (7.852 to NC)	NC (12.255 to NC)	NC (7.885 to NC)	NC (14.784 to NC)	
Comparison vs. Pd											

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_greg_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.7 Subgroup analyses by geographical region
16.2.6.2.3.7.1 Time to progression based on disease assessment by the IRC according to geographical region - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[b]**
Log-Rank test p-value[a] vs Pd	-	0.1315		0.0962		0.8923		0.1846		0.0368	
Hazard ratio (95% CI) vs Pd	-	0.66 (0.38 to 1.14)		0.51 (0.22 to 1.15)		1.13 (0.19 to 6.85)		0.52 (0.19 to 1.39)		0.52 (0.28 to 0.97)	
P-value	-	0.1342		0.1028		0.8923		0.1922		0.0402	
TTP probability (95% CI)[a]											
2 Months	0.793 (0.663 to 0.877)	0.830 (0.689 to 0.911)	0.882 (0.606 to 0.969)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.857 (0.334 to 0.979)	0.857 (0.539 to 0.962)	1.000 (1.000 to 1.000)	0.785 (0.600 to 0.891)	0.949 (0.812 to 0.987)	
4 Months	0.645 (0.505 to 0.755)	0.669 (0.511 to 0.786)	0.647 (0.377 to 0.823)	0.844 (0.636 to 0.939)	0.800 (0.204 to 0.969)	0.714 (0.258 to 0.920)	0.635 (0.331 to 0.830)	0.895 (0.641 to 0.973)	0.596 (0.408 to 0.742)	0.812 (0.645 to 0.906)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_greg_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.8 Subgroup analyses by regulatory region
16.2.6.2.3.8.1 Time to progression based on disease assessment by the IRC according to regulatory region - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	46 (47.4)	32 (41.6)	32 (57.1)	30 (39.0)	0.5604
Number (%) of patients censored	51 (52.6)	45 (58.4)	24 (42.9)	47 (61.0)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	2.79 (1.413 to 3.811)	3.09 (1.971 to 8.969)	2.86 (1.971 to 3.285)	5.85 (3.811 to 8.246)	
Median (95% CI)	7.75 (4.698 to 10.251)	11.53 (9.396 to NC)	7.82 (3.285 to 10.382)	13.31 (8.542 to NC)	
75% quantile (95% CI)	NC (11.072 to NC)	NC (13.897 to NC)	NC (10.053 to NC)	NC (15.211 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0462		0.0063	
Hazard ratio (95% CI) vs Pd	-	0.63 (0.40 to 1.00)		0.51 (0.31 to 0.83)	
P-value	-	0.0481		0.0074	
TTP probability (95% CI)[a]					
2 Months	0.792 (0.683 to 0.867)	0.839 (0.728 to 0.908)	0.860 (0.729 to 0.931)	1.000 (1.000 to 1.000)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_rreg_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.9 Subgroup analyses by baseline ECOG PS
16.2.6.2.3.9.1 Time to progression based on disease assessment by the IRC according to baseline ECOG PS - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	71 (51.8)	53 (38.4)	7 (43.8)	9 (56.3)	0.6002
Number (%) of patients censored	66 (48.2)	85 (61.6)	9 (56.3)	7 (43.8)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	2.83 (1.971 to 3.285)	5.78 (3.680 to 8.115)	2.76 (0.066 to 8.049)	2.63 (0.263 to 5.881)	
Median (95% CI)	7.75 (5.027 to 10.053)	12.71 (11.203 to NC)	4.04 (2.760 to NC)	11.56 (2.431 to 15.211)	
75% quantile (95% CI)	NC (11.203 to NC)	NC (NC to NC)	8.57 (4.041 to NC)	15.21 (5.881 to 15.211)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0010		0.5794	
Hazard ratio (95% CI) vs Pd	-	0.55 (0.39 to 0.79)		0.75 (0.26 to 2.11)	
P-value	-	0.0011		0.5806	
TTP probability (95% CI)[a]					
2 Months	0.818 (0.734 to 0.877)	0.929 (0.868 to 0.963)	0.844 (0.504 to 0.959)	0.844 (0.504 to 0.959)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_ecog_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.10 Subgroup analyses by ISS staging
16.2.6.2.3.10.1 Time to progression based on disease assessment by the IRC according to ISS staging - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	28 (54.9)	23 (35.9)	30 (53.6)	20 (37.7)	19 (44.2)	18 (52.9)	0.6899
Number (%) of patients censored	23 (45.1)	41 (64.1)	26 (46.4)	33 (62.3)	24 (55.8)	16 (47.1)	
Kaplan-Meier estimates of TTP in months							
25% quantile (95% CI)	4.73 (2.595 to 7.852)	8.25 (3.713 to 11.565)	2.76 (1.938 to 2.858)	4.44 (2.990 to 7.491)	1.97 (1.150 to 3.088)	2.76 (1.971 to 6.472)	
Median (95% CI)	9.76 (7.754 to 12.485)	14.78 (11.565 to NC)	4.76 (2.858 to 10.053)	NC (5.881 to NC)	5.59 (2.333 to 7.819)	8.54 (2.825 to 13.897)	
75% quantile (95% CI)	NC (12.057 to NC)	NC (14.784 to NC)	NC (9.758 to NC)	NC (NC to NC)	9.53 (5.749 to NC)	13.90 (9.495 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0757		0.0152		0.1856	
Hazard ratio (95% CI) vs Pd	-	0.61 (0.35 to 1.06)		0.50 (0.28 to 0.88)		0.64 (0.33 to 1.24)	
P-value	-	0.0787		0.0172		0.1891	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_seiss_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.11 Subgroup analyses by R-ISS stage
16.2.6.2.3.11.1 Time to progression based on disease assessment by the IRC according to R-ISS stage - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	17 (54.8)	12 (30.8)	51 (52.0)	40 (40.4)	10 (41.7)	10 (62.5)	0.9503
Number (%) of patients censored	14 (45.2)	27 (69.2)	47 (48.0)	59 (59.6)	14 (58.3)	6 (37.5)	
Kaplan-Meier estimates of TTP in months							
25% quantile (95% CI)	5.65 (2.891 to 8.279)	11.20 (3.844 to 14.784)	2.76 (1.938 to 3.088)	4.44 (3.088 to 7.031)	1.45 (0.066 to 2.793)	1.97 (1.807 to 2.825)	
Median (95% CI)	10.38 (7.754 to NC)	14.78 (11.203 to NC)	7.39 (4.041 to 9.758)	12.71 (8.542 to NC)	2.79 (1.446 to 3.811)	2.83 (1.971 to 13.897)	
75% quantile (95% CI)	NC (12.057 to NC)	NC (14.784 to NC)	NC (10.053 to NC)	NC (15.211 to NC)	3.81 (2.793 to NC)	13.90 (2.760 to 13.897)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0981		0.0040		0.4012	
Hazard ratio (95% CI) vs Pd	-	0.54 (0.26 to 1.13)		0.55 (0.36 to 0.83)		0.68 (0.27 to 1.69)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_seriss_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.2.3.12.1 Time to progression based on disease assessment by the IRC according to cytogenetic abnormality (del17p) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	11 (47.8)	4 (28.6)	52 (54.7)	51 (43.2)	0.8416
Number (%) of patients censored	12 (52.2)	10 (71.4)	43 (45.3)	67 (56.8)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	2.83 (1.446 to 7.392)	2.63 (1.807 to NC)	2.76 (1.938 to 3.285)	5.78 (3.515 to 7.622)	
Median (95% CI)	7.89 (2.825 to 11.203)	NC (1.971 to NC)	7.03 (4.041 to 9.758)	12.25 (9.396 to 14.784)	
75% quantile (95% CI)	11.20 (7.392 to NC)	NC (NC to NC)	NC (10.382 to NC)	NC (14.784 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2646		0.0033	
Hazard ratio (95% CI) vs Pd	-	0.53 (0.17 to 1.66)		0.56 (0.38 to 0.83)	
P-value	-	0.2727		0.0037	
TTP probability (95% CI)[a]					
2 Months	0.933 (0.613 to 0.990)	0.818 (0.447 to 0.951)	0.802 (0.698 to 0.874)	0.937 (0.871 to 0.969)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_cyto_de_i_t_x.rtf (20APR2021 10:48)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.13 Subgroup analyses by cytogenetic abnormality
16.2.6.2.3.13.1 Time to progression based on disease assessment by the IRC according to cytogenetic abnormality - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	20 (55.6)	9 (37.5)	42 (53.8)	45 (43.7)	0.5332
Number (%) of patients censored	16 (44.4)	15 (62.5)	36 (46.2)	58 (56.3)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	2.79 (1.183 to 2.858)	2.83 (1.807 to 9.396)	2.86 (1.938 to 4.271)	5.82 (3.088 to 8.115)	
Median (95% CI)	3.81 (2.793 to 7.885)	9.40 (2.825 to NC)	8.05 (4.698 to 10.382)	12.25 (9.495 to 14.784)	
75% quantile (95% CI)	11.07 (4.731 to NC)	NC (9.396 to NC)	NC (12.057 to NC)	NC (13.897 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0670		0.0286	
Hazard ratio (95% CI) vs Pd	-	0.49 (0.22 to 1.07)		0.63 (0.41 to 0.96)	
P-value	-	0.0731		0.0301	
TTP probability (95% CI)[a]					
2 Months	0.807 (0.596 to 0.915)	0.842 (0.587 to 0.946)	0.838 (0.727 to 0.907)	0.939 (0.869 to 0.972)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_care_de_i_t_x.rtf (20APR2021 10:48)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.14 Subgroup analyses by previous autologous stem-cell
16.2.6.2.3.14.1 Time to progression based on disease assessment by the IRC according to previous autologous stem-cell - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	50 (55.6)	32 (38.6)	28 (44.4)	30 (42.3)	0.6516
Number (%) of patients censored	40 (44.4)	51 (61.4)	35 (55.6)	41 (57.7)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	2.83 (1.971 to 3.745)	5.59 (2.990 to 9.495)	2.83 (1.938 to 3.811)	4.44 (2.760 to 7.622)	
Median (95% CI)	7.75 (4.731 to 9.758)	13.31 (11.203 to 15.211)	7.39 (3.285 to NC)	12.25 (8.115 to NC)	
75% quantile (95% CI)	NC (10.053 to NC)	NC (13.897 to NC)	NC (11.072 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0044		0.0987	
Hazard ratio (95% CI) vs Pd	-	0.53 (0.34 to 0.83)		0.65 (0.39 to 1.09)	
P-value	-	0.0051		0.1012	
TTP probability (95% CI)[a]					
2 Months	0.806 (0.698 to 0.878)	0.919 (0.829 to 0.963)	0.839 (0.704 to 0.916)	0.925 (0.828 to 0.968)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_auto_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.15 Subgroup analyses by previous allogenic transplantation
16.2.6.2.3.15.1 Time to progression based on disease assessment by the IRC according to previous allogenic transplantation - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	1 (50.0)	1 (50.0)	77 (51.0)	61 (40.1)	0.4915
Number (%) of patients censored	1 (50.0)	1 (50.0)	74 (49.0)	91 (59.9)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	7.03 (7.031 to NC)	2.99 (2.990 to NC)	2.79 (1.971 to 3.154)	4.70 (3.515 to 7.491)	
Median (95% CI)	NC (7.031 to NC)	NC (2.990 to NC)	7.75 (4.764 to 9.758)	12.71 (11.203 to 15.211)	
75% quantile (95% CI)	NC (7.031 to NC)	NC (2.990 to NC)	NC (11.203 to NC)	NC (15.211 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.0008	
Hazard ratio (95% CI) vs Pd	-	1.41 (0.08 to 23.57)		0.57 (0.40 to 0.79)	
P-value	-	0.8092		0.0009	
TTP probability (95% CI)[a]					
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.816 (0.736 to 0.874)	0.920 (0.861 to 0.955)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_allt_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.16 Subgroup analyses by MM type at SE
16.2.6.2.3.16.1 Time to progression based on disease assessment by the IRC according to MM type at SE - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	49 (48.5)	42 (40.4)	23 (56.1)	12 (36.4)	0.5030
Number (%) of patients censored	52 (51.5)	62 (59.6)	18 (43.9)	21 (63.6)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	2.86 (2.333 to 4.698)	4.70 (3.088 to 8.246)	1.97 (1.413 to 4.041)	7.03 (1.971 to 11.400)	
Median (95% CI)	7.89 (5.585 to 10.251)	12.71 (9.495 to 15.211)	5.65 (2.793 to 11.072)	13.90 (8.115 to NC)	
75% quantile (95% CI)	NC (11.203 to NC)	NC (14.784 to NC)	12.06 (9.528 to NC)	NC (13.897 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0295		0.0090	
Hazard ratio (95% CI) vs Pd	-	0.63 (0.42 to 0.96)		0.39 (0.19 to 0.81)	
P-value	-	0.0309		0.0116	
TTP probability (95% CI)[a]					
2 Months	0.858 (0.764 to 0.917)	0.948 (0.880 to 0.978)	0.735 (0.551 to 0.852)	0.900 (0.720 to 0.967)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_semm_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.17 Subgroup analyses by MM type at initial diagnosis
16.2.6.2.3.17.1 Time to progression based on disease assessment by the IRC according to MM type at initial diagnosis - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	48 (48.0)	41 (40.2)	29 (55.8)	21 (41.2)	0.4868
Number (%) of patients censored	52 (52.0)	61 (59.8)	23 (44.2)	30 (58.8)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	2.86 (2.333 to 4.271)	5.59 (3.515 to 8.542)	1.97 (1.413 to 3.088)	3.84 (1.971 to 8.115)	
Median (95% CI)	7.85 (5.585 to 10.251)	12.71 (9.495 to 15.211)	5.03 (2.858 to 10.382)	11.53 (7.031 to NC)	
75% quantile (95% CI)	NC (11.203 to NC)	NC (14.784 to NC)	12.06 (9.528 to NC)	NC (13.897 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0318		0.0158	
Hazard ratio (95% CI) vs Pd	-	0.64 (0.42 to 0.96)		0.50 (0.28 to 0.89)	
P-value	-	0.0332		0.0179	
TTP probability (95% CI)[a]					
2 Months	0.857 (0.761 to 0.916)	0.947 (0.878 to 0.978)	0.744 (0.586 to 0.850)	0.865 (0.724 to 0.937)	

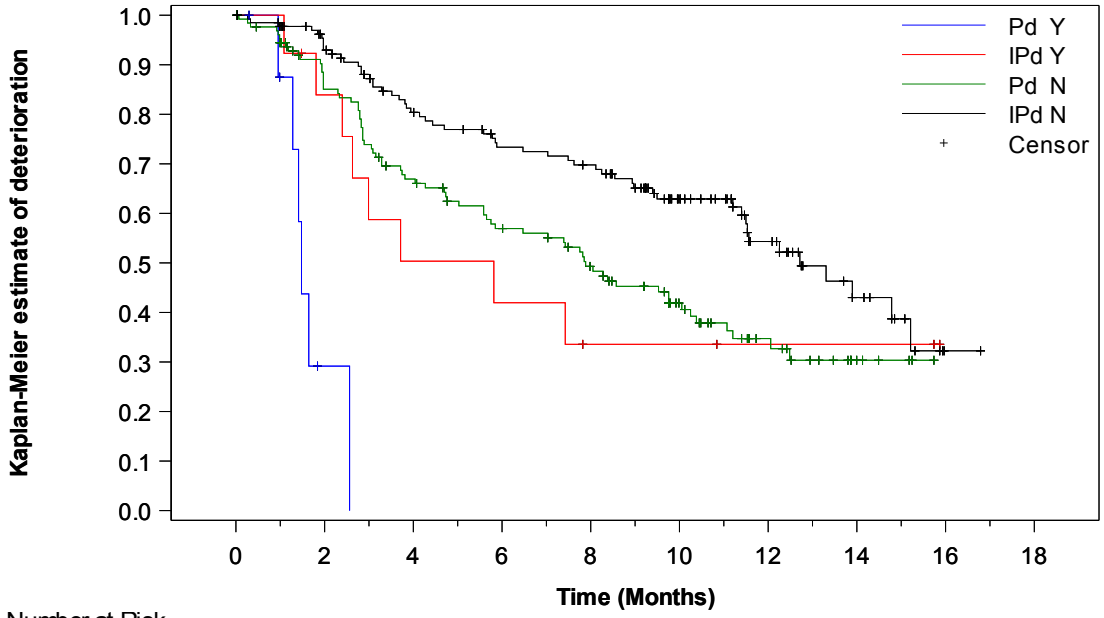
Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_dghc_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.18 Subgroup analyses by existing plasmacytoma
16.2.6.2.3.18.1 Time to progression based on disease assessment by the IRC according to existing plasmacytoma - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	6 (60.0)	8 (57.1)	72 (50.3)	54 (38.6)	0.0075
Number (%) of patients censored	4 (40.0)	6 (42.9)	71 (49.7)	86 (61.4)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	1.28 (0.953 to 1.478)	2.63 (1.084 to 3.713)	2.86 (2.595 to 3.811)	5.85 (3.811 to 8.542)	
Median (95% CI)	1.48 (0.953 to 2.563)	5.82 (1.807 to NC)	7.89 (5.651 to 10.053)	12.71 (11.400 to 15.211)	
75% quantile (95% CI)	2.56 (1.413 to 2.563)	NC (3.713 to NC)	NC (12.057 to NC)	NC (14.784 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0018		0.0016	
Hazard ratio (95% CI) vs Pd	-	0.13 (0.03 to 0.57)		0.57 (0.40 to 0.81)	
P-value	-	0.0063		0.0019	
TTP probability (95% CI)[a]					
2 Months	0.292 (0.042 to 0.619)	0.839 (0.494 to 0.957)	0.851 (0.773 to 0.903)	0.930 (0.869 to 0.963)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_mri_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.18 Subgroup analyses by existing plasmacytoma
16.2.6.2.3.18.2 Time to progression based on disease assessment by the IRC according to existing plasmacytoma - Kaplan-Meier curve- ITT population



Number at Risk

Pd Y	10	0	0	0	0	0	0
IPd Y	14	7	5	3	2	2	0
Pd N	143	86	62	43	17	3	0
IPd N	140	105	82	68	28	7	0

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.19 Subgroup analyses by baseline creatinine clearance
16.2.6.2.3.19.1 Time to progression based on disease assessment by the IRC according to baseline creatinine clearance - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	50 (52.1)	33 (37.9)	24 (49.0)	24 (43.6)	0.7037
Number (%) of patients censored	46 (47.9)	54 (62.1)	25 (51.0)	31 (56.4)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	3.06 (1.971 to 4.764)	4.70 (3.515 to 8.936)	2.76 (1.446 to 3.088)	6.47 (2.760 to 8.969)	
Median (95% CI)	8.28 (5.749 to 10.382)	12.71 (11.203 to NC)	3.81 (2.858 to 9.758)	12.25 (8.542 to 14.784)	
75% quantile (95% CI)	NC (11.072 to NC)	NC (15.211 to NC)	NC (7.819 to NC)	NC (13.306 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0123		0.0105	
Hazard ratio (95% CI) vs Pd	-	0.57 (0.37 to 0.89)		0.48 (0.27 to 0.85)	
P-value	-	0.0135		0.0123	
TTP probability (95% CI)[a]					
2 Months	0.837 (0.739 to 0.900)	0.939 (0.860 to 0.974)	0.811 (0.643 to 0.905)	0.958 (0.844 to 0.989)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_crcl_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.2.3.20.1 Time to progression based on disease assessment by the IRC according to previous therapy with anti-CD38 mAB - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	0 (0.0)	2 (100.0)	78 (51.7)	60 (39.5)	0.9792
Number (%) of patients censored	2 (100.0)	0 (0.0)	73 (48.3)	92 (60.5)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	NC (NC to NC)	3.71 (3.713 to 11.400)	2.83 (1.971 to 3.285)	4.70 (3.285 to 7.491)	
Median (95% CI)	NC (NC to NC)	7.56 (3.713 to 11.400)	7.75 (5.027 to 9.758)	12.71 (11.203 to 15.211)	
75% quantile (95% CI)	NC (NC to NC)	11.40 (3.713 to 11.400)	NC (11.203 to NC)	NC (15.211 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0007	
Hazard ratio (95% CI) vs Pd	-			0.56 (0.40 to 0.79)	
P-value	-			0.0009	
TTP probability (95% CI)[a]					
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.818 (0.739 to 0.876)	0.920 (0.861 to 0.955)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_prmab_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.21 Subgroup analyses by refractory to PI status
16.2.6.2.3.21.1 Time to progression based on disease assessment by the IRC according to refractory to PI status - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	59 (51.3)	49 (41.5)	19 (50.0)	13 (36.1)	0.7279
Number (%) of patients censored	56 (48.7)	69 (58.5)	19 (50.0)	23 (63.9)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	2.60 (1.906 to 2.858)	4.14 (3.088 to 5.881)	4.73 (2.563 to 7.754)	8.11 (1.971 to 11.565)	
Median (95% CI)	7.03 (3.745 to 10.053)	12.71 (8.936 to NC)	8.28 (5.651 to NC)	12.25 (11.532 to NC)	
75% quantile (95% CI)	NC (10.382 to NC)	NC (15.211 to NC)	NC (9.528 to NC)	13.90 (12.255 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0021		0.1751	
Hazard ratio (95% CI) vs Pd	-	0.55 (0.38 to 0.81)		0.62 (0.30 to 1.25)	
P-value	-	0.0024		0.1793	
TTP probability (95% CI)[a]					
2 Months	0.777 (0.679 to 0.849)	0.935 (0.869 to 0.969)	0.938 (0.775 to 0.984)	0.878 (0.706 to 0.952)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.22 Subgroup analyses by refractory to IMID status
16.2.6.2.3.22.1 Time to progression based on disease assessment by the IRC according to refractory to IMID status - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	74 (51.4)	61 (41.5)	4 (44.4)	1 (14.3)	0.7543
Number (%) of patients censored	70 (48.6)	86 (58.5)	5 (55.6)	6 (85.7)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	2.79 (1.971 to 3.088)	4.44 (3.285 to 7.425)	9.53 (1.906 to NC)	NC (2.168 to NC)	
Median (95% CI)	7.03 (4.698 to 8.575)	12.25 (9.495 to 15.211)	NC (1.906 to NC)	NC (2.168 to NC)	
75% quantile (95% CI)	NC (11.072 to NC)	NC (15.211 to NC)	NC (9.758 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0006		0.3046	
Hazard ratio (95% CI) vs Pd	-	0.55 (0.39 to 0.78)		0.33 (0.04 to 3.00)	
P-value	-	0.0007		0.3283	
TTP probability (95% CI)[a]					
2 Months	0.814 (0.731 to 0.873)	0.917 (0.856 to 0.953)	0.889 (0.433 to 0.984)	1.000 (1.000 to 1.000)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_refr1_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.3 Time to progression based on disease assessment by the IRC
16.2.6.2.3.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.2.3.23.1 Time to progression based on disease assessment by the IRC according to refractory to refractory to lenalidomide in last previous regimen - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	51 (58.0)	35 (37.6)	27 (41.5)	27 (44.3)	0.1219
Number (%) of patients censored	37 (42.0)	58 (62.4)	38 (58.5)	34 (55.7)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	2.76 (1.938 to 3.154)	7.03 (3.088 to 9.495)	3.09 (1.906 to 5.585)	3.84 (2.990 to 5.848)	
Median (95% CI)	5.75 (3.713 to 8.279)	12.25 (11.400 to NC)	10.05 (5.027 to NC)	13.31 (5.848 to NC)	
75% quantile (95% CI)	12.48 (8.575 to NC)	NC (13.897 to NC)	NC (11.072 to NC)	NC (14.784 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0002		0.4242	
Hazard ratio (95% CI) vs Pd	-	0.45 (0.29 to 0.70)		0.80 (0.47 to 1.37)	
P-value	-	0.0003		0.4251	
TTP probability (95% CI)[a]					
2 Months	0.824 (0.717 to 0.894)	0.891 (0.801 to 0.942)	0.811 (0.677 to 0.894)	0.966 (0.869 to 0.991)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_llen_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.2 Subgroup analyses by age (IRT)
16.2.6.2.4.2.1 Time to first response based on disease assessment by the IRC according to age (IRT) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	24 (34.3)	32 (59.3)	21 (38.9)	44 (64.7)	9 (31.0)	17 (53.1)	0.9538
Number (%) of patients censored	46 (65.7)	22 (40.7)	33 (61.1)	24 (35.3)	20 (69.0)	15 (46.9)	
Kaplan-Meier estimates of TT1R in months							
25% quantile (95% CI)	1.94 (1.018 to 2.825)	1.05 (0.986 to 1.117)	1.91 (1.051 to 2.037)	1.08 (0.986 to 1.248)	2.86 (1.018 to 2.957)	1.08 (0.986 to 1.216)	
Median (95% CI)	3.02 (2.070 to NC)	1.91 (1.117 to 3.088)	2.96 (1.938 to NC)	1.94 (1.248 to 2.103)	2.96 (1.906 to NC)	1.97 (1.117 to NC)	
75% quantile (95% CI)	NC (5.060 to NC)	5.06 (3.055 to 6.505)	NC (4.172 to NC)	4.67 (2.103 to NC)	5.03 (2.957 to NC)	NC (2.267 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0199		0.0170		0.1662	
Hazard ratio (95% CI) vs Pd	-	1.86 (1.09 to 3.17)		1.87 (1.11 to 3.15)		1.77 (0.78 to 3.99)	
P-value	-	0.0219		0.0188		0.1717	
TT1R probability (95% CI)[a]							

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_age_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.3 Subgroup analyses by nb of prior lines (IRT)
16.2.6.2.4.3.1 Time to first response based on disease assessment by the IRC according to nb of prior lines (IRT) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	39 (38.6)	58 (56.9)	15 (28.8)	35 (67.3)	0.4362
Number (%) of patients censored	62 (61.4)	44 (43.1)	37 (71.2)	17 (32.7)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.91 (1.084 to 2.037)	1.12 (1.018 to 1.248)	1.94 (1.084 to 2.957)	1.05 (1.018 to 1.117)	
Median (95% CI)	2.89 (2.234 to 5.651)	1.97 (1.380 to 2.267)	4.17 (1.938 to NC)	1.31 (1.117 to 1.971)	
75% quantile (95% CI)	NC (5.060 to NC)	5.16 (2.793 to NC)	NC (4.172 to NC)	4.67 (1.971 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0112		0.0090	
Hazard ratio (95% CI) vs Pd	-	1.68 (1.12 to 2.53)		2.20 (1.20 to 4.03)	
P-value	-	0.0121		0.0109	
TT1R probability (95% CI)[a]					
2 Months	0.298 (0.197 to 0.406)	0.542 (0.424 to 0.646)	0.300 (0.147 to 0.470)	0.652 (0.495 to 0.772)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_plne_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.4 Subgroup analyses by gender
16.2.6.2.4.4.1 Time to first response based on disease assessment by the IRC according to gender - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	28 (40.0)	51 (57.3)	26 (31.3)	42 (64.6)	0.0720
Number (%) of patients censored	42 (60.0)	38 (42.7)	57 (68.7)	23 (35.4)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.91 (1.018 to 2.234)	1.05 (0.986 to 1.150)	1.94 (1.314 to 2.793)	1.08 (1.018 to 1.117)	
Median (95% CI)	2.96 (2.037 to 5.651)	1.97 (1.446 to 3.088)	3.02 (2.136 to NC)	1.38 (1.117 to 1.971)	
75% quantile (95% CI)	NC (4.172 to NC)	6.51 (3.187 to NC)	NC (5.027 to NC)	2.17 (1.971 to 5.322)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1550		<.0001	
Hazard ratio (95% CI) vs Pd	-	1.40 (0.88 to 2.22)		2.73 (1.66 to 4.47)	
P-value	-	0.1569		<.0001	
TT1R probability (95% CI)[a]					
2 Months	0.313 (0.194 to 0.439)	0.514 (0.395 to 0.620)	0.282 (0.163 to 0.413)	0.687 (0.533 to 0.800)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_sex_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.5 Subgroup analyses by race
16.2.6.2.4.5.1 Time to first response based on disease assessment by the IRC according to race - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	43 (34.1)	74 (62.7)	10 (52.6)	16 (66.7)	0.3781
Number (%) of patients censored	83 (65.9)	44 (37.3)	9 (47.4)	8 (33.3)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.91 (1.117 to 2.793)	1.08 (1.051 to 1.150)	1.38 (0.986 to 2.037)	0.99 (0.953 to 1.117)	
Median (95% CI)	3.42 (2.858 to NC)	1.97 (1.380 to 2.103)	2.04 (1.380 to 3.023)	1.22 (0.986 to 1.971)	
75% quantile (95% CI)	NC (NC to NC)	5.16 (2.793 to NC)	3.02 (2.037 to NC)	3.19 (1.314 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0004		0.4425	
Hazard ratio (95% CI) vs Pd	-	1.96 (1.34 to 2.85)		1.36 (0.62 to 3.02)	
P-value	-	0.0005		0.4443	
TT1R probability (95% CI)[a]					
2 Months	0.289 (0.198 to 0.386)	0.567 (0.462 to 0.659)	0.398 (0.136 to 0.655)	0.729 (0.475 to 0.875)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_race_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.6 Subgroup analyses by ethnic origin
16.2.6.2.4.6.1 Time to first response based on disease assessment by the IRC according to ethnic origin - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	0 (0.0)	3 (75.0)	49 (36.6)	82 (63.1)	0.9831
Number (%) of patients censored	3 (100.0)	1 (25.0)	85 (63.4)	48 (36.9)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	NC (NC to NC)	1.87 (1.248 to 5.158)	1.91 (1.117 to 2.037)	1.05 (1.018 to 1.117)	
Median (95% CI)	NC (NC to NC)	3.83 (1.248 to NC)	2.96 (2.793 to 5.027)	1.84 (1.216 to 1.971)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.248 to NC)	NC (5.060 to NC)	5.06 (2.168 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3621		0.0005	
Hazard ratio (95% CI) vs Pd	-			1.86 (1.31 to 2.66)	
P-value	-	0.9981		0.0006	
TT1R probability (95% CI)[a]					
2 Months		0.250 (0.009 to 0.665)	0.308 (0.216 to 0.405)	0.609 (0.509 to 0.694)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_ethn_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.7 Subgroup analyses by geographical region
16.2.6.2.4.7.1 Time to first response based on disease assessment by the IRC according to geographical region - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[b]**
Number (%) of events	25 (32.9)	24 (43.6)	7 (35.0)	22 (78.6)	3 (60.0)	5 (71.4)	9 (60.0)	15 (71.4)	10 (27.0)	27 (62.8)	0.5074
Number (%) of patients censored	51 (67.1)	31 (56.4)	13 (65.0)	6 (21.4)	2 (40.0)	2 (28.6)	6 (40.0)	6 (28.6)	27 (73.0)	16 (37.2)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	2.07 (1.248 to 2.858)	1.22 (1.117 to 1.938)	1.31 (0.986 to 4.172)	1.00 (0.986 to 1.084)	1.91 (1.906 to 2.037)	1.15 (0.986 to 2.004)	1.38 (0.986 to 2.037)	0.99 (0.953 to 1.084)	1.25 (1.018 to 2.957)	1.05 (1.018 to 1.117)	
Median (95% CI)	2.89 (2.825 to 5.651)	2.27 (1.840 to 4.337)	4.17 (1.117 to NC)	1.25 (1.051 to 1.971)	1.97 (1.906 to NC)	1.87 (0.986 to 5.158)	2.04 (1.051 to 5.060)	1.12 (0.986 to 1.971)	NC (1.906 to NC)	1.97 (1.117 to 5.060)	
75% quantile (95% CI)	NC (5.027 to NC)	6.31 (3.055 to NC)	NC (3.417 to NC)	1.97 (1.511 to NC)	NC (1.906 to NC)	2.00 (1.873 to 5.158)	3.02 (1.938 to NC)	3.19 (1.117 to NC)	NC (NC to NC)	6.51 (2.825 to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.1583		0.0082		0.5134		0.4075		0.0510	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_greg_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.7 Subgroup analyses by geographical region
16.2.6.2.4.7.1 Time to first response based on disease assessment by the IRC according to geographical region - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[b]**
Hazard ratio (95% CI) vs Pd	-	1.50 (0.85 to 2.62)		3.09 (1.29 to 7.39)		1.66 (0.36 to 7.76)		1.42 (0.62 to 3.25)		2.03 (0.98 to 4.20)	
P-value	-	0.1610		0.0115		0.5172		0.4098		0.0560	
TT1R probability (95% CI)[a]											
2 Months	0.218 (0.115 to 0.341)	0.430 (0.267 to 0.583)	0.274 (0.083 to 0.509)	0.765 (0.541 to 0.890)	0.500 (0.058 to 0.845)	0.524 (0.092 to 0.839)	0.437 (0.146 to 0.701)	0.737 (0.479 to 0.881)	0.366 (0.182 to 0.552)	0.556 (0.383 to 0.698)	
4 Months	0.579 (0.397 to 0.724)	0.667 (0.458 to 0.811)	0.481 (0.185 to 0.728)	0.875 (0.628 to 0.962)	0.750 (0.128 to 0.961)	0.762 (0.158 to 0.961)	0.775 (0.367 to 0.937)	0.803 (0.533 to 0.926)	0.429 (0.221 to 0.623)	0.617 (0.439 to 0.754)	
6 Months	0.700 (0.474 to 0.843)	0.715 (0.499 to 0.850)	0.611 (0.250 to 0.839)	0.875 (0.628 to 0.962)	0.750 (0.128 to 0.961)	0.762 (0.158 to 0.961)	0.887 (0.432 to 0.983)	0.803 (0.533 to 0.926)	0.429 (0.221 to 0.623)	0.745 (0.545 to 0.867)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_greg_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.8 Subgroup analyses by regulatory region
16.2.6.2.4.8.1 Time to first response based on disease assessment by the IRC according to regulatory region - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	32 (33.0)	39 (50.6)	22 (39.3)	54 (70.1)	0.3438
Number (%) of patients censored	65 (67.0)	38 (49.4)	34 (60.7)	23 (29.9)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.94 (1.248 to 2.793)	1.18 (1.117 to 1.840)	1.38 (1.051 to 2.234)	1.02 (0.986 to 1.084)	
Median (95% CI)	2.89 (2.793 to 5.651)	2.10 (1.840 to 3.088)	3.02 (1.938 to NC)	1.25 (1.084 to 1.971)	
75% quantile (95% CI)	NC (5.027 to NC)	5.16 (3.055 to NC)	NC (4.172 to NC)	3.19 (1.971 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0476		0.0052	
Hazard ratio (95% CI) vs Pd	-	1.60 (1.00 to 2.56)		2.00 (1.22 to 3.29)	
P-value	-	0.0496		0.0062	
TT1R probability (95% CI)[a]					
2 Months	0.273 (0.168 to 0.389)	0.468 (0.331 to 0.595)	0.332 (0.193 to 0.478)	0.678 (0.554 to 0.775)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_rreg_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.9 Subgroup analyses by baseline ECOG PS
16.2.6.2.4.9.1 Time to first response based on disease assessment by the IRC according to baseline ECOG PS - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	50 (36.5)	88 (63.8)	4 (25.0)	5 (31.3)	0.4449
Number (%) of patients censored	87 (63.5)	50 (36.2)	12 (75.0)	11 (68.8)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.91 (1.117 to 2.136)	1.05 (1.018 to 1.117)	1.91 (1.380 to 2.004)	1.91 (0.986 to 5.158)	
Median (95% CI)	3.02 (2.825 to 5.060)	1.58 (1.216 to 1.971)	2.00 (1.380 to NC)	5.16 (1.840 to NC)	
75% quantile (95% CI)	NC (5.060 to NC)	4.67 (2.497 to NC)	NC (1.938 to NC)	NC (1.971 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0003		0.8835	
Hazard ratio (95% CI) vs Pd	-	1.89 (1.34 to 2.68)		1.10 (0.29 to 4.14)	
P-value	-	0.0003		0.8836	
TT1R probability (95% CI)[a]					
2 Months	0.291 (0.203 to 0.385)	0.598 (0.502 to 0.682)	0.407 (0.089 to 0.716)	0.462 (0.130 to 0.746)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_ecog_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.10 Subgroup analyses by ISS staging
16.2.6.2.4.10.1 Time to first response based on disease assessment by the IRC according to ISS staging - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	23 (45.1)	42 (65.6)	20 (35.7)	34 (64.2)	10 (23.3)	15 (44.1)	0.6703
Number (%) of patients censored	28 (54.9)	22 (34.4)	36 (64.3)	19 (35.8)	33 (76.7)	19 (55.9)	
Kaplan-Meier estimates of TT1R in months							
25% quantile (95% CI)	1.94 (1.051 to 2.793)	1.08 (0.986 to 1.150)	1.91 (1.051 to 2.234)	1.08 (1.018 to 1.150)	2.14 (1.018 to 2.957)	1.18 (0.986 to 1.971)	
Median (95% CI)	3.02 (2.037 to NC)	1.94 (1.150 to 2.793)	3.42 (1.938 to NC)	1.38 (1.150 to 2.004)	2.96 (2.136 to NC)	2.10 (1.183 to NC)	
75% quantile (95% CI)	NC (5.651 to NC)	4.67 (2.793 to NC)	NC (5.027 to NC)	3.06 (1.971 to NC)	NC (2.957 to NC)	NC (2.136 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0044		0.0129		0.4245	
Hazard ratio (95% CI) vs Pd	-	2.08 (1.24 to 3.48)		2.00 (1.15 to 3.48)		1.39 (0.62 to 3.14)	
P-value	-	0.0053		0.0147		0.4266	
TT1R probability (95% CI)[a]							

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_seiss_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.11 Subgroup analyses by R-ISS stage
16.2.6.2.4.11.1 Time to first response based on disease assessment by the IRC according to R-ISS stage - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	16 (51.6)	28 (71.8)	36 (36.7)	60 (60.6)	2 (8.3)	5 (31.3)	0.7915
Number (%) of patients censored	15 (48.4)	11 (28.2)	62 (63.3)	39 (39.4)	22 (91.7)	11 (68.8)	
Kaplan-Meier estimates of TT1R in months							
25% quantile (95% CI)	2.00 (1.018 to 2.858)	1.05 (0.986 to 1.380)	1.31 (1.051 to 1.938)	1.08 (1.051 to 1.117)	2.50 (2.136 to NC)	1.18 (0.986 to 5.060)	
Median (95% CI)	2.96 (2.037 to NC)	1.94 (1.117 to 3.187)	3.42 (2.234 to 5.060)	1.84 (1.183 to 2.103)	NC (2.136 to NC)	5.06 (1.051 to NC)	
75% quantile (95% CI)	NC (3.778 to NC)	4.67 (1.971 to NC)	NC (5.027 to NC)	6.31 (2.136 to NC)	NC (2.136 to NC)	NC (1.906 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0388		0.0099		0.2161	
Hazard ratio (95% CI) vs Pd	-	1.90 (1.02 to 3.52)		1.72 (1.13 to 2.60)		2.79 (0.51 to 15.24)	
P-value	-	0.0421		0.0108		0.2362	
TT1R probability (95% CI)[a]							

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_seriss_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.2.4.12.1 Time to first response based on disease assessment by the IRC according to cytogenetic abnormality (del17p) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	5 (21.7)	7 (50.0)	35 (36.8)	75 (63.6)	0.0717
Number (%) of patients censored	18 (78.3)	7 (50.0)	60 (63.2)	43 (36.4)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	3.71 (0.953 to NC)	0.99 (0.986 to 1.150)	1.91 (1.084 to 2.070)	1.08 (1.051 to 1.117)	
Median (95% CI)	NC (2.858 to NC)	1.15 (0.986 to NC)	2.96 (2.136 to 5.060)	1.94 (1.248 to 2.004)	
75% quantile (95% CI)	NC (5.651 to NC)	NC (1.084 to NC)	NC (5.027 to NC)	5.16 (2.267 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0037		0.0039	
Hazard ratio (95% CI) vs Pd	-	7.79 (1.56 to 38.89)		1.79 (1.20 to 2.68)	
P-value	-	0.0123		0.0044	
TT1R probability (95% CI)[a]					
2 Months	0.137 (0.022 to 0.358)	0.682 (0.310 to 0.882)	0.317 (0.207 to 0.432)	0.588 (0.483 to 0.679)	

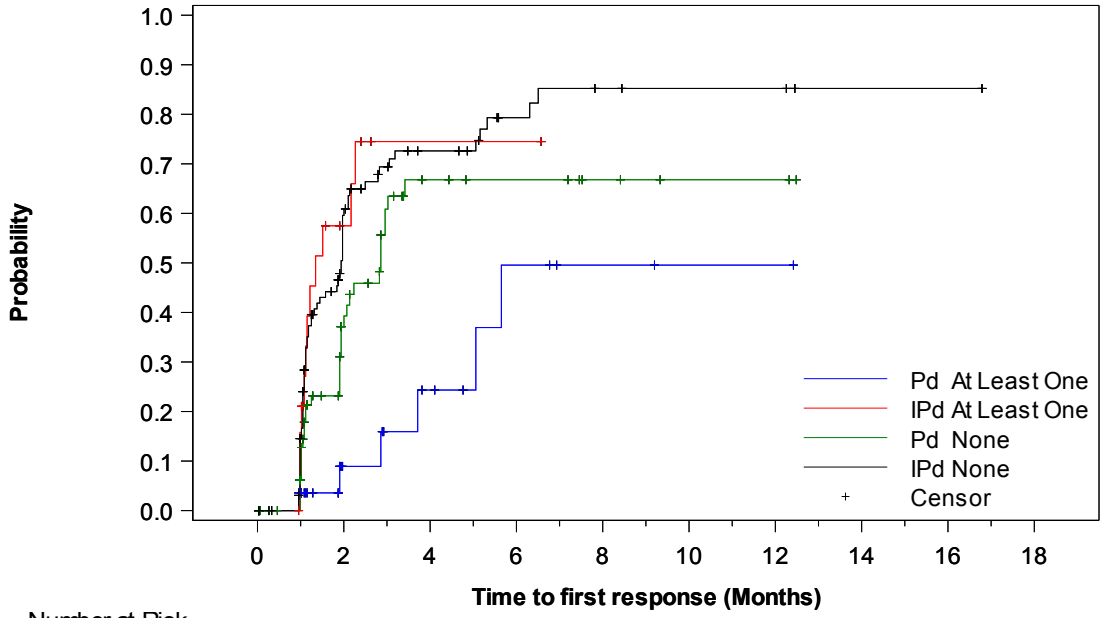
Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_cyto_de_i_t_x.rtf (20APR2021 10:48)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.13 Subgroup analyses by cytogenetic abnormality
16.2.6.2.4.13.1 Time to first response based on disease assessment by the IRC according to cytogenetic abnormality - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	6 (16.7)	12 (50.0)	33 (42.3)	67 (65.0)	0.0340
Number (%) of patients censored	30 (83.3)	12 (50.0)	45 (57.7)	36 (35.0)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	5.06 (1.906 to NC)	1.08 (0.986 to 1.216)	1.91 (1.051 to 1.938)	1.08 (1.018 to 1.150)	
Median (95% CI)	NC (3.713 to NC)	1.35 (1.084 to 2.267)	2.86 (1.938 to 3.417)	1.94 (1.248 to 2.004)	
75% quantile (95% CI)	NC (5.651 to NC)	NC (1.347 to NC)	NC (3.023 to NC)	5.16 (2.136 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0003		0.0291	
Hazard ratio (95% CI) vs Pd	-	5.61 (2.00 to 15.75)		1.59 (1.04 to 2.41)	
P-value	-	0.0011		0.0305	
TT1R probability (95% CI)[a]					
2 Months	0.089 (0.015 to 0.252)	0.575 (0.313 to 0.768)	0.371 (0.246 to 0.497)	0.596 (0.483 to 0.692)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_care_de_i_t_x.rtf (20APR2021 10:48)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.13 Subgroup analyses by cytogenetic abnormality
16.2.6.2.4.13.2 Time to first response based on disease assessment by the IRC according to cytogenetic abnormality - Kaplan-Meier curve- ITT population



Number at Risk

Pd At Least One	36	10	4	2	1	0	0
IPd At Least One	24	1	1	0	0	0	0
Pd None	78	15	7	3	2	0	0
IPd None	103	20	7	3	3	1	0

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.14 Subgroup analyses by previous autologous stem-cell
16.2.6.2.4.14.1 Time to first response based on disease assessment by the IRC according to previous autologous stem-cell - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	32 (35.6)	49 (59.0)	22 (34.9)	44 (62.0)	0.8389
Number (%) of patients censored	58 (64.4)	34 (41.0)	41 (65.1)	27 (38.0)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.91 (1.051 to 2.070)	1.12 (1.018 to 1.248)	1.94 (1.084 to 2.793)	1.08 (0.986 to 1.117)	
Median (95% CI)	3.02 (2.136 to NC)	1.94 (1.314 to 2.497)	2.96 (2.037 to 4.172)	1.84 (1.150 to 2.103)	
75% quantile (95% CI)	NC (5.060 to NC)	4.67 (2.825 to NC)	NC (3.713 to NC)	5.16 (2.103 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0110		0.0154	
Hazard ratio (95% CI) vs Pd	-	1.77 (1.13 to 2.77)		1.87 (1.12 to 3.12)	
P-value	-	0.0121		0.0172	
TT1R probability (95% CI)[a]					
2 Months	0.298 (0.190 to 0.414)	0.567 (0.437 to 0.677)	0.297 (0.163 to 0.444)	0.597 (0.459 to 0.711)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_auto_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.15 Subgroup analyses by previous allogenic transplantation
16.2.6.2.4.15.1 Time to first response based on disease assessment by the IRC according to previous allogenic transplantation - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	2 (100.0)	2 (100.0)	52 (34.4)	91 (59.9)	0.2812
Number (%) of patients censored	0 (0.0)	0 (0.0)	99 (65.6)	61 (40.1)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.02 (1.018 to 2.070)	1.12 (1.117 to 3.187)	1.91 (1.248 to 2.136)	1.08 (1.051 to 1.117)	
Median (95% CI)	1.54 (1.018 to 2.070)	2.15 (1.117 to 3.187)	3.02 (2.858 to 5.060)	1.94 (1.314 to 2.004)	
75% quantile (95% CI)	2.07 (1.018 to 2.070)	3.19 (1.117 to 3.187)	NC (5.651 to NC)	5.16 (2.825 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4328		0.0003	
Hazard ratio (95% CI) vs Pd	-	0.39 (0.03 to 4.44)		1.87 (1.33 to 2.63)	
P-value	-	0.4482		0.0003	
TT1R probability (95% CI)[a]					
2 Months	0.500 (0.006 to 0.910)	0.500 (0.006 to 0.910)	0.294 (0.207 to 0.385)	0.583 (0.489 to 0.666)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_allt_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.16 Subgroup analyses by MM type at SE
16.2.6.2.4.16.1 Time to first response based on disease assessment by the IRC according to MM type at SE - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	37 (36.6)	65 (62.5)	15 (36.6)	21 (63.6)	0.8547
Number (%) of patients censored	64 (63.4)	39 (37.5)	26 (63.4)	12 (36.4)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.94 (1.117 to 2.136)	1.05 (1.018 to 1.117)	1.25 (0.986 to 2.234)	1.12 (0.986 to 1.380)	
Median (95% CI)	3.02 (2.136 to 5.060)	1.84 (1.150 to 1.971)	2.96 (1.380 to NC)	1.91 (1.150 to 2.103)	
75% quantile (95% CI)	NC (5.060 to NC)	4.67 (2.497 to NC)	NC (2.957 to NC)	2.17 (1.971 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0013		0.1410	
Hazard ratio (95% CI) vs Pd	-	1.92 (1.28 to 2.89)		1.64 (0.84 to 3.19)	
P-value	-	0.0016		0.1450	
TT1R probability (95% CI)[a]					
2 Months	0.278 (0.177 to 0.388)	0.603 (0.490 to 0.698)	0.405 (0.216 to 0.586)	0.626 (0.408 to 0.783)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_semm_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.17 Subgroup analyses by MM type at initial diagnosis
16.2.6.2.4.17.1 Time to first response based on disease assessment by the IRC according to MM type at initial diagnosis - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	37 (37.0)	64 (62.7)	17 (32.7)	28 (54.9)	0.6050
Number (%) of patients censored	63 (63.0)	38 (37.3)	35 (67.3)	23 (45.1)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.94 (1.117 to 2.070)	1.05 (1.018 to 1.117)	1.38 (1.018 to 2.825)	1.15 (0.986 to 1.873)	
Median (95% CI)	3.02 (2.136 to 5.060)	1.58 (1.150 to 1.971)	2.96 (1.906 to NC)	1.97 (1.248 to 3.187)	
75% quantile (95% CI)	NC (5.027 to NC)	4.67 (2.267 to NC)	NC (3.713 to NC)	5.32 (2.168 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0016		0.1265	
Hazard ratio (95% CI) vs Pd	-	1.91 (1.27 to 2.87)		1.59 (0.87 to 2.92)	
P-value	-	0.0019		0.1299	
TT1R probability (95% CI)[a]					
2 Months	0.282 (0.179 to 0.394)	0.618 (0.503 to 0.713)	0.333 (0.183 to 0.491)	0.517 (0.348 to 0.662)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_dghc_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.18 Subgroup analyses by existing plasmacytoma
16.2.6.2.4.18.1 Time to first response based on disease assessment by the IRC according to existing plasmacytoma - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	1 (10.0)	7 (50.0)	53 (37.1)	86 (61.4)	0.5666
Number (%) of patients censored	9 (90.0)	7 (50.0)	90 (62.9)	54 (38.6)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	NC (0.953 to NC)	0.99 (0.986 to 1.117)	1.91 (1.117 to 2.037)	1.08 (1.051 to 1.150)	
Median (95% CI)	NC (0.953 to NC)	1.12 (0.986 to 5.060)	2.96 (2.793 to 5.060)	1.94 (1.347 to 2.004)	
75% quantile (95% CI)	NC (NC to NC)	5.06 (1.084 to 5.060)	NC (5.651 to NC)	5.16 (2.793 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1848		0.0006	
Hazard ratio (95% CI) vs Pd	-	3.80 (0.46 to 31.62)		1.81 (1.28 to 2.55)	
P-value	-	0.2175		0.0007	
TT1R probability (95% CI)[a]					
2 Months	0.143 (0.007 to 0.465)	0.545 (0.229 to 0.780)	0.301 (0.213 to 0.394)	0.585 (0.487 to 0.670)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_mri_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.19 Subgroup analyses by baseline creatinine clearance
16.2.6.2.4.19.1 Time to first response based on disease assessment by the IRC according to baseline creatinine clearance - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	41 (42.7)	59 (67.8)	12 (24.5)	31 (56.4)	0.9021
Number (%) of patients censored	55 (57.3)	28 (32.2)	37 (75.5)	24 (43.6)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.91 (1.051 to 2.037)	1.05 (1.018 to 1.117)	2.14 (1.248 to 2.957)	1.08 (0.986 to 1.248)	
Median (95% CI)	2.89 (2.037 to 5.027)	1.51 (1.150 to 1.971)	4.17 (2.136 to NC)	1.97 (1.248 to 5.060)	
75% quantile (95% CI)	NC (5.027 to NC)	3.09 (2.103 to 6.308)	NC (4.172 to NC)	NC (2.497 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0016		0.0367	
Hazard ratio (95% CI) vs Pd	-	1.89 (1.26 to 2.82)		2.01 (1.03 to 3.93)	
P-value	-	0.0019		0.0406	
TT1R probability (95% CI)[a]					
2 Months	0.329 (0.223 to 0.438)	0.635 (0.513 to 0.734)	0.245 (0.105 to 0.415)	0.521 (0.365 to 0.657)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.2.4.20.1 Time to first response based on disease assessment by the IRC according to previous therapy with anti-CD38 mAB - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	0 (0.0)	0 (0.0)	54 (35.8)	93 (61.2)	0.9996
Number (%) of patients censored	2 (100.0)	2 (100.0)	97 (64.2)	59 (38.8)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	1.91 (1.248 to 2.037)	1.08 (1.051 to 1.117)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	3.02 (2.825 to 5.060)	1.91 (1.248 to 1.971)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.651 to NC)	5.06 (2.793 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0002	
Hazard ratio (95% CI) vs Pd	-			1.89 (1.35 to 2.64)	
P-value	-			0.0002	
TT1R probability (95% CI)[a]					
2 Months			0.298 (0.212 to 0.389)	0.592 (0.498 to 0.674)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_prmab_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.21 Subgroup analyses by refractory to PI status
16.2.6.2.4.21.1 Time to first response based on disease assessment by the IRC according to refractory to PI status - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	37 (32.2)	71 (60.2)	17 (44.7)	22 (61.1)	0.3935
Number (%) of patients censored	78 (67.8)	47 (39.8)	21 (55.3)	14 (38.9)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.94 (1.117 to 2.136)	1.08 (1.051 to 1.150)	1.91 (1.018 to 2.858)	1.08 (0.986 to 1.971)	
Median (95% CI)	3.71 (2.234 to 5.651)	1.84 (1.216 to 1.971)	2.89 (1.906 to NC)	2.10 (1.117 to 3.187)	
75% quantile (95% CI)	NC (5.060 to NC)	5.06 (2.168 to NC)	NC (2.957 to NC)	5.16 (2.267 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0006		0.2423	
Hazard ratio (95% CI) vs Pd	-	1.99 (1.34 to 2.97)		1.46 (0.77 to 2.75)	
P-value	-	0.0007		0.2454	
TT1R probability (95% CI)[a]					
2 Months	0.262 (0.168 to 0.366)	0.624 (0.517 to 0.714)	0.379 (0.207 to 0.551)	0.440 (0.257 to 0.609)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.22 Subgroup analyses by refractory to IMID status
16.2.6.2.4.22.1 Time to first response based on disease assessment by the IRC according to refractory to IMID status - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	47 (32.6)	88 (59.9)	7 (77.8)	5 (71.4)	0.2100
Number (%) of patients censored	97 (67.4)	59 (40.1)	2 (22.2)	2 (28.6)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.94 (1.380 to 2.793)	1.08 (1.051 to 1.150)	1.08 (0.986 to 1.248)	1.02 (0.986 to 1.577)	
Median (95% CI)	3.71 (2.858 to 5.651)	1.94 (1.314 to 2.103)	1.25 (0.986 to 2.136)	1.58 (0.986 to NC)	
75% quantile (95% CI)	NC (5.651 to NC)	5.16 (2.825 to NC)	2.14 (1.248 to NC)	1.97 (1.051 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0001		0.9863	
Hazard ratio (95% CI) vs Pd	-	1.98 (1.39 to 2.82)		0.99 (0.31 to 3.14)	
P-value	-	0.0002		0.9863	
TT1R probability (95% CI)[a]					
2 Months	0.259 (0.175 to 0.351)	0.569 (0.474 to 0.654)	0.741 (0.303 to 0.927)	0.821 (0.252 to 0.972)	

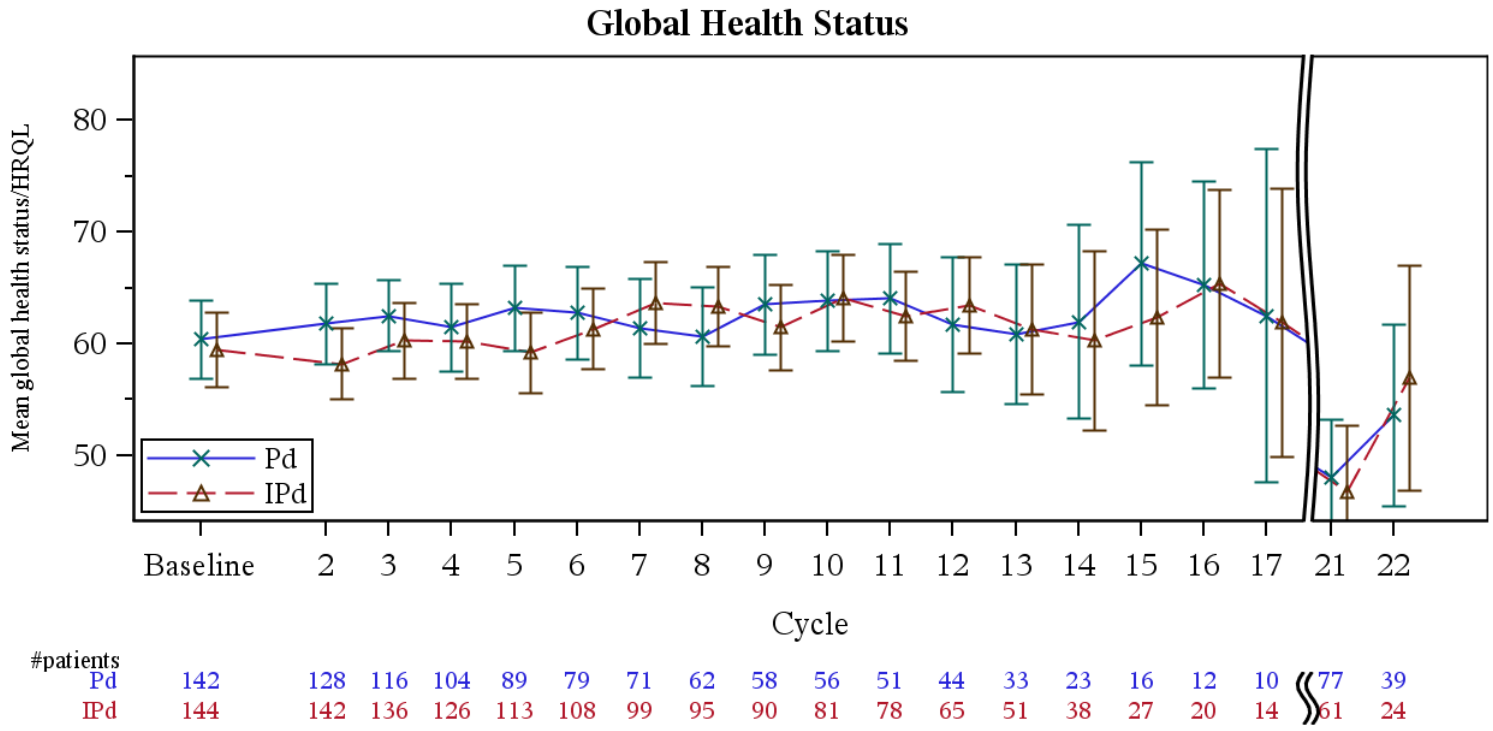
Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_refr1_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.2 Secondary efficacy endpoints
16.2.6.2.4 Time to first response based on disease assessment by the IRC
16.2.6.2.4.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.2.4.23.1 Time to first response based on disease assessment by the IRC according to refractory to refractory to lenalidomide in last previous regimen - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[b]**
Number (%) of events	26 (29.5)	52 (55.9)	28 (43.1)	41 (67.2)	0.4216
Number (%) of patients censored	62 (70.5)	41 (44.1)	37 (56.9)	20 (32.8)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	2.00 (1.117 to 2.891)	1.08 (1.051 to 1.248)	1.31 (1.084 to 2.037)	1.05 (0.986 to 1.150)	
Median (95% CI)	5.06 (2.858 to NC)	1.97 (1.347 to 2.793)	2.23 (1.906 to 3.713)	1.45 (1.150 to 1.971)	
75% quantile (95% CI)	NC (NC to NC)	5.16 (3.055 to NC)	5.03 (2.957 to NC)	4.67 (1.971 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0018		0.0557	
Hazard ratio (95% CI) vs Pd	-	2.09 (1.30 to 3.34)		1.60 (0.98 to 2.59)	
P-value	-	0.0022		0.0579	
TT1R probability (95% CI)[a]					
2 Months	0.248 (0.146 to 0.363)	0.506 (0.384 to 0.615)	0.370 (0.227 to 0.513)	0.682 (0.535 to 0.791)	

Cutoff date = 11OCT2018
One-sided significance level is 0.025.
[a] Estimated using the Kaplan-Meier method
[b] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_llen_de_i_t_x.rtf (12FEB2021 17:16)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Global health status
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-C30 - Mean and 95% CI for global health status score over time (LOCF) - ITT population



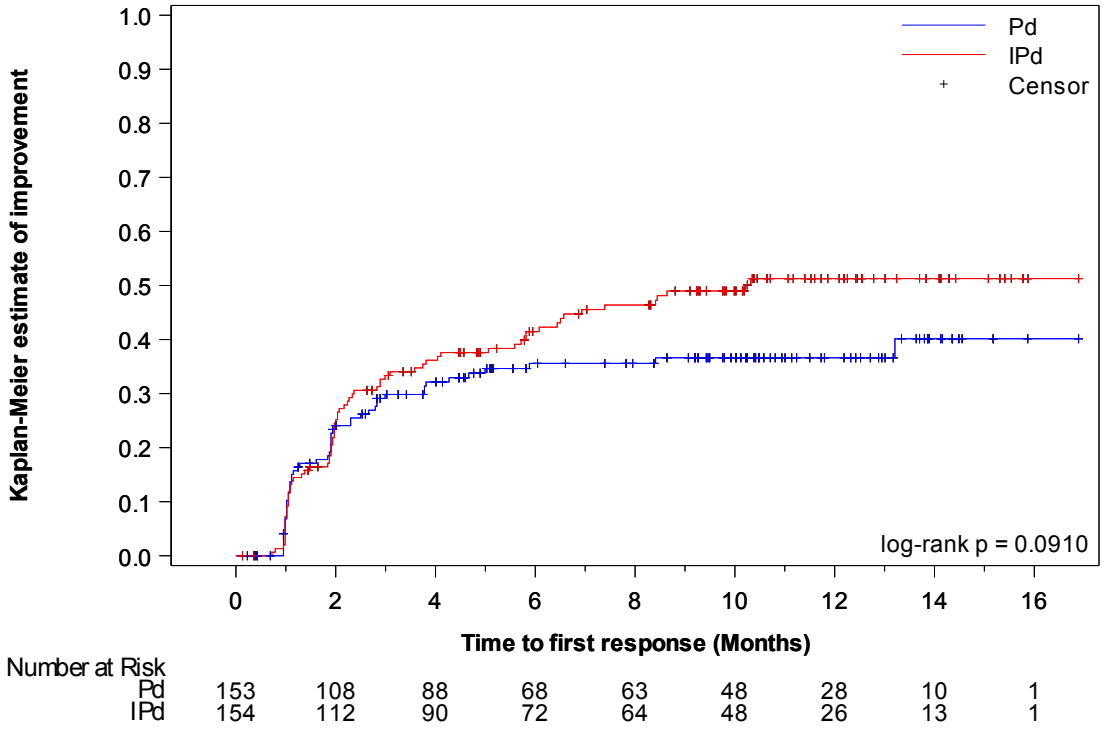
A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_line_i_f.sas OUT=REPORT/OUTPUT/eff_qlq_line_c30_glb_de_i_f_x.rtf (12FEB2021 17:15)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Global health status
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-C30 - Time to first improvement by 15 pt in global health (LOCF) - ITT population

First improvement 15 points Global health status	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	52 (34.0)	72 (46.8)
Number (%) of patients censored	101 (66.0)	82 (53.2)
Kaplan-Meier estimates of global health status in months		
25% quantile (95% CI)	2.30 (1.610 to 3.811)	2.00 (1.873 to 2.891)
Median (95% CI)	NC (13.207 to NC)	10.22 (6.078 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0910
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.36 (0.95 to 1.94)
P-value	-	0.0923
Probability (95% CI)[c]		
2 Months	0.24 (0.175 to 0.313)	0.25 (0.180 to 0.316)
4 Months	0.32 (0.246 to 0.399)	0.36 (0.285 to 0.439)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imp15l_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Global health status
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-C30 - Time to first improvement by 15 pt in global health - Kaplan-Meier curve (LOCF) - ITT population



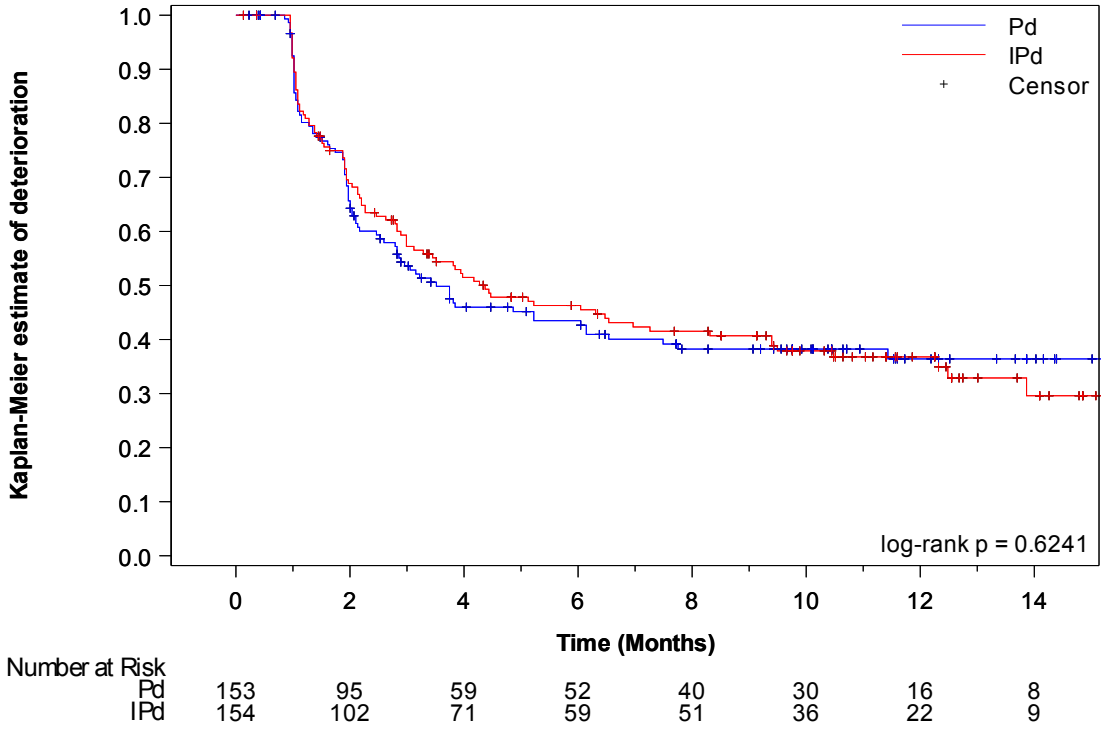
A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imp15l_de_i_f_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Global health status
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-C30 - Time to first deterioration by 15 pt in global health (LOCF) - ITT population

First deterioration 15 points Global health status	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	87 (56.9)	93 (60.4)
Number (%) of patients censored	66 (43.1)	61 (39.6)
Kaplan-Meier estimates of global health status in months		
25% quantile (95% CI)	1.74 (1.084 to 1.971)	1.64 (1.183 to 2.037)
Median (95% CI)	3.52 (2.595 to 6.144)	4.37 (2.990 to 7.261)
75% quantile (95% CI)	NC (NC to NC)	NC (12.485 to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6241
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.93 (0.69 to 1.25)
P-value	-	0.6236
Probability (95% CI)[c]		
2 Months	0.66 (0.573 to 0.728)	0.69 (0.608 to 0.756)
4 Months	0.46 (0.376 to 0.540)	0.51 (0.431 to 0.592)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_det15l_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Global health status
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-C30 - Time to first deterioration by 15 pt in global health - Kaplan-Meier curve (LOCF) - ITT population



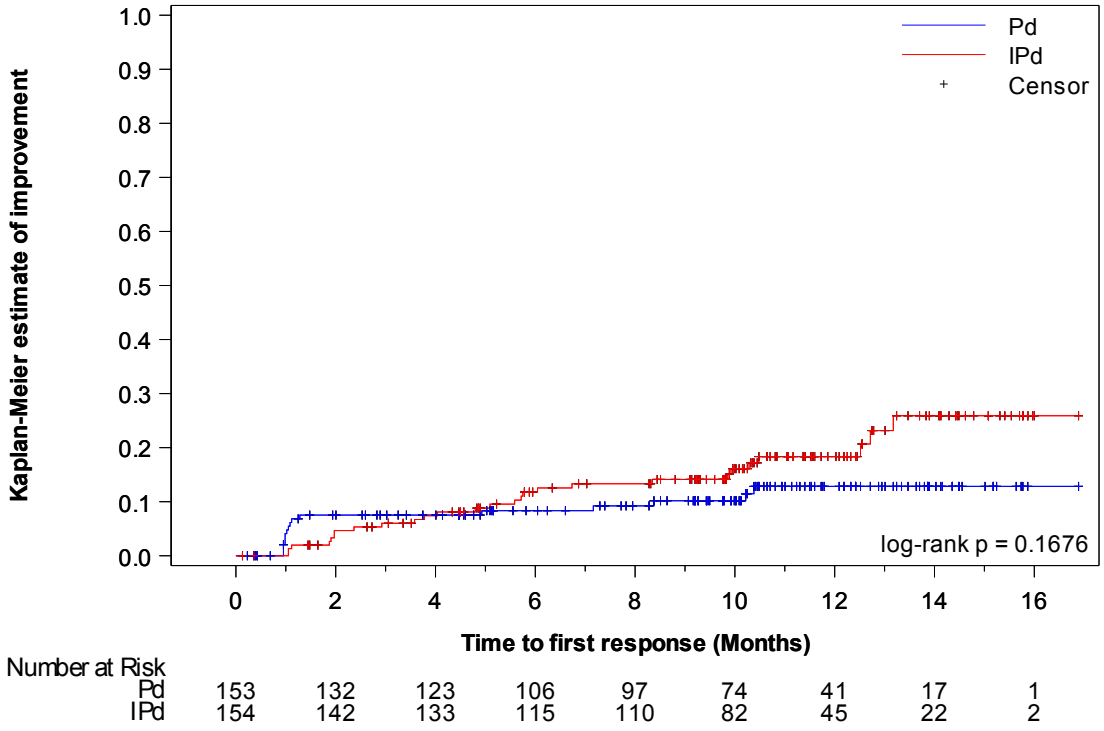
A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_det15l_de_i_f_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Global health status
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in global health (LOCF) - ITT population

First permanent improvement 15 points Global health status	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	16 (10.5)	27 (17.5)
Number (%) of patients censored	137 (89.5)	127 (82.5)
Kaplan-Meier estimates of global health status in months		
25% quantile (95% CI)	NC (NC to NC)	13.17 (10.480 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1676
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.54 (0.83 to 2.86)
P-value	-	0.1709
Probability (95% CI)[c]		
2 Months	0.08 (0.040 to 0.125)	0.05 (0.021 to 0.089)
4 Months	0.08 (0.040 to 0.125)	0.07 (0.039 to 0.123)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imp15pl_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Global health status
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-C30 - Time until permanent improvement by 15 pt in global health - Kaplan-Meier curve (LOCF) - ITT population



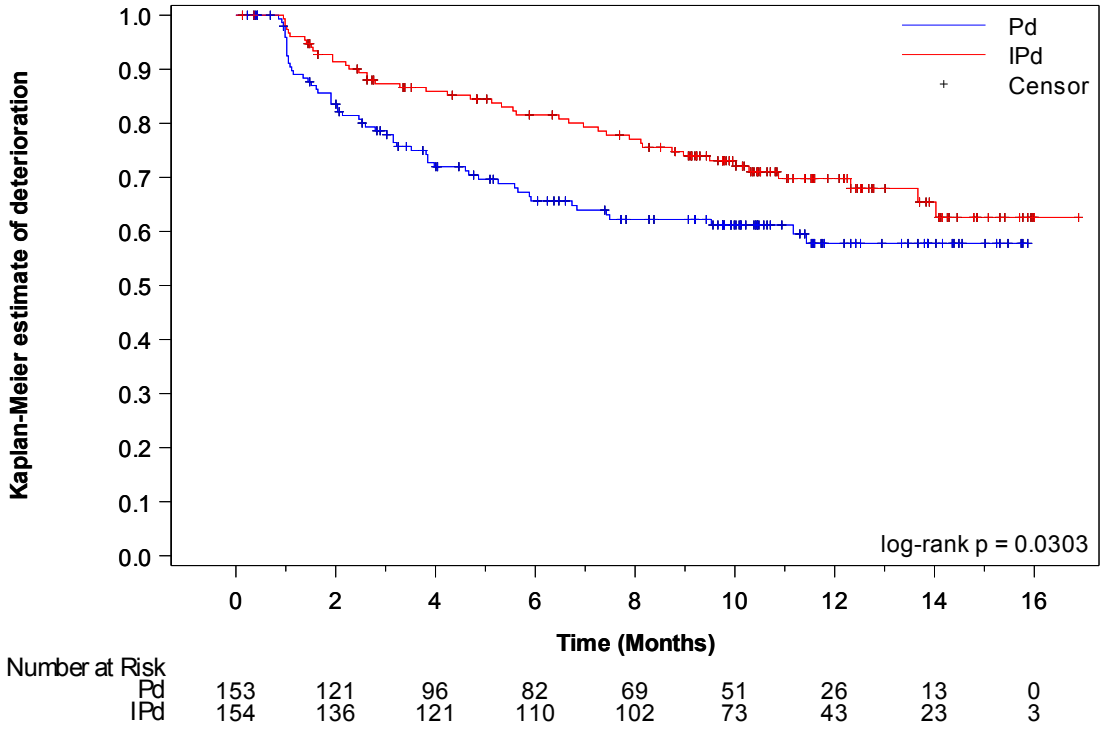
A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imp15pl_de_i_f_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Global health status
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in global health (LOCF) - ITT population

First permanent deterioration 15 points Global health status	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	55 (35.9)	44 (28.6)
Number (%) of patients censored	98 (64.1)	110 (71.4)
Kaplan-Meier estimates of global health status in months		
25% quantile (95% CI)	3.52 (2.037 to 5.651)	8.74 (5.618 to 13.667)
Median (95% CI)	NC (11.433 to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0303
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.65 (0.43 to 0.96)
P-value	-	0.0316
Probability (95% CI)[c]		
2 Months	0.84 (0.765 to 0.887)	0.91 (0.856 to 0.949)
4 Months	0.72 (0.638 to 0.786)	0.86 (0.792 to 0.906)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_det15pl_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Global health status
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-C30 - Time until permanent deterioration by 15 pt in global health - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_det15pl_de_i_f_x.rtf (08APR2021 15:30)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (34.3)	30 (55.6)	20 (37.0)	31 (45.6)	8 (27.6)	11 (34.4)	0.6015
Number (%) of patients censored	46 (65.7)	24 (44.4)	34 (63.0)	37 (54.4)	21 (72.4)	21 (65.6)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	1.91 (1.051 to 4.665)	1.91 (1.084 to 2.070)	2.83 (1.248 to 8.411)	2.23 (1.084 to 5.815)	1.97 (1.018 to NC)	2.83 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	5.59 (2.070 to NC)	NC (5.881 to NC)	10.22 (5.815 to NC)	NC (2.497 to NC)	NC (5.717 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0711		0.4840		0.9722	
Hazard ratio (95% CI) vs Pd	-	1.63 (0.95 to 2.79)		1.22 (0.70 to 2.14)		1.02 (0.41 to 2.53)	
P-value	-	0.0739		0.4847		0.9722	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (50.0)	30 (55.6)	31 (57.4)	43 (63.2)	21 (72.4)	20 (62.5)	0.2185
Number (%) of patients censored	35 (50.0)	24 (44.4)	23 (42.6)	25 (36.8)	8 (27.6)	12 (37.5)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	1.91 (1.084 to 2.004)	1.64 (1.084 to 2.267)	1.87 (1.084 to 2.168)	1.91 (1.084 to 2.136)	1.02 (0.953 to 1.938)	1.15 (1.018 to 2.990)	
Median (95% CI)	4.86 (2.793 to NC)	3.94 (2.267 to NC)	5.22 (2.168 to 11.433)	4.37 (2.793 to 8.312)	2.10 (1.018 to 3.055)	5.13 (1.873 to 12.485)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.864 to NC)	NC (11.433 to NC)	NC (9.396 to NC)	3.75 (2.464 to NC)	12.48 (9.396 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7862		0.7387		0.0645	
Hazard ratio (95% CI) vs Pd	-	1.07 (0.66 to 1.74)		1.08 (0.68 to 1.72)		0.56 (0.30 to 1.04)	
P-value	-	0.7855		0.7387		0.0680	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (14.3)	10 (18.5)	5 (9.3)	13 (19.1)	1 (3.4)	4 (12.5)	0.6657
Number (%) of patients censored	60 (85.7)	44 (81.5)	49 (90.7)	55 (80.9)	28 (96.6)	28 (87.5)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	NC (10.382 to NC)	NC (4.041 to NC)	NC (10.218 to NC)	12.71 (9.856 to NC)	NC (NC to NC)	NC (5.717 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.175 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6907		0.2250		0.3066	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.50 to 2.87)		1.87 (0.67 to 5.26)		2.97 (0.33 to 26.66)	
P-value	-	0.6911		0.2326		0.3302	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imppl_age_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (30.0)	18 (33.3)	20 (37.0)	18 (26.5)	14 (48.3)	8 (25.0)	0.1286
Number (%) of patients censored	49 (70.0)	36 (66.7)	34 (63.0)	50 (73.5)	15 (51.7)	24 (75.0)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	4.67 (1.906 to NC)	5.32 (1.938 to NC)	3.02 (1.150 to 9.528)	8.97 (6.472 to NC)	2.53 (0.986 to 5.651)	12.32 (5.125 to 14.029)	
Median (95% CI)	NC (NC to NC)	NC (7.885 to NC)	NC (7.491 to NC)	NC (NC to NC)	5.91 (3.844 to NC)	13.67 (12.320 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.425 to NC)	NC (13.667 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8685		0.0713		0.0199	
Hazard ratio (95% CI) vs Pd	-	1.05 (0.56 to 1.98)		0.56 (0.30 to 1.06)		0.37 (0.15 to 0.88)	
P-value	-	0.8682		0.0753		0.0252	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detpl_age_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (33.7)	43 (42.2)	18 (34.6)	29 (55.8)	0.4477
Number (%) of patients censored	67 (66.3)	59 (57.8)	34 (65.4)	23 (44.2)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.30 (1.248 to 4.665)	2.07 (1.840 to 4.107)	2.50 (1.018 to 13.207)	1.97 (1.051 to 2.825)	
Median (95% CI)	NC (NC to NC)	NC (6.439 to NC)	NC (5.881 to NC)	5.82 (2.267 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4248		0.1043	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.77 to 1.88)		1.62 (0.90 to 2.92)	
P-value	-	0.4255		0.1077	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	55 (54.5)	60 (58.8)	32 (61.5)	33 (63.5)	0.3418
Number (%) of patients censored	46 (45.5)	42 (41.2)	20 (38.5)	19 (36.5)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.91 (1.347 to 2.103)	1.87 (1.084 to 2.267)	1.08 (1.018 to 1.906)	1.51 (1.084 to 2.037)	
Median (95% CI)	5.22 (2.825 to 11.433)	4.37 (2.891 to 9.396)	2.83 (1.906 to 3.844)	4.17 (2.037 to 12.485)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.320 to NC)	NC (3.745 to NC)	13.86 (9.495 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7477		0.3263	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.74 to 1.53)		0.78 (0.48 to 1.28)	
P-value	-	0.7479		0.3274	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detl_plne_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	13 (12.9)	19 (18.6)	3 (5.8)	8 (15.4)	0.4257
Number (%) of patients censored	88 (87.1)	83 (81.4)	49 (94.2)	44 (84.6)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (10.382 to NC)	12.71 (9.856 to NC)	NC (NC to NC)	NC (5.092 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4199		0.1758	
Hazard ratio (95% CI) vs Pd	-	1.34 (0.66 to 2.70)		2.43 (0.64 to 9.16)	
P-value	-	0.4215		0.1900	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imppl_plne_de_i_t_x.rtf (08APR2021 14:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	35 (34.7)	30 (29.4)	20 (38.5)	14 (26.9)	0.4067
Number (%) of patients censored	66 (65.3)	72 (70.6)	32 (61.5)	38 (73.1)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	3.98 (2.037 to 7.491)	8.74 (3.285 to 14.029)	3.15 (1.051 to 4.862)	10.02 (5.125 to NC)	
Median (95% CI)	NC (11.170 to NC)	NC (14.029 to NC)	NC (4.665 to NC)	NC (13.667 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2169		0.0594	
Hazard ratio (95% CI) vs Pd	-	0.74 (0.45 to 1.20)		0.52 (0.26 to 1.04)	
P-value	-	0.2187		0.0638	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detpl_plne_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (32.9)	45 (50.6)	29 (34.9)	27 (41.5)	0.2816
Number (%) of patients censored	47 (67.1)	44 (49.4)	54 (65.1)	38 (58.5)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.83 (1.248 to 13.207)	1.97 (1.314 to 2.891)	1.94 (1.084 to 3.778)	2.04 (1.117 to 5.717)	
Median (95% CI)	NC (13.207 to NC)	8.41 (3.745 to NC)	NC (5.881 to NC)	NC (5.717 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0583		0.7743	
Hazard ratio (95% CI) vs Pd	-	1.62 (0.98 to 2.68)		1.08 (0.64 to 1.82)	
P-value	-	0.0608		0.7738	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_impl_sex_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (52.9)	53 (59.6)	50 (60.2)	40 (61.5)	0.6787
Number (%) of patients censored	33 (47.1)	36 (40.4)	33 (39.8)	25 (38.5)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.51 (1.084 to 1.971)	1.91 (1.117 to 2.464)	1.87 (1.018 to 2.004)	1.40 (1.051 to 2.136)	
Median (95% CI)	3.84 (2.004 to NC)	4.44 (2.891 to 10.480)	3.15 (2.103 to 6.045)	3.98 (2.201 to 9.396)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.320 to NC)	NC (7.491 to NC)	NC (9.396 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7992		0.7476	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.69 to 1.61)		0.93 (0.62 to 1.42)	
P-value	-	0.8001		0.7484	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (8.6)	18 (20.2)	10 (12.0)	9 (13.8)	0.1990
Number (%) of patients censored	64 (91.4)	71 (79.8)	73 (88.0)	56 (86.2)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (NC to NC)	12.71 (6.045 to NC)	NC (10.218 to NC)	NC (10.283 to NC)	
Median (95% CI)	NC (NC to NC)	NC (13.175 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0643		0.9926	
Hazard ratio (95% CI) vs Pd	-	2.33 (0.93 to 5.88)		1.00 (0.40 to 2.45)	
P-value	-	0.0725		0.9926	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (34.3)	22 (24.7)	31 (37.3)	22 (33.8)	0.6751
Number (%) of patients censored	46 (65.7)	67 (75.3)	52 (62.7)	43 (66.2)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	3.98 (1.511 to 6.834)	12.32 (4.698 to NC)	3.22 (1.906 to 5.914)	8.15 (2.267 to 10.875)	
Median (95% CI)	NC (11.433 to NC)	NC (14.029 to NC)	NC (7.491 to NC)	NC (10.875 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0967		0.2551	
Hazard ratio (95% CI) vs Pd	-	0.62 (0.34 to 1.10)		0.73 (0.42 to 1.26)	
P-value	-	0.1000		0.2570	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detpl_sex_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (34.1)	55 (46.6)	7 (36.8)	13 (54.2)	0.5682
Number (%) of patients censored	83 (65.9)	63 (53.4)	12 (63.2)	11 (45.8)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.97 (1.281 to 3.811)	2.04 (1.873 to 3.581)	2.30 (0.953 to NC)	1.97 (0.986 to 2.990)	
Median (95% CI)	NC (13.207 to NC)	10.22 (5.815 to NC)	NC (2.300 to NC)	6.93 (1.971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.316 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2343		0.2582	
Hazard ratio (95% CI) vs Pd	-	1.27 (0.85 to 1.90)		1.69 (0.67 to 4.25)	
P-value	-	0.2354		0.2636	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	72 (57.1)	75 (63.6)	12 (63.2)	15 (62.5)	0.8852
Number (%) of patients censored	54 (42.9)	43 (36.4)	7 (36.8)	9 (37.5)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.87 (1.150 to 1.971)	1.87 (1.216 to 2.201)	1.08 (0.986 to 2.891)	1.12 (0.953 to 2.037)	
Median (95% CI)	3.52 (2.530 to 6.144)	4.37 (2.891 to 7.261)	3.22 (1.084 to NC)	2.99 (1.117 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.320 to NC)	NC (3.220 to NC)	NC (3.515 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9801		0.9719	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.72 to 1.38)		0.99 (0.46 to 2.13)	
P-value	-	0.9801		0.9719	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (9.5)	21 (17.8)	3 (15.8)	3 (12.5)	0.2933
Number (%) of patients censored	114 (90.5)	97 (82.2)	16 (84.2)	21 (87.5)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (NC to NC)	13.17 (10.283 to NC)	NC (0.953 to NC)	NC (2.924 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1259		0.7241	
Hazard ratio (95% CI) vs Pd	-	1.73 (0.85 to 3.51)		0.75 (0.15 to 3.72)	
P-value	-	0.1307		0.7250	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imppl_race_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (36.5)	36 (30.5)	7 (36.8)	5 (20.8)	0.5022
Number (%) of patients censored	80 (63.5)	82 (69.5)	12 (63.2)	19 (79.2)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	3.52 (2.037 to 5.651)	8.11 (4.698 to 14.029)	3.22 (1.018 to NC)	13.67 (1.938 to NC)	
Median (95% CI)	NC (11.170 to NC)	NC (NC to NC)	NC (3.220 to NC)	NC (10.875 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.667 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0825		0.0551	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.44 to 1.05)		0.29 (0.07 to 1.12)	
P-value	-	0.0841		0.0717	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detpl_race_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	1 (25.0)	44 (32.8)	65 (50.0)	0.3340
Number (%) of patients censored	2 (66.7)	3 (75.0)	90 (67.2)	65 (50.0)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (1.018 to NC)	2.50 (1.873 to 4.665)	2.00 (1.873 to 2.891)	
Median (95% CI)	NC (1.281 to NC)	NC (1.018 to NC)	NC (13.207 to NC)	8.41 (5.717 to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6949		0.0309	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.04 to 9.30)		1.52 (1.04 to 2.23)	
P-value	-	0.6985		0.0321	
Hazard ratio inverted (95% CI) vs IPd		-		0.66 (0.45 to 0.96)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_impl_ethn_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	2 (50.0)	78 (58.2)	83 (63.8)	0.6490
Number (%) of patients censored	2 (66.7)	2 (50.0)	56 (41.8)	47 (36.2)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.35 (1.347 to NC)	3.25 (2.136 to NC)	1.74 (1.084 to 1.938)	1.51 (1.084 to 1.938)	
Median (95% CI)	NC (1.347 to NC)	NC (2.136 to NC)	3.15 (2.136 to 5.224)	3.98 (2.825 to 6.965)	
75% quantile (95% CI)	NC (1.347 to NC)	NC (2.136 to NC)	NC (NC to NC)	NC (12.320 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4504		0.9236	
Hazard ratio (95% CI) vs Pd	-	0.35 (0.02 to 5.89)		1.02 (0.75 to 1.38)	
P-value	-	0.4689		0.9236	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	1 (25.0)	12 (9.0)	21 (16.2)	0.1754
Number (%) of patients censored	2 (66.7)	3 (75.0)	122 (91.0)	109 (83.8)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	12.52 (12.517 to NC)	NC (NC to NC)	NC (10.480 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (12.517 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (12.517 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.1538	
Hazard ratio (95% CI) vs Pd	-			1.67 (0.82 to 3.39)	
P-value	-	0.9985		0.1583	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	0 (0.0)	50 (37.3)	38 (29.2)	0.9785
Number (%) of patients censored	2 (66.7)	4 (100.0)	84 (62.7)	92 (70.8)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	5.26 (NC to NC)	NC (NC to NC)	3.22 (2.037 to 5.585)	8.97 (5.618 to 13.667)	
Median (95% CI)	5.26 (NC to NC)	NC (NC to NC)	NC (9.528 to NC)	NC (14.029 to NC)	
75% quantile (95% CI)	5.26 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0455		0.0291	
Hazard ratio (95% CI) vs Pd	-			0.63 (0.41 to 0.96)	
P-value	-	1.0000		0.0306	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	26 (34.2)	17 (30.9)	5 (25.0)	15 (53.6)	2 (40.0)	3 (42.9)	6 (40.0)	12 (57.1)	13 (35.1)	25 (58.1)	0.3948
Number (%) of patients censored	50 (65.8)	38 (69.1)	15 (75.0)	13 (46.4)	3 (60.0)	4 (57.1)	9 (60.0)	9 (42.9)	24 (64.9)	18 (41.9)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	1.91 (1.084 to 5.881)	3.09 (1.051 to NC)	2.50 (0.986 to NC)	1.99 (0.986 to 5.585)	2.83 (1.906 to NC)	1.94 (1.018 to NC)	2.30 (0.986 to NC)	1.97 (0.986 to 2.990)	2.66 (1.018 to 13.207)	2.04 (1.117 to 2.891)	
Median (95% CI)	NC (8.411 to NC)	NC (NC to NC)	NC (2.497 to NC)	7.39 (2.366 to NC)	NC (1.906 to NC)	NC (1.018 to NC)	NC (2.300 to NC)	6.93 (1.971 to NC)	13.21 (4.271 to NC)	5.82 (2.333 to NC)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.444 to NC)	NC (1.906 to NC)	NC (6.078 to NC)	NC (NC to NC)	NC (6.932 to NC)	NC (13.207 to NC)	NC (8.641 to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.5278		0.1285		0.8962		0.2826		0.1448	
Hazard ratio (95% CI) vs Pd	-	0.82 (0.45 to 1.51)		2.15 (0.78 to 5.93)		1.13 (0.19 to 6.75)		1.70 (0.64 to 4.56)		1.64 (0.84 to 3.21)	
P-value	-	0.5285		0.1380		0.8963		0.2882		0.1489	
Improvement probability (95% CI)[b]											

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Number (%) of events	38 (50.0)	30 (54.5)	15 (75.0)	15 (53.6)	3 (60.0)	6 (85.7)	9 (60.0)	13 (61.9)	22 (59.5)	29 (67.4)	0.3410
Number (%) of patients censored	38 (50.0)	25 (45.5)	5 (25.0)	13 (46.4)	2 (40.0)	1 (14.3)	6 (40.0)	8 (38.1)	15 (40.5)	14 (32.6)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	1.94 (1.084 to 2.464)	1.54 (1.051 to 2.990)	0.99 (0.953 to 2.825)	2.05 (0.986 to 3.844)	2.04 (1.347 to NC)	0.95 (0.953 to 2.136)	1.08 (1.018 to 2.891)	1.12 (0.953 to 2.037)	1.51 (1.018 to 1.938)	1.91 (1.051 to 2.628)	
Median (95% CI)	6.05 (2.858 to NC)	5.13 (2.990 to NC)	2.96 (0.986 to 6.144)	6.54 (2.793 to NC)	2.60 (1.347 to NC)	2.14 (0.953 to 3.515)	3.22 (1.051 to NC)	2.99 (1.117 to NC)	2.17 (1.906 to NC)	4.17 (1.971 to 9.495)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.320 to NC)	7.75 (2.957 to NC)	NC (NC to NC)	NC (1.347 to NC)	3.52 (1.084 to NC)	NC (3.220 to NC)	NC (2.990 to NC)	NC (3.745 to NC)	13.86 (8.312 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.8730		0.0772		0.4136		0.8982		0.8349	
Hazard ratio (95% CI) vs Pd	-	1.04 (0.64 to 1.68)		0.53 (0.26 to 1.08)		1.77 (0.44 to 7.14)		1.06 (0.45 to 2.51)		0.94 (0.54 to 1.64)	
P-value	-	0.8727		0.0822		0.4199		0.8986		0.8342	
Deterioration probability (95% CI)[b]											
2 Months	0.719 (0.599 to 0.808)	0.722 (0.582 to 0.822)	0.579 (0.332 to 0.763)	0.750 (0.546 to 0.872)	0.800 (0.204 to 0.969)	0.571 (0.172 to 0.837)	0.600 (0.318 to 0.797)	0.615 (0.376 to 0.786)	0.576 (0.398 to 0.719)	0.662 (0.497 to 0.784)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detl_greg_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	7 (9.2)	9 (16.4)	0 (0.0)	7 (25.0)	1 (20.0)	1 (14.3)	2 (13.3)	3 (14.3)	6 (16.2)	7 (16.3)	0.8464
Number (%) of patients censored	69 (90.8)	46 (83.6)	20 (100.0)	21 (75.0)	4 (80.0)	6 (85.7)	13 (86.7)	18 (85.7)	31 (83.8)	36 (83.7)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (NC to NC)	13.17 (5.749 to NC)	NC (NC to NC)	10.28 (1.971 to NC)	NC (7.162 to NC)	12.52 (12.517 to NC)	NC (0.986 to NC)	NC (2.924 to NC)	NC (1.018 to NC)	NC (9.856 to NC)	
Median (95% CI)	NC (NC to NC)	NC (13.175 to NC)	NC (NC to NC)	NC (10.283 to NC)	NC (7.162 to NC)	NC (12.517 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.162 to NC)	NC (12.517 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imppl_greg_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.2623		0.0246		0.2733		0.9541		0.6896	
Hazard ratio (95% CI) vs Pd	-	1.75 (0.65 to 4.70)						1.05 (0.18 to 6.31)		0.80 (0.27 to 2.39)	
P-value	-	0.2684		0.9959		0.9984		0.9544		0.6902	
Improvement probability (95% CI)[b]											
2 Months	0.070 (0.026 to 0.145)	0.056 (0.015 to 0.140)		0.071 (0.013 to 0.204)			0.133 (0.022 to 0.346)		0.111 (0.035 to 0.236)	0.048 (0.009 to 0.144)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	23 (30.3)	17 (30.9)	10 (50.0)	9 (32.1)	3 (60.0)	2 (28.6)	5 (33.3)	4 (19.0)	14 (37.8)	12 (27.9)	0.5306
Number (%) of patients censored	53 (69.7)	38 (69.1)	10 (50.0)	19 (67.9)	2 (40.0)	5 (71.4)	10 (66.7)	17 (81.0)	23 (62.2)	31 (72.1)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	5.88 (3.154 to 11.170)	5.32 (1.643 to 14.029)	1.64 (0.953 to 3.811)	7.89 (1.938 to NC)	2.60 (2.037 to NC)	8.97 (2.628 to NC)	3.22 (1.018 to NC)	13.67 (5.552 to NC)	1.91 (1.051 to 9.528)	8.11 (2.628 to NC)	
Median (95% CI)	NC (11.170 to NC)	NC (12.320 to NC)	3.98 (1.643 to NC)	NC (8.148 to NC)	5.26 (2.037 to NC)	NC (2.628 to NC)	NC (1.906 to NC)	NC (10.875 to NC)	NC (3.844 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.975 to NC)	NC (NC to NC)	NC (2.037 to NC)	NC (8.969 to NC)	NC (NC to NC)	NC (13.667 to NC)	NC (NC to NC)	NC (NC to NC)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.9426		0.0844		0.2172		0.0674		0.1685	
Hazard ratio (95% CI) vs Pd	-	0.98 (0.52 to 1.83)		0.46 (0.19 to 1.14)		0.34 (0.06 to 2.05)		0.24 (0.05 to 1.26)		0.58 (0.27 to 1.27)	
P-value	-	0.9427		0.0922		0.2389		0.0916		0.1735	
Deterioration probability (95% CI)[b]											
2 Months	0.916 (0.822 to 0.961)	0.870 (0.747 to 0.936)	0.684 (0.428 to 0.844)	0.929 (0.743 to 0.982)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.800 (0.500 to 0.931)	1.000 (1.000 to 1.000)	0.747 (0.570 to 0.860)	0.904 (0.764 to 0.963)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (33.0)	28 (36.4)	20 (35.7)	44 (57.1)	0.1408
Number (%) of patients censored	65 (67.0)	49 (63.6)	36 (64.3)	33 (42.9)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.94 (1.281 to 5.881)	2.33 (1.873 to 6.078)	2.50 (1.117 to 13.207)	1.97 (1.084 to 2.234)	
Median (95% CI)	NC (NC to NC)	NC (8.411 to NC)	NC (4.994 to NC)	6.51 (2.990 to 10.316)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9752		0.0413	
Hazard ratio (95% CI) vs Pd	-	0.99 (0.60 to 1.65)		1.72 (1.01 to 2.92)	
P-value	-	0.9752		0.0439	
Hazard ratio inverted (95% CI) vs IPd		-		0.58 (0.34 to 0.99)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	53 (54.6)	46 (59.7)	34 (60.7)	47 (61.0)	0.7378
Number (%) of patients censored	44 (45.4)	31 (40.3)	22 (39.3)	30 (39.0)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.94 (1.150 to 2.037)	1.59 (1.084 to 2.267)	1.15 (1.018 to 1.906)	1.87 (1.084 to 2.136)	
Median (95% CI)	3.75 (2.464 to 11.433)	4.37 (2.891 to 9.396)	3.22 (1.906 to 7.754)	4.27 (2.628 to 9.495)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.320 to NC)	NC (7.754 to NC)	NC (10.480 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9752		0.7205	
Hazard ratio (95% CI) vs Pd	-	1.01 (0.68 to 1.49)		0.92 (0.59 to 1.43)	
P-value	-	0.9752		0.7206	
Deterioration probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (9.3)	10 (13.0)	7 (12.5)	17 (22.1)	0.7382
Number (%) of patients censored	88 (90.7)	67 (87.0)	49 (87.5)	60 (77.9)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (NC to NC)	NC (12.517 to NC)	NC (10.382 to NC)	12.71 (6.045 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5529		0.2837	
Hazard ratio (95% CI) vs Pd	-	1.31 (0.53 to 3.23)		1.61 (0.67 to 3.89)	
P-value	-	0.5541		0.2885	
Improvement probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (33.0)	25 (32.5)	23 (41.1)	19 (24.7)	0.0999
Number (%) of patients censored	65 (67.0)	52 (67.5)	33 (58.9)	58 (75.3)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	5.26 (2.793 to 7.491)	6.67 (2.628 to 12.320)	1.91 (1.051 to 3.811)	10.87 (6.965 to NC)	
Median (95% CI)	NC (11.170 to NC)	NC (12.320 to NC)	NC (3.811 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6103		0.0117	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.52 to 1.47)		0.46 (0.25 to 0.86)	
P-value	-	0.6106		0.0138	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (32.1)	65 (47.1)	8 (50.0)	7 (43.8)	0.3339
Number (%) of patients censored	93 (67.9)	73 (52.9)	8 (50.0)	9 (56.3)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.83 (1.906 to 5.881)	2.04 (1.906 to 2.990)	1.08 (0.953 to 2.300)	1.02 (0.986 to 6.439)	
Median (95% CI)	NC (13.207 to NC)	10.32 (5.815 to NC)	2.79 (0.986 to NC)	6.44 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.793 to NC)	NC (6.439 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0673		0.7825	
Hazard ratio (95% CI) vs Pd	-	1.43 (0.97 to 2.09)		0.87 (0.31 to 2.39)	
P-value	-	0.0687		0.7830	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_impl_ecog_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	79 (57.7)	88 (63.8)	8 (50.0)	5 (31.3)	0.3622
Number (%) of patients censored	58 (42.3)	50 (36.2)	8 (50.0)	11 (68.8)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.74 (1.084 to 1.971)	1.54 (1.117 to 1.938)	1.35 (0.986 to 2.793)	2.83 (0.953 to NC)	
Median (95% CI)	3.75 (2.464 to 6.144)	3.98 (2.825 to 6.538)	3.22 (1.084 to NC)	NC (2.136 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.320 to NC)	NC (3.220 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9364		0.3617	
Hazard ratio (95% CI) vs Pd	-	1.01 (0.75 to 1.37)		0.60 (0.20 to 1.83)	
P-value	-	0.9364		0.3670	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (8.0)	23 (16.7)	5 (31.3)	4 (25.0)	0.1176
Number (%) of patients censored	126 (92.0)	115 (83.3)	11 (68.8)	12 (75.0)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (NC to NC)	NC (10.283 to NC)	1.08 (0.953 to NC)	12.52 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	13.17 (12.517 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.517 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0662		0.4854	
Hazard ratio (95% CI) vs Pd	-	1.94 (0.94 to 3.97)		0.63 (0.17 to 2.35)	
P-value	-	0.0713		0.4892	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imppl_ecog_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (35.8)	43 (31.2)	6 (37.5)	1 (6.3)	0.1437
Number (%) of patients censored	88 (64.2)	95 (68.8)	10 (62.5)	15 (93.8)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	3.84 (2.037 to 5.881)	8.11 (5.322 to 12.320)	2.79 (0.986 to NC)	NC (2.628 to NC)	
Median (95% CI)	NC (11.433 to NC)	NC (14.029 to NC)	NC (2.530 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1046		0.0520	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.47 to 1.07)		0.16 (0.02 to 1.33)	
P-value	-	0.1062		0.0898	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detpl_ecog_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (39.2)	28 (43.8)	19 (33.9)	26 (49.1)	13 (30.2)	17 (50.0)	0.7321
Number (%) of patients censored	31 (60.8)	36 (56.3)	37 (66.1)	27 (50.9)	30 (69.8)	17 (50.0)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	1.15 (1.018 to 3.811)	1.97 (1.084 to 5.060)	2.83 (1.906 to 8.411)	2.27 (1.873 to 5.815)	1.94 (1.084 to NC)	1.48 (0.986 to 2.168)	
Median (95% CI)	NC (2.990 to NC)	NC (5.060 to NC)	NC (8.411 to NC)	8.41 (5.717 to NC)	NC (3.778 to NC)	3.75 (1.971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7374		0.2492		0.1831	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.62 to 1.96)		1.41 (0.78 to 2.56)		1.63 (0.79 to 3.35)	
P-value	-	0.7375		0.2516		0.1874	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_impl_seiss_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (64.7)	41 (64.1)	31 (55.4)	33 (62.3)	21 (48.8)	16 (47.1)	0.5534
Number (%) of patients censored	18 (35.3)	23 (35.9)	25 (44.6)	20 (37.7)	22 (51.2)	18 (52.9)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	1.97 (1.051 to 2.595)	1.87 (1.084 to 2.201)	1.35 (1.018 to 1.971)	1.22 (1.018 to 2.267)	1.45 (0.986 to 1.938)	1.97 (0.986 to 5.224)	
Median (95% CI)	3.52 (2.103 to 5.224)	3.84 (2.464 to 9.396)	3.42 (1.938 to NC)	4.37 (2.201 to 12.320)	3.75 (1.906 to NC)	9.49 (4.271 to NC)	
75% quantile (95% CI)	NC (5.224 to NC)	NC (9.396 to NC)	NC (11.433 to NC)	13.86 (6.965 to NC)	NC (6.144 to NC)	NC (12.485 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9628		0.7881		0.3242	
Hazard ratio (95% CI) vs Pd	-	0.99 (0.63 to 1.56)		1.07 (0.65 to 1.75)		0.72 (0.37 to 1.39)	
P-value	-	0.9628		0.7882		0.3263	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (11.8)	9 (14.1)	5 (8.9)	13 (24.5)	5 (11.6)	5 (14.7)	0.4174
Number (%) of patients censored	45 (88.2)	55 (85.9)	51 (91.1)	40 (75.5)	38 (88.4)	29 (85.3)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	NC (NC to NC)	NC (12.517 to NC)	NC (10.218 to NC)	10.28 (3.778 to NC)	NC (8.378 to NC)	NC (5.585 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.175 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7231		0.0521		0.9428	
Hazard ratio (95% CI) vs Pd	-	1.21 (0.43 to 3.39)		2.67 (0.95 to 7.50)		0.96 (0.28 to 3.32)	
P-value	-	0.7235		0.0620		0.9427	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (35.3)	16 (25.0)	22 (39.3)	14 (26.4)	14 (32.6)	11 (32.4)	0.7012
Number (%) of patients censored	33 (64.7)	48 (75.0)	34 (60.7)	39 (73.6)	29 (67.4)	23 (67.6)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	4.67 (2.595 to NC)	10.28 (3.285 to NC)	2.46 (1.018 to 5.651)	10.02 (5.552 to NC)	3.84 (1.347 to 9.528)	7.26 (1.380 to 13.667)	
Median (95% CI)	NC (11.170 to NC)	NC (14.029 to NC)	NC (5.257 to NC)	NC (12.320 to NC)	NC (5.585 to NC)	13.67 (8.115 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.667 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2394		0.0380		0.4875	
Hazard ratio (95% CI) vs Pd	-	0.67 (0.34 to 1.31)		0.50 (0.25 to 0.97)		0.76 (0.34 to 1.67)	
P-value	-	0.2426		0.0418		0.4888	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (35.5)	19 (48.7)	36 (36.7)	45 (45.5)	5 (20.8)	8 (50.0)	0.3459
Number (%) of patients censored	20 (64.5)	20 (51.3)	62 (63.3)	54 (54.5)	19 (79.2)	8 (50.0)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	1.91 (1.018 to NC)	1.91 (0.986 to 3.811)	2.30 (1.610 to 4.271)	2.27 (1.938 to 5.717)	NC (0.953 to NC)	1.05 (0.723 to 2.037)	
Median (95% CI)	NC (2.990 to NC)	10.22 (2.990 to NC)	NC (8.411 to NC)	NC (6.505 to NC)	NC (NC to NC)	3.75 (1.018 to NC)	
75% quantile (95% CI)	NC (13.207 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.037 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3236		0.5278		0.0868	
Hazard ratio (95% CI) vs Pd	-	1.45 (0.69 to 3.05)		1.15 (0.74 to 1.79)		2.57 (0.84 to 7.87)	
P-value	-	0.3264		0.5281		0.0987	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (71.0)	24 (61.5)	55 (56.1)	63 (63.6)	10 (41.7)	6 (37.5)	0.2823
Number (%) of patients censored	9 (29.0)	15 (38.5)	43 (43.9)	36 (36.4)	14 (58.3)	10 (62.5)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	1.94 (1.018 to 2.037)	2.04 (1.380 to 2.891)	1.74 (1.018 to 2.004)	1.28 (1.051 to 1.938)	1.51 (0.953 to 2.004)	2.27 (0.986 to 9.495)	
Median (95% CI)	2.89 (1.971 to 5.224)	4.44 (2.464 to NC)	3.75 (2.530 to 11.433)	3.84 (2.267 to 6.308)	6.05 (1.511 to NC)	9.49 (1.938 to NC)	
75% quantile (95% CI)	NC (3.515 to NC)	NC (10.480 to NC)	NC (NC to NC)	13.86 (12.320 to NC)	NC (6.045 to NC)	NC (9.495 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2914		0.4542		0.3290	
Hazard ratio (95% CI) vs Pd	-	0.73 (0.41 to 1.31)		1.15 (0.80 to 1.65)		0.60 (0.21 to 1.69)	
P-value	-	0.2933		0.4552		0.3335	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (9.7)	7 (17.9)	9 (9.2)	19 (19.2)	4 (16.7)	1 (6.3)	0.2234
Number (%) of patients censored	28 (90.3)	32 (82.1)	89 (90.8)	80 (80.8)	20 (83.3)	15 (93.8)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	NC (1.117 to NC)	12.71 (6.045 to NC)	NC (NC to NC)	13.17 (6.735 to NC)	8.38 (0.953 to NC)	NC (10.480 to NC)	
Median (95% CI)	NC (NC to NC)	NC (12.715 to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.378 to NC)	NC (10.480 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3520		0.0831		0.1937	
Hazard ratio (95% CI) vs Pd	-	1.88 (0.49 to 7.28)		1.99 (0.90 to 4.40)		0.26 (0.03 to 2.33)	
P-value	-	0.3601		0.0893		0.2266	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imppl_seriss_de_i_t_x.rtf (08APR2021 14:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (35.5)	8 (20.5)	36 (36.7)	31 (31.3)	8 (33.3)	5 (31.3)	0.8623
Number (%) of patients censored	20 (64.5)	31 (79.5)	62 (63.3)	68 (68.7)	16 (66.7)	11 (68.8)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	5.88 (2.037 to NC)	14.03 (2.464 to NC)	3.81 (1.643 to 5.585)	8.15 (5.125 to 12.320)	1.91 (1.117 to 6.834)	5.62 (0.986 to NC)	
Median (95% CI)	NC (6.735 to NC)	NC (14.029 to NC)	NC (9.528 to NC)	NC (13.667 to NC)	6.83 (1.906 to NC)	NC (4.698 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.834 to NC)	NC (7.261 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1680		0.1632		0.4406	
Hazard ratio (95% CI) vs Pd	-	0.53 (0.21 to 1.32)		0.71 (0.44 to 1.15)		0.64 (0.21 to 1.99)	
P-value	-	0.1750		0.1653		0.4441	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (34.8)	6 (42.9)	29 (30.5)	59 (50.0)	0.5516
Number (%) of patients censored	15 (65.2)	8 (57.1)	66 (69.5)	59 (50.0)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.28 (0.953 to NC)	1.94 (0.986 to 6.571)	2.83 (1.840 to NC)	1.97 (1.380 to 2.891)	
Median (95% CI)	NC (1.281 to NC)	6.57 (1.840 to NC)	NC (NC to NC)	8.44 (5.060 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (6.571 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8233		0.0231	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.39 to 3.26)		1.66 (1.07 to 2.60)	
P-value	-	0.8234		0.0246	
Hazard ratio inverted (95% CI) vs IPd		-		0.60 (0.39 to 0.94)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (39.1)	5 (35.7)	55 (57.9)	76 (64.4)	0.9408
Number (%) of patients censored	14 (60.9)	9 (64.3)	40 (42.1)	42 (35.6)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.10 (1.117 to 5.224)	2.99 (1.018 to NC)	1.35 (1.018 to 1.906)	1.87 (1.084 to 2.136)	
Median (95% CI)	NC (2.103 to NC)	NC (1.511 to NC)	3.52 (1.971 to 7.491)	4.17 (2.825 to 6.538)	
75% quantile (95% CI)	NC (5.224 to NC)	NC (3.844 to NC)	NC (NC to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9502		0.8980	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.32 to 2.89)		1.02 (0.72 to 1.45)	
P-value	-	0.9504		0.8981	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (17.4)	1 (7.1)	9 (9.5)	24 (20.3)	0.1471
Number (%) of patients censored	19 (82.6)	13 (92.9)	86 (90.5)	94 (79.7)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	8.38 (1.051 to NC)	NC (8.345 to NC)	NC (NC to NC)	12.71 (9.922 to NC)	
Median (95% CI)	NC (4.928 to NC)	NC (8.345 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3438		0.0660	
Hazard ratio (95% CI) vs Pd	-	0.36 (0.04 to 3.25)		2.02 (0.94 to 4.35)	
P-value	-	0.3642		0.0717	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (26.1)	3 (21.4)	35 (36.8)	35 (29.7)	0.7518
Number (%) of patients censored	17 (73.9)	11 (78.6)	60 (63.2)	83 (70.3)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	5.65 (1.117 to NC)	6.67 (1.018 to NC)	3.81 (1.511 to 6.735)	8.74 (5.552 to 14.029)	
Median (95% CI)	NC (4.862 to NC)	NC (4.698 to NC)	NC (11.170 to NC)	NC (14.029 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6967		0.0782	
Hazard ratio (95% CI) vs Pd	-	0.76 (0.19 to 3.04)		0.66 (0.41 to 1.05)	
P-value	-	0.6977		0.0803	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (30.6)	9 (37.5)	25 (32.1)	54 (52.4)	0.4660
Number (%) of patients censored	25 (69.4)	15 (62.5)	53 (67.9)	49 (47.6)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.30 (1.150 to NC)	2.04 (0.986 to 8.411)	2.79 (1.084 to NC)	1.94 (1.084 to 2.267)	
Median (95% CI)	NC (5.881 to NC)	8.41 (2.037 to NC)	NC (NC to NC)	6.44 (3.581 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (8.411 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7903		0.0318	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.47 to 2.72)		1.67 (1.04 to 2.69)	
P-value	-	0.7904		0.0337	
Hazard ratio inverted (95% CI) vs IPd		-		0.60 (0.37 to 0.96)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (50.0)	13 (54.2)	44 (56.4)	66 (64.1)	0.5501
Number (%) of patients censored	18 (50.0)	11 (45.8)	34 (43.6)	37 (35.9)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.97 (1.347 to 3.055)	1.28 (0.986 to 2.267)	1.08 (1.018 to 1.906)	1.87 (1.084 to 2.267)	
Median (95% CI)	5.22 (2.103 to NC)	2.99 (1.511 to NC)	3.75 (1.938 to NC)	4.37 (2.891 to 6.965)	
75% quantile (95% CI)	NC (6.144 to NC)	NC (3.844 to NC)	NC (NC to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4938		0.9331	
Hazard ratio (95% CI) vs Pd	-	1.28 (0.63 to 2.62)		1.02 (0.69 to 1.49)	
P-value	-	0.4949		0.9332	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (11.1)	2 (8.3)	9 (11.5)	22 (21.4)	0.3404
Number (%) of patients censored	32 (88.9)	22 (91.7)	69 (88.5)	81 (78.6)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (4.928 to NC)	NC (5.717 to NC)	NC (10.382 to NC)	12.71 (9.856 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6527		0.1543	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.12 to 3.71)		1.74 (0.80 to 3.79)	
P-value	-	0.6548		0.1598	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (33.3)	7 (29.2)	27 (34.6)	30 (29.1)	0.7535
Number (%) of patients censored	24 (66.7)	17 (70.8)	51 (65.4)	73 (70.9)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	3.84 (1.906 to 7.425)	5.62 (0.986 to NC)	3.98 (1.150 to 11.170)	8.15 (5.322 to NC)	
Median (95% CI)	NC (4.862 to NC)	NC (5.618 to NC)	NC (11.170 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5834		0.1758	
Hazard ratio (95% CI) vs Pd	-	0.77 (0.30 to 1.96)		0.70 (0.42 to 1.18)	
P-value	-	0.5845		0.1781	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (33.3)	42 (50.6)	22 (34.9)	30 (42.3)	0.1424
Number (%) of patients censored	60 (66.7)	41 (49.4)	41 (65.1)	41 (57.7)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.79 (1.840 to 5.881)	1.91 (1.117 to 2.267)	1.91 (1.084 to 4.994)	2.99 (1.938 to 6.439)	
Median (95% CI)	NC (NC to NC)	6.57 (2.891 to NC)	13.21 (4.994 to NC)	NC (6.505 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.207 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0294		0.9146	
Hazard ratio (95% CI) vs Pd	-	1.68 (1.05 to 2.68)		0.97 (0.56 to 1.68)	
P-value	-	0.0311		0.9144	
Hazard ratio inverted (95% CI) vs IPd		-		1.03 (0.59 to 1.79)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (55.6)	45 (54.2)	37 (58.7)	48 (67.6)	0.6313
Number (%) of patients censored	40 (44.4)	38 (45.8)	26 (41.3)	23 (32.4)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.74 (1.084 to 2.037)	2.04 (1.643 to 2.891)	1.35 (0.986 to 1.938)	1.08 (1.018 to 1.511)	
Median (95% CI)	3.84 (2.825 to 11.433)	6.31 (3.121 to 13.864)	2.60 (1.938 to 6.538)	3.52 (1.873 to 7.261)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.864 to NC)	NC (6.538 to NC)	12.32 (8.312 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5782		0.8911	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.60 to 1.33)		1.03 (0.67 to 1.58)	
P-value	-	0.5787		0.8913	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (11.1)	16 (19.3)	6 (9.5)	11 (15.5)	0.6183
Number (%) of patients censored	80 (88.9)	67 (80.7)	57 (90.5)	60 (84.5)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (NC to NC)	12.71 (6.045 to NC)	NC (10.382 to NC)	NC (10.283 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1585		0.6856	
Hazard ratio (95% CI) vs Pd	-	1.75 (0.80 to 3.87)		1.23 (0.45 to 3.34)	
P-value	-	0.1639		0.6861	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (36.7)	24 (28.9)	22 (34.9)	20 (28.2)	0.7004
Number (%) of patients censored	57 (63.3)	59 (71.1)	41 (65.1)	51 (71.8)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	3.81 (1.906 to 6.735)	6.67 (2.793 to NC)	3.22 (1.150 to 7.425)	10.28 (6.965 to 14.029)	
Median (95% CI)	NC (11.170 to NC)	NC (NC to NC)	NC (7.425 to NC)	NC (13.667 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1990		0.0896	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.42 to 1.20)		0.59 (0.32 to 1.09)	
P-value	-	0.2012		0.0931	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	2 (100.0)	50 (33.1)	70 (46.1)	0.3204
Number (%) of patients censored	0 (0.0)	0 (0.0)	101 (66.9)	82 (53.9)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.02 (1.018 to 1.084)	1.08 (1.084 to 2.267)	2.50 (1.873 to 4.665)	2.04 (1.873 to 2.990)	
Median (95% CI)	1.05 (1.018 to 1.084)	1.68 (1.084 to 2.267)	NC (13.207 to NC)	10.32 (6.078 to NC)	
75% quantile (95% CI)	1.08 (1.018 to 1.084)	2.27 (1.084 to 2.267)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.1015	
Hazard ratio (95% CI) vs Pd	-	0.31 (0.03 to 3.50)		1.35 (0.94 to 1.94)	
P-value	-	0.3429		0.1028	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_impl_allt_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	87 (57.6)	92 (60.5)	0.9790
Number (%) of patients censored	2 (100.0)	1 (50.0)	64 (42.4)	60 (39.5)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (NC to NC)	2.04 (2.037 to NC)	1.64 (1.084 to 1.938)	1.64 (1.117 to 2.136)	
Median (95% CI)	NC (NC to NC)	NC (2.037 to NC)	3.42 (2.530 to 6.045)	4.37 (2.990 to 7.261)	
75% quantile (95% CI)	NC (NC to NC)	NC (2.037 to NC)	NC (NC to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.7755	
Hazard ratio (95% CI) vs Pd	-			0.96 (0.71 to 1.28)	
P-value	-	0.9990		0.7753	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	15 (9.9)	27 (17.8)	0.9889
Number (%) of patients censored	1 (50.0)	2 (100.0)	136 (90.1)	125 (82.2)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.02 (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	13.17 (10.283 to NC)	
Median (95% CI)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.1141	
Hazard ratio (95% CI) vs Pd	-			1.65 (0.88 to 3.11)	
P-value	-	0.9990		0.1180	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	55 (36.4)	44 (28.9)	0.9997
Number (%) of patients censored	2 (100.0)	2 (100.0)	96 (63.6)	108 (71.1)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	3.52 (2.037 to 5.585)	8.74 (5.552 to 13.667)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.170 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0338	
Hazard ratio (95% CI) vs Pd	-			0.65 (0.44 to 0.97)	
P-value	-			0.0351	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (37.6)	54 (51.9)	12 (29.3)	12 (36.4)	0.7655
Number (%) of patients censored	63 (62.4)	50 (48.1)	29 (70.7)	21 (63.6)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.30 (1.281 to 3.778)	1.97 (1.314 to 2.333)	2.30 (0.986 to NC)	2.89 (0.986 to NC)	
Median (95% CI)	NC (8.411 to NC)	7.39 (4.107 to NC)	NC (NC to NC)	NC (5.815 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1572		0.7939	
Hazard ratio (95% CI) vs Pd	-	1.35 (0.89 to 2.04)		1.11 (0.50 to 2.48)	
P-value	-	0.1588		0.7936	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	59 (58.4)	62 (59.6)	22 (53.7)	21 (63.6)	0.6382
Number (%) of patients censored	42 (41.6)	42 (40.4)	19 (46.3)	12 (36.4)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.91 (1.018 to 1.971)	1.91 (1.281 to 2.267)	1.87 (1.150 to 2.464)	1.22 (0.986 to 2.201)	
Median (95% CI)	3.75 (2.136 to 6.538)	4.47 (2.990 to 7.261)	5.22 (2.037 to NC)	3.45 (2.037 to 12.320)	
75% quantile (95% CI)	NC (11.433 to NC)	NC (13.864 to NC)	NC (NC to NC)	12.32 (4.271 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6279		0.4636	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.64 to 1.31)		1.25 (0.69 to 2.28)	
P-value	-	0.6271		0.4645	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (11.9)	24 (23.1)	2 (4.9)	0 (0.0)	0.8088
Number (%) of patients censored	89 (88.1)	80 (76.9)	39 (95.1)	33 (100.0)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (10.382 to NC)	12.52 (6.735 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0956		0.1784	
Hazard ratio (95% CI) vs Pd	-	1.79 (0.89 to 3.58)			
P-value	-	0.1004		0.9965	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (36.6)	27 (26.0)	13 (31.7)	11 (33.3)	0.6399
Number (%) of patients censored	64 (63.4)	77 (74.0)	28 (68.3)	22 (66.7)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	3.52 (1.906 to 6.735)	10.02 (5.618 to NC)	3.84 (1.610 to NC)	8.97 (1.084 to NC)	
Median (95% CI)	NC (11.170 to NC)	NC (14.029 to NC)	NC (9.528 to NC)	NC (10.283 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0249		0.8170	
Hazard ratio (95% CI) vs Pd	-	0.57 (0.35 to 0.94)		0.91 (0.41 to 2.03)	
P-value	-	0.0268		0.8175	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (37.0)	53 (52.0)	14 (26.9)	18 (35.3)	0.7768
Number (%) of patients censored	63 (63.0)	49 (48.0)	38 (73.1)	33 (64.7)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.30 (1.610 to 3.811)	1.95 (1.314 to 2.333)	2.66 (0.986 to NC)	2.83 (1.380 to 8.641)	
Median (95% CI)	NC (8.411 to NC)	7.39 (4.107 to NC)	NC (NC to NC)	NC (6.078 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1242		0.5799	
Hazard ratio (95% CI) vs Pd	-	1.39 (0.91 to 2.11)		1.22 (0.61 to 2.45)	
P-value	-	0.1258		0.5805	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_impl_dghc_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	59 (59.0)	61 (59.8)	28 (53.8)	32 (62.7)	0.4370
Number (%) of patients censored	41 (41.0)	41 (40.2)	24 (46.2)	19 (37.3)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.91 (1.018 to 1.971)	1.91 (1.281 to 2.628)	1.64 (1.051 to 2.168)	1.22 (1.018 to 2.168)	
Median (95% CI)	3.75 (2.103 to 6.538)	4.47 (2.990 to 7.261)	3.22 (2.037 to NC)	3.45 (2.136 to 12.320)	
75% quantile (95% CI)	NC (11.433 to NC)	NC (13.864 to NC)	NC (NC to NC)	NC (9.396 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5753		0.5647	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.63 to 1.29)		1.16 (0.70 to 1.93)	
P-value	-	0.5745		0.5655	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (11.0)	23 (22.5)	4 (7.7)	3 (5.9)	0.2352
Number (%) of patients censored	89 (89.0)	79 (77.5)	48 (92.3)	48 (94.1)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (NC to NC)	12.52 (8.345 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (13.175 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0757		0.6604	
Hazard ratio (95% CI) vs Pd	-	1.90 (0.92 to 3.89)		0.72 (0.16 to 3.20)	
P-value	-	0.0809		0.6619	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (37.0)	27 (26.5)	18 (34.6)	17 (33.3)	0.4114
Number (%) of patients censored	63 (63.0)	75 (73.5)	34 (65.4)	34 (66.7)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	3.52 (1.906 to 6.735)	10.02 (5.618 to NC)	3.84 (1.610 to 9.528)	8.74 (2.267 to 12.320)	
Median (95% CI)	NC (11.170 to NC)	NC (14.029 to NC)	NC (5.257 to NC)	NC (10.283 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0262		0.5758	
Hazard ratio (95% CI) vs Pd	-	0.57 (0.35 to 0.94)		0.83 (0.43 to 1.61)	
P-value	-	0.0282		0.5764	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detpl_dghc_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (30.0)	10 (71.4)	49 (34.3)	62 (44.3)	0.3269
Number (%) of patients censored	7 (70.0)	4 (28.6)	94 (65.7)	78 (55.7)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	3.81 (0.953 to NC)	1.91 (1.380 to 2.267)	2.30 (1.610 to 4.271)	2.07 (1.873 to 3.088)	
Median (95% CI)	NC (0.953 to NC)	3.93 (1.906 to 6.505)	NC (13.207 to NC)	NC (6.571 to NC)	
75% quantile (95% CI)	NC (3.811 to NC)	6.16 (2.267 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1111		0.2460	
Hazard ratio (95% CI) vs Pd	-	2.75 (0.75 to 10.09)		1.25 (0.86 to 1.81)	
P-value	-	0.1261		0.2470	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (40.0)	9 (64.3)	83 (58.0)	84 (60.0)	0.9283
Number (%) of patients censored	6 (60.0)	5 (35.7)	60 (42.0)	56 (40.0)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.02 (0.920 to NC)	1.38 (0.986 to 3.975)	1.87 (1.150 to 1.971)	1.87 (1.183 to 2.037)	
Median (95% CI)	NC (0.920 to NC)	3.98 (1.084 to NC)	3.52 (2.595 to 6.144)	4.37 (2.990 to 8.312)	
75% quantile (95% CI)	NC (1.741 to NC)	13.86 (3.975 to NC)	NC (NC to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8560		0.8772	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.26 to 3.02)		0.98 (0.72 to 1.32)	
P-value	-	0.8561		0.8772	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	2 (14.3)	15 (10.5)	25 (17.9)	0.7016
Number (%) of patients censored	9 (90.0)	12 (85.7)	128 (89.5)	115 (82.1)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (0.953 to NC)	NC (1.906 to NC)	NC (NC to NC)	13.17 (10.283 to NC)	
Median (95% CI)	NC (0.953 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9350		0.1495	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.10 to 12.25)		1.59 (0.84 to 3.02)	
P-value	-	0.9351		0.1533	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (20.0)	5 (35.7)	53 (37.1)	39 (27.9)	0.7188
Number (%) of patients censored	8 (80.0)	9 (64.3)	90 (62.9)	101 (72.1)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (0.920 to NC)	9.49 (1.084 to NC)	3.52 (2.037 to 5.585)	8.74 (5.552 to 13.667)	
Median (95% CI)	NC (0.920 to NC)	NC (7.885 to NC)	NC (11.170 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.029 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5580		0.0324	
Hazard ratio (95% CI) vs Pd	-	0.56 (0.08 to 3.99)		0.64 (0.42 to 0.97)	
P-value	-	0.5634		0.0341	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (35.4)	41 (47.1)	16 (32.7)	27 (49.1)	0.9621
Number (%) of patients censored	62 (64.6)	46 (52.9)	33 (67.3)	28 (50.9)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.50 (1.117 to 4.994)	1.97 (1.314 to 3.581)	1.97 (1.117 to NC)	2.04 (1.478 to 3.745)	
Median (95% CI)	NC (13.207 to NC)	10.32 (5.060 to NC)	NC (4.665 to NC)	8.64 (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2310		0.3493	
Hazard ratio (95% CI) vs Pd	-	1.32 (0.84 to 2.08)		1.34 (0.72 to 2.49)	
P-value	-	0.2326		0.3510	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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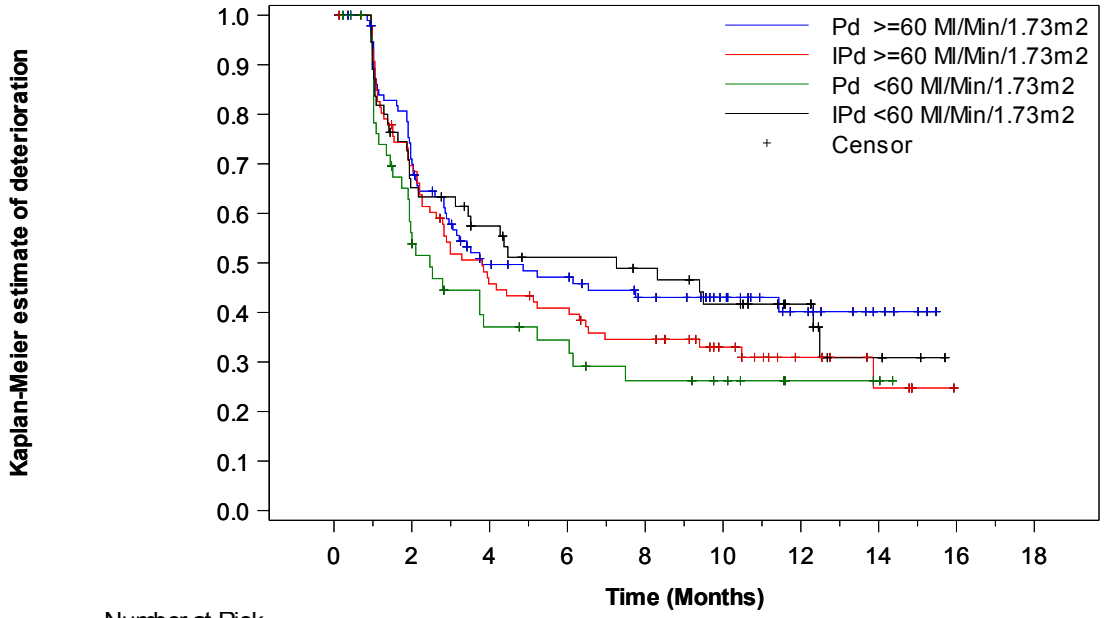
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	52 (54.2)	58 (66.7)	32 (65.3)	32 (58.2)	0.0451
Number (%) of patients censored	44 (45.8)	29 (33.3)	17 (34.7)	23 (41.8)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.94 (1.150 to 2.136)	1.54 (1.117 to 2.201)	1.15 (1.018 to 1.938)	1.64 (1.051 to 2.168)	
Median (95% CI)	3.81 (2.858 to NC)	3.81 (2.464 to 6.045)	2.46 (1.741 to 5.224)	7.26 (2.168 to 12.485)	
75% quantile (95% CI)	NC (NC to NC)	13.86 (6.965 to NC)	NC (3.844 to NC)	NC (12.320 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2396		0.1288	
Hazard ratio (95% CI) vs Pd	-	1.25 (0.86 to 1.82)		0.68 (0.42 to 1.12)	
P-value	-	0.2406		0.1310	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detl_crcl_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-C30 - Time to first deterioration by 10 pt in global health according to baseline creatinine clearance (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd >=60 Ml/Min/1.73m2	96	52	37	28	12	3	0
lPd >=60 Ml/Min/1.73m2	87	43	33	24	9	1	0
Pd <60 Ml/Min/1.73m2	49	18	13	9	3	0	0
lPd <60 Ml/Min/1.73m2	55	33	23	20	11	2	0

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detl_crcl_de_i_f_x.rtf (08APR2021 14:38)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (12.5)	15 (17.2)	3 (6.1)	9 (16.4)	0.4266
Number (%) of patients censored	84 (87.5)	72 (82.8)	46 (93.9)	46 (83.6)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (NC to NC)	13.17 (9.856 to NC)	NC (10.218 to NC)	NC (9.922 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5035		0.1984	
Hazard ratio (95% CI) vs Pd	-	1.29 (0.61 to 2.77)		2.30 (0.62 to 8.50)	
P-value	-	0.5047		0.2114	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imppl_crcl_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.7 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (32.3)	26 (29.9)	22 (44.9)	15 (27.3)	0.1562
Number (%) of patients censored	65 (67.7)	61 (70.1)	27 (55.1)	40 (72.7)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	4.60 (2.136 to 11.170)	8.15 (5.125 to NC)	2.46 (1.018 to 3.975)	10.02 (4.698 to NC)	
Median (95% CI)	NC (11.433 to NC)	NC (14.029 to NC)	7.49 (3.844 to NC)	NC (13.667 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3623		0.0118	
Hazard ratio (95% CI) vs Pd	-	0.79 (0.47 to 1.32)		0.44 (0.23 to 0.85)	
P-value	-	0.3639		0.0143	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detpl_crcl_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	51 (33.8)	71 (46.7)	0.7239
Number (%) of patients censored	1 (50.0)	1 (50.0)	100 (66.2)	81 (53.3)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	1.91 (1.906 to NC)	2.30 (1.840 to 4.271)	2.04 (1.873 to 2.891)	
Median (95% CI)	NC (1.281 to NC)	NC (1.906 to NC)	NC (13.207 to NC)	10.22 (6.078 to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (1.906 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.1050	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		1.35 (0.94 to 1.93)	
P-value	-	0.8092		0.1063	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	2 (100.0)	86 (57.0)	91 (59.9)	0.7388
Number (%) of patients censored	1 (50.0)	0 (0.0)	65 (43.0)	61 (40.1)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.10 (2.103 to NC)	2.83 (2.825 to 12.320)	1.64 (1.084 to 1.938)	1.64 (1.117 to 2.037)	
Median (95% CI)	NC (2.103 to NC)	7.57 (2.825 to 12.320)	3.52 (2.595 to 6.144)	4.37 (2.990 to 7.261)	
75% quantile (95% CI)	NC (2.103 to NC)	12.32 (2.825 to 12.320)	NC (NC to NC)	NC (13.864 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.8434	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		0.97 (0.72 to 1.30)	
P-value	-	0.8092		0.8434	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	15 (9.9)	26 (17.1)	0.4288
Number (%) of patients censored	1 (50.0)	1 (50.0)	136 (90.1)	126 (82.9)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	5.09 (5.092 to NC)	NC (NC to NC)	13.17 (10.480 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.1439	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		1.60 (0.85 to 3.02)	
P-value	-	0.8092		0.1476	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	55 (36.4)	43 (28.3)	0.9820
Number (%) of patients censored	2 (100.0)	1 (50.0)	96 (63.6)	109 (71.7)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (NC to NC)	12.32 (NC to NC)	3.52 (2.037 to 5.585)	8.74 (5.552 to 14.029)	
Median (95% CI)	NC (NC to NC)	12.32 (NC to NC)	NC (11.170 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	12.32 (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0298	
Hazard ratio (95% CI) vs Pd	-			0.64 (0.43 to 0.96)	
P-value	-			0.0311	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detpl_prmab_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (33.9)	50 (42.4)	13 (34.2)	22 (61.1)	0.1410
Number (%) of patients censored	76 (66.1)	68 (57.6)	25 (65.8)	14 (38.9)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.30 (1.610 to 4.994)	2.23 (1.906 to 4.041)	2.83 (1.018 to NC)	1.48 (1.018 to 2.168)	
Median (95% CI)	NC (13.207 to NC)	NC (6.505 to NC)	NC (4.271 to NC)	5.72 (1.938 to 10.316)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.411 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5203		0.0336	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.75 to 1.74)		2.07 (1.04 to 4.12)	
P-value	-	0.5206		0.0376	
Hazard ratio inverted (95% CI) vs IPd		-		0.48 (0.24 to 0.96)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_impl_refr4_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	65 (56.5)	75 (63.6)	22 (57.9)	18 (50.0)	0.6557
Number (%) of patients censored	50 (43.5)	43 (36.4)	16 (42.1)	18 (50.0)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.51 (1.084 to 1.938)	1.51 (1.051 to 1.971)	1.97 (1.018 to 2.858)	1.91 (1.183 to 2.267)	
Median (95% CI)	3.42 (2.037 to 7.491)	4.17 (2.891 to 7.261)	4.86 (2.530 to NC)	4.37 (2.201 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.480 to NC)	NC (6.538 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9662		0.6817	
Hazard ratio (95% CI) vs Pd	-	1.01 (0.72 to 1.40)		0.88 (0.47 to 1.64)	
P-value	-	0.9663		0.6819	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detl_refr4_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (10.4)	18 (15.3)	4 (10.5)	9 (25.0)	0.3347
Number (%) of patients censored	103 (89.6)	100 (84.7)	34 (89.5)	27 (75.0)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (NC to NC)	NC (12.715 to NC)	NC (8.378 to NC)	10.28 (2.366 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.517 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4963		0.1179	
Hazard ratio (95% CI) vs Pd	-	1.29 (0.62 to 2.67)		2.49 (0.76 to 8.12)	
P-value	-	0.4975		0.1306	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imppl_refr4_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (37.4)	37 (31.4)	12 (31.6)	7 (19.4)	0.7371
Number (%) of patients censored	72 (62.6)	81 (68.6)	26 (68.4)	29 (80.6)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	3.22 (2.037 to 5.257)	7.89 (5.125 to 12.320)	5.88 (1.051 to NC)	NC (2.201 to NC)	
Median (95% CI)	NC (7.491 to NC)	NC (14.029 to NC)	NC (9.528 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0661		0.2193	
Hazard ratio (95% CI) vs Pd	-	0.66 (0.43 to 1.03)		0.56 (0.22 to 1.43)	
P-value	-	0.0680		0.2256	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detpl_refr4_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	47 (32.6)	67 (45.6)	5 (55.6)	5 (71.4)	0.4797
Number (%) of patients censored	97 (67.4)	80 (54.4)	4 (44.4)	2 (28.6)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.30 (1.610 to 4.271)	2.07 (1.873 to 3.088)	2.99 (1.084 to 13.207)	1.02 (0.986 to 1.971)	
Median (95% CI)	NC (NC to NC)	10.32 (6.439 to NC)	13.21 (1.084 to NC)	1.97 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.665 to NC)	NC (1.971 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1430		0.1300	
Hazard ratio (95% CI) vs Pd	-	1.32 (0.91 to 1.92)		2.71 (0.71 to 10.35)	
P-value	-	0.1443		0.1446	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_impl_refr1_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	81 (56.3)	90 (61.2)	6 (66.7)	3 (42.9)	0.3233
Number (%) of patients censored	63 (43.8)	57 (38.8)	3 (33.3)	4 (57.1)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.74 (1.117 to 1.938)	1.54 (1.117 to 2.037)	2.17 (0.986 to 6.045)	4.44 (1.938 to NC)	
Median (95% CI)	3.52 (2.530 to 6.538)	3.98 (2.891 to 6.538)	6.05 (0.986 to NC)	NC (1.938 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.485 to NC)	NC (2.825 to NC)	NC (10.480 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9496		0.2719	
Hazard ratio (95% CI) vs Pd	-	1.01 (0.75 to 1.36)		0.47 (0.11 to 1.88)	
P-value	-	0.9496		0.2831	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detl_refr1_de_i_t_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (11.1)	26 (17.7)	0 (0.0)	1 (14.3)	0.9873
Number (%) of patients censored	128 (88.9)	121 (82.3)	9 (100.0)	6 (85.7)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (NC to NC)	13.17 (10.283 to NC)	NC (NC to NC)	NC (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2597		0.2568	
Hazard ratio (95% CI) vs Pd	-	1.43 (0.77 to 2.66)			
P-value	-	0.2623		0.9984	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	52 (36.1)	43 (29.3)	3 (33.3)	1 (14.3)	0.6852
Number (%) of patients censored	92 (63.9)	104 (70.7)	6 (66.7)	6 (85.7)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	3.52 (2.037 to 5.585)	8.74 (5.552 to 13.667)	9.53 (0.986 to NC)	NC (1.938 to NC)	
Median (95% CI)	NC (11.170 to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (1.938 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0407		0.4371	
Hazard ratio (95% CI) vs Pd	-	0.66 (0.44 to 0.99)		0.42 (0.04 to 4.05)	
P-value	-	0.0422		0.4512	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-C30 - Time to first improvement by 10 pt in global health according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (35.2)	44 (47.3)	21 (32.3)	28 (45.9)	0.9206
Number (%) of patients censored	57 (64.8)	49 (52.7)	44 (67.7)	33 (54.1)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.91 (1.117 to 3.811)	2.00 (1.117 to 3.088)	2.83 (1.906 to 13.207)	2.04 (1.906 to 3.745)	
Median (95% CI)	NC (NC to NC)	10.22 (5.060 to NC)	NC (5.881 to NC)	NC (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1956		0.3604	
Hazard ratio (95% CI) vs Pd	-	1.35 (0.85 to 2.14)		1.30 (0.74 to 2.29)	
P-value	-	0.1973		0.3618	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-C30 - Time to first deterioration by 10 pt in global health according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	54 (61.4)	52 (55.9)	33 (50.8)	41 (67.2)	0.2665
Number (%) of patients censored	34 (38.6)	41 (44.1)	32 (49.2)	20 (32.8)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.61 (1.051 to 1.938)	1.64 (1.117 to 2.037)	1.91 (1.018 to 2.825)	1.94 (1.084 to 2.825)	
Median (95% CI)	2.86 (1.971 to 5.224)	4.27 (2.464 to 12.320)	3.84 (2.825 to NC)	5.13 (2.891 to 9.396)	
75% quantile (95% CI)	NC (11.433 to NC)	NC (12.320 to NC)	NC (NC to NC)	13.86 (9.396 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4189		0.4771	
Hazard ratio (95% CI) vs Pd	-	0.85 (0.58 to 1.25)		1.18 (0.75 to 1.87)	
P-value	-	0.4182		0.4776	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (13.6)	17 (18.3)	4 (6.2)	10 (16.4)	0.3775
Number (%) of patients censored	76 (86.4)	76 (81.7)	61 (93.8)	51 (83.6)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (10.382 to NC)	12.71 (9.856 to NC)	NC (NC to NC)	NC (8.345 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5244		0.1438	
Hazard ratio (95% CI) vs Pd	-	1.27 (0.61 to 2.66)		2.32 (0.73 to 7.39)	
P-value	-	0.5254		0.1557	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Global health status
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (39.8)	22 (23.7)	20 (30.8)	22 (36.1)	0.1740
Number (%) of patients censored	53 (60.2)	71 (76.3)	45 (69.2)	39 (63.9)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	3.15 (1.643 to 5.881)	10.02 (4.698 to NC)	3.84 (1.906 to NC)	7.26 (5.125 to 13.667)	
Median (95% CI)	NC (6.834 to NC)	NC (NC to NC)	NC (9.528 to NC)	NC (10.875 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0152		0.6520	
Hazard ratio (95% CI) vs Pd	-	0.52 (0.31 to 0.89)		0.87 (0.47 to 1.60)	
P-value	-	0.0170		0.6523	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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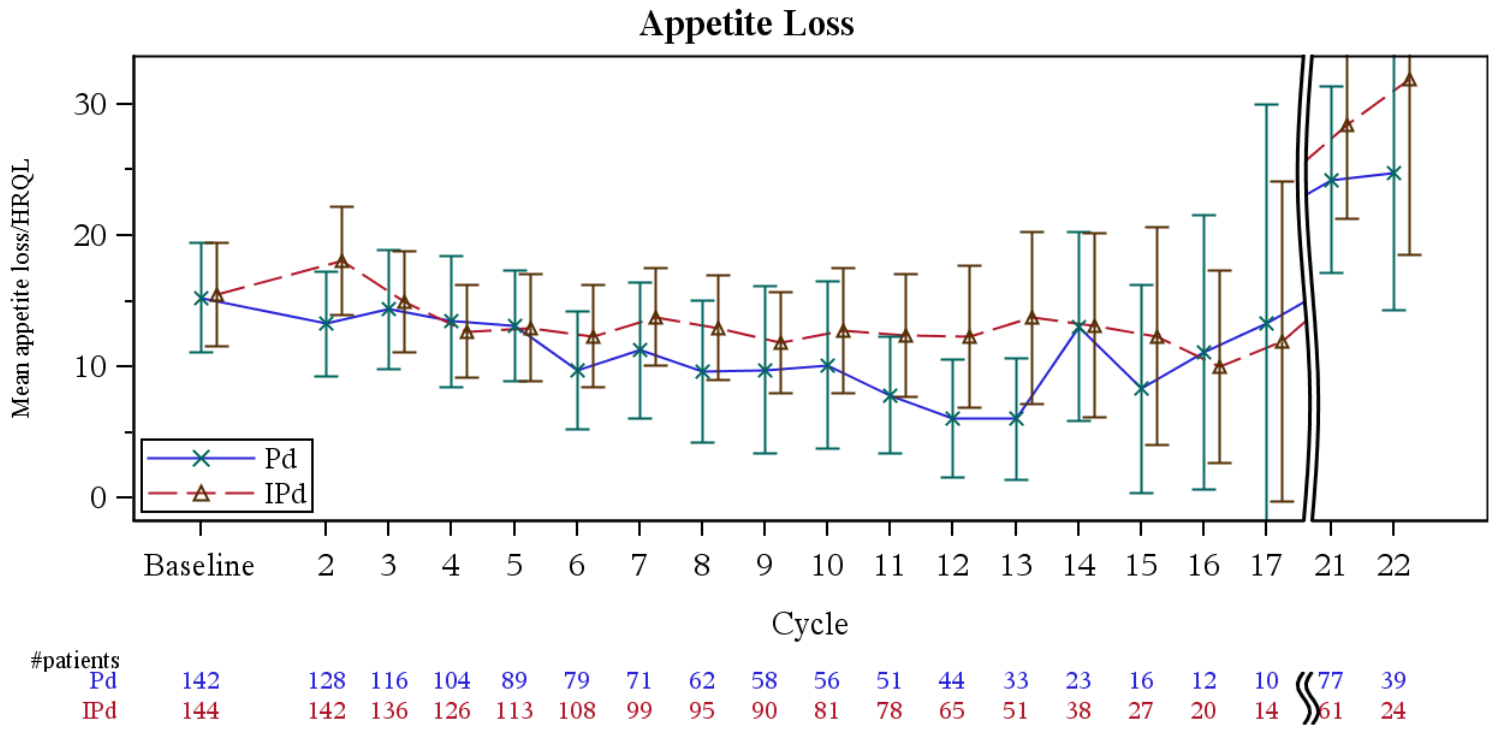
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Appetite loss
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-C30 - Mean and 95% CI for appetite loss score over time (LOCF) - ITT population



A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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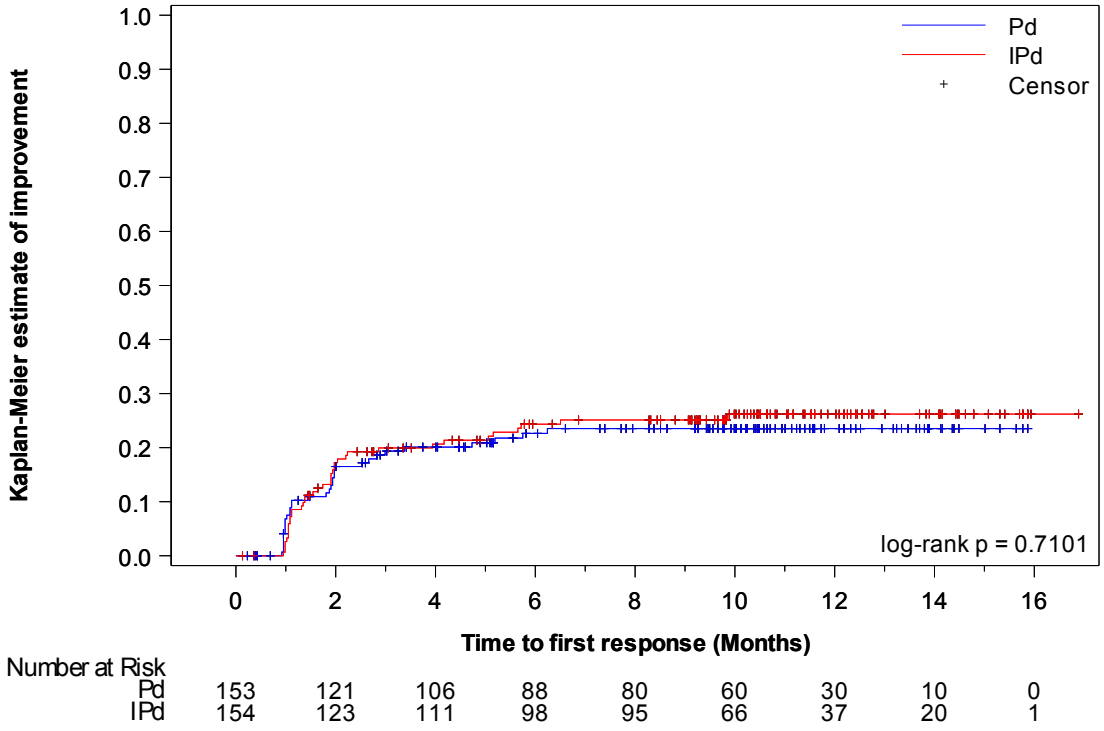
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Appetite loss
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-C30 - Time to first improvement by 15 pt in appetite loss (LOCF) - ITT population

First improvement 15 points Appetite loss (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	33 (21.6)	38 (24.7)
Number (%) of patients censored	120 (78.4)	116 (75.3)
Kaplan-Meier estimates of appetite loss in months		
25% quantile (95% CI)	NC (2.661 to NC)	6.51 (2.037 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.7101
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.09 (0.68 to 1.74)
P-value	-	0.7107
Probability (95% CI)[c]		
2 Months	0.16 (0.104 to 0.222)	0.17 (0.117 to 0.237)
4 Months	0.20 (0.140 to 0.270)	0.21 (0.146 to 0.275)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_imp15l_de_i_t_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Appetite loss
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-C30 - Time to first improvement by 15 pt in appetite loss - Kaplan-Meier curve (LOCF) - ITT population



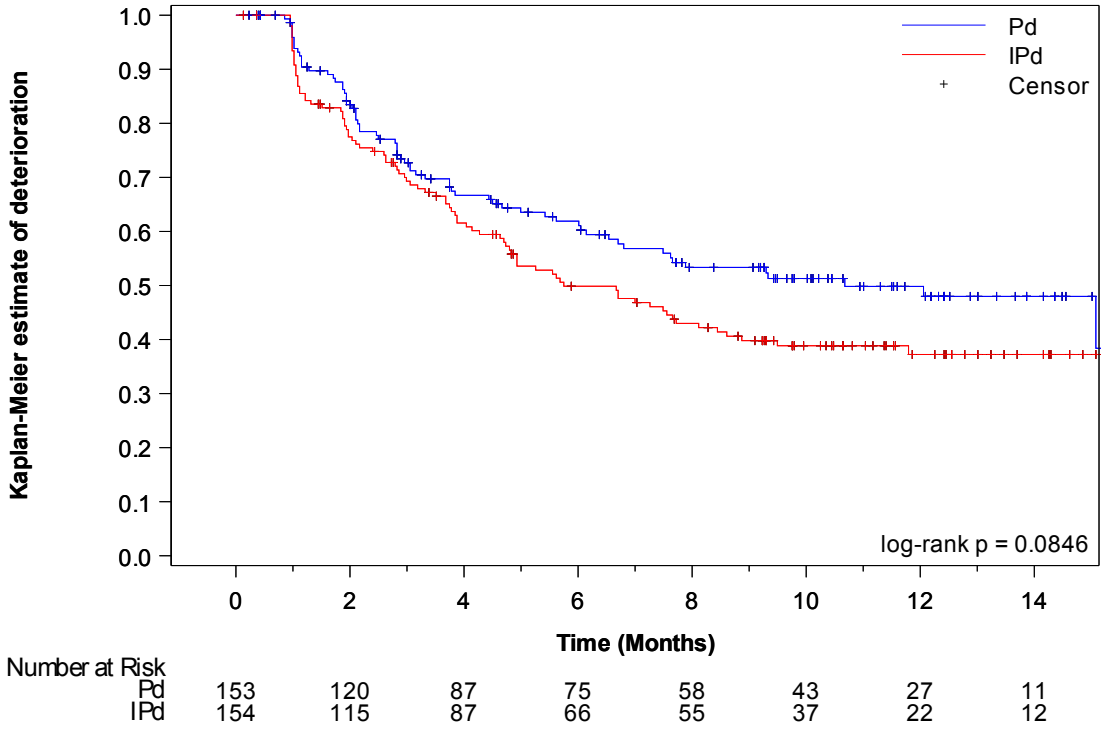
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_imp15l_de_i_f_x.rtf (08APR2021 15:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Appetite loss
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-C30 - Time to first deterioration by 15 pt in appetite loss (LOCF) - ITT population

First deterioration 15 points Appetite loss (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	68 (44.4)	88 (57.1)
Number (%) of patients censored	85 (55.6)	66 (42.9)
Kaplan-Meier estimates of appetite loss in months		
25% quantile (95% CI)	2.83 (2.103 to 3.778)	2.40 (1.873 to 3.187)
Median (95% CI)	10.68 (6.538 to NC)	5.75 (4.698 to 8.444)
75% quantile (95% CI)	NC (15.080 to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0846
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.32 (0.96 to 1.82)
P-value	-	0.0856
Probability (95% CI)[c]		
2 Months	0.84 (0.771 to 0.892)	0.77 (0.700 to 0.834)
4 Months	0.67 (0.582 to 0.738)	0.62 (0.532 to 0.689)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_det15l_de_i_t_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Appetite loss
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-C30 - Time to first deterioration by 15 pt in appetite loss - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_det15l_de_i_f_x.rtf (08APR2021 15:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Appetite loss
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in appetite loss (LOCF) - ITT population

First permanent improvement 15 points Appetite loss (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	17 (11.1)	24 (15.6)
Number (%) of patients censored	136 (88.9)	130 (84.4)
Kaplan-Meier estimates of appetite loss in months		
25% quantile (95% CI)	NC (NC to NC)	15.74 (14.554 to NC)
Median (95% CI)	NC (NC to NC)	NC (15.737 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4425
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.28 (0.68 to 2.38)
P-value	-	0.4436
Probability (95% CI)[c]		
2 Months	0.06 (0.030 to 0.109)	0.08 (0.043 to 0.129)
4 Months	0.09 (0.051 to 0.144)	0.10 (0.059 to 0.155)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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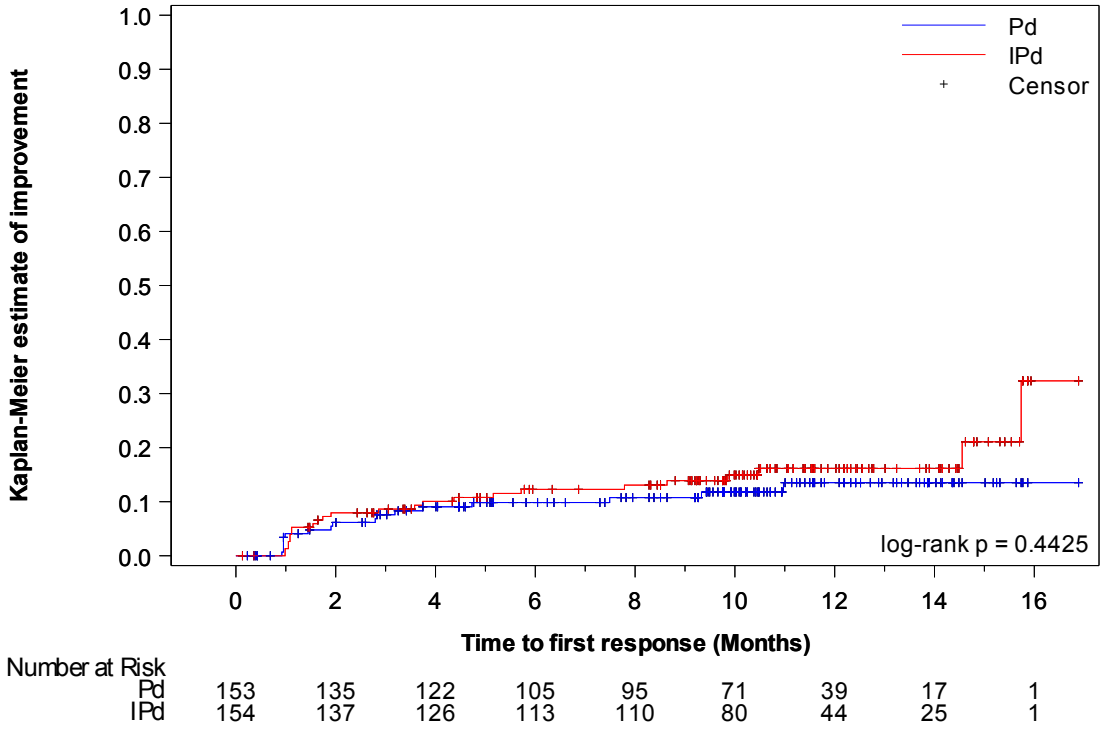
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Appetite loss
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-C30 - Time until permanent improvement by 15 pt in appetite loss - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_imp15pl_de_i_f_x.rtf (08APR2021 15:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Appetite loss
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in appetite loss (LOCF) - ITT population

First permanent deterioration 15 points Appetite loss (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	26 (17.0)	32 (20.8)
Number (%) of patients censored	127 (83.0)	122 (79.2)
Kaplan-Meier estimates of appetite loss in months		
25% quantile (95% CI)	NC (9.331 to NC)	NC (8.115 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6816
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.11 (0.66 to 1.87)
P-value	-	0.6828
Probability (95% CI)[c]		
2 Months	0.95 (0.901 to 0.977)	0.96 (0.913 to 0.982)
4 Months	0.89 (0.821 to 0.929)	0.93 (0.878 to 0.963)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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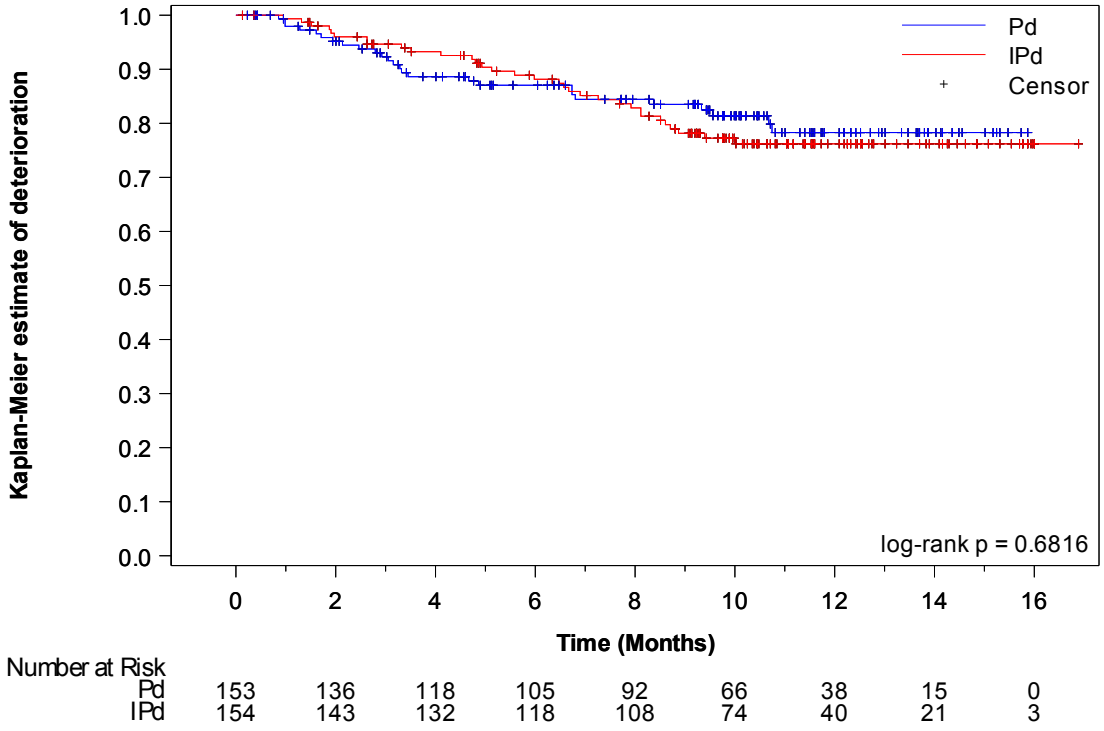
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Appetite loss
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-C30 - Time until permanent deterioration by 15 pt in appetite loss - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_det15pl_de_i_f_x.rtf (08APR2021 15:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (22.9)	19 (35.2)	11 (20.4)	11 (16.2)	6 (20.7)	8 (25.0)	0.3745
Number (%) of patients censored	54 (77.1)	35 (64.8)	43 (79.6)	57 (83.8)	23 (79.3)	24 (75.0)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	NC (1.873 to NC)	2.20 (1.117 to NC)	NC (1.971 to NC)	NC (5.158 to NC)	NC (1.117 to NC)	5.72 (1.117 to NC)	
Median (95% CI)	NC (NC to NC)	NC (6.505 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1836		0.4557		0.8680	
Hazard ratio (95% CI) vs Pd	-	1.56 (0.80 to 3.04)		0.73 (0.32 to 1.68)		1.09 (0.38 to 3.15)	
P-value	-	0.1873		0.4576		0.8680	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (45.7)	21 (38.9)	21 (38.9)	48 (70.6)	15 (51.7)	19 (59.4)	0.0133
Number (%) of patients censored	38 (54.3)	33 (61.1)	33 (61.1)	20 (29.4)	14 (48.3)	13 (40.6)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	3.75 (2.004 to 6.702)	3.75 (1.906 to 4.830)	3.06 (1.906 to 6.045)	1.94 (1.051 to 3.055)	1.28 (0.953 to 2.497)	2.02 (0.986 to 3.877)	
Median (95% CI)	9.33 (6.801 to NC)	NC (4.830 to NC)	15.08 (6.012 to NC)	4.73 (3.515 to 5.749)	4.44 (2.037 to NC)	6.70 (2.957 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	11.79 (6.669 to NC)	NC (5.618 to NC)	NC (7.655 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4223		0.0010		0.8088	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.46 to 1.39)		2.34 (1.39 to 3.96)		0.92 (0.47 to 1.81)	
P-value	-	0.4233		0.0014		0.8088	
Hazard ratio inverted (95% CI) vs IPd		-		0.43 (0.25 to 0.72)		1.09 (0.55 to 2.14)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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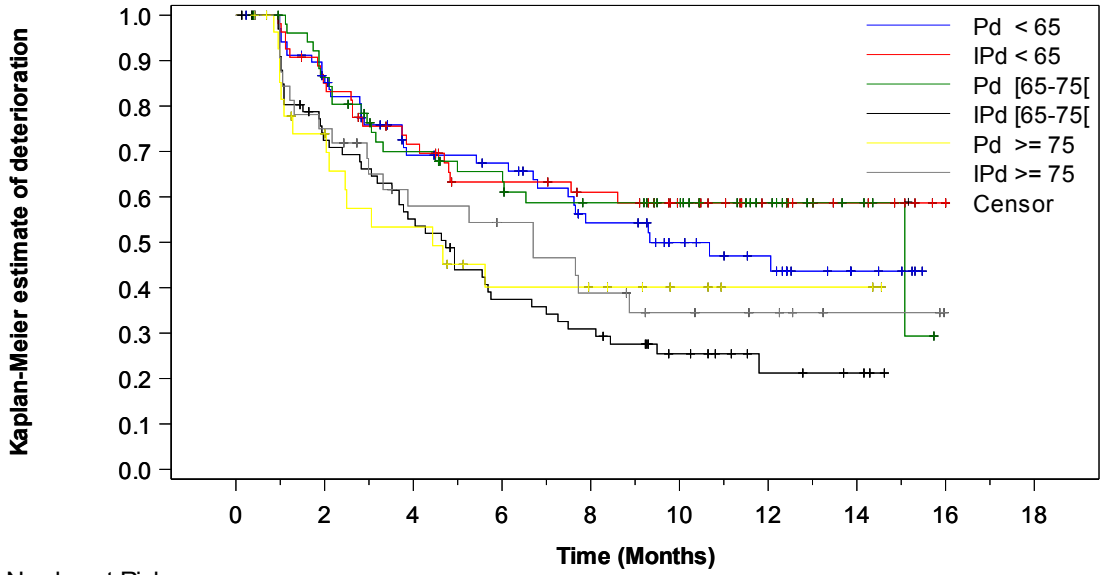
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to age (IRT) (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd < 65	70	48	38	27	14	4	0
IPd < 65	54	39	29	25	12	5	0
Pd [65-75[	54	37	29	24	11	2	0
IPd [65-75[	68	42	23	16	5	0	0
Pd >= 75	29	14	8	6	2	0	0
IPd >= 75	32	19	14	8	5	2	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (14.3)	12 (22.2)	5 (9.3)	7 (10.3)	2 (6.9)	5 (15.6)	0.6923
Number (%) of patients censored	60 (85.7)	42 (77.8)	49 (90.7)	61 (89.7)	27 (93.1)	27 (84.4)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	NC (9.331 to NC)	15.74 (1.741 to 15.737)	NC (NC to NC)	NC (14.554 to NC)	NC (10.973 to NC)	NC (1.117 to NC)	
Median (95% CI)	NC (NC to NC)	15.74 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.973 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	15.74 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2941		0.9276		0.4116	
Hazard ratio (95% CI) vs Pd	-	1.56 (0.67 to 3.62)		0.95 (0.30 to 3.00)		1.97 (0.38 to 10.16)	
P-value	-	0.2981		0.9272		0.4203	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.7 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (15.7)	10 (18.5)	7 (13.0)	13 (19.1)	8 (27.6)	9 (28.1)	0.6912
Number (%) of patients censored	59 (84.3)	44 (81.5)	47 (87.0)	55 (80.9)	21 (72.4)	23 (71.9)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	NC (9.331 to NC)	NC (6.669 to NC)	NC (6.735 to NC)	NC (7.261 to NC)	4.67 (0.986 to NC)	7.92 (4.731 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.378 to NC)	NC (8.871 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7915		0.5185		0.6171	
Hazard ratio (95% CI) vs Pd	-	1.12 (0.48 to 2.64)		1.35 (0.54 to 3.39)		0.78 (0.30 to 2.04)	
P-value	-	0.7916		0.5201		0.6180	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (17.8)	23 (22.5)	15 (28.8)	15 (28.8)	0.5620
Number (%) of patients censored	83 (82.2)	79 (77.5)	37 (71.2)	37 (71.2)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (2.990 to NC)	NC (2.201 to NC)	3.38 (1.084 to NC)	2.86 (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5171		0.8353	
Hazard ratio (95% CI) vs Pd	-	1.23 (0.66 to 2.27)		0.93 (0.45 to 1.90)	
P-value	-	0.5179		0.8352	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	42 (41.6)	58 (56.9)	26 (50.0)	30 (57.7)	0.3417
Number (%) of patients censored	59 (58.4)	44 (43.1)	26 (50.0)	22 (42.3)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	3.06 (2.103 to 5.618)	2.60 (1.840 to 3.680)	2.50 (1.150 to 3.154)	2.17 (1.084 to 3.515)	
Median (95% CI)	NC (6.538 to NC)	5.75 (4.698 to 8.608)	7.89 (3.055 to NC)	6.70 (3.318 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	15.08 (15.080 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0482		0.7999	
Hazard ratio (95% CI) vs Pd	-	1.49 (1.00 to 2.22)		1.07 (0.63 to 1.81)	
P-value	-	0.0496		0.8002	
Hazard ratio inverted (95% CI) vs IPd		-		0.93 (0.55 to 1.58)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_detl_plne_de_i_t_x.rtf (08APR2021 14:50)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	11 (10.9)	14 (13.7)	6 (11.5)	10 (19.2)	0.6019
Number (%) of patients censored	90 (89.1)	88 (86.3)	46 (88.5)	42 (80.8)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	15.74 (14.554 to NC)	NC (10.973 to NC)	NC (2.858 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.737 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7650		0.3846	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.51 to 2.50)		1.56 (0.57 to 4.30)	
P-value	-	0.7652		0.3885	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (15.8)	17 (16.7)	10 (19.2)	15 (28.8)	0.6405
Number (%) of patients censored	85 (84.2)	85 (83.3)	42 (80.8)	37 (71.2)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (9.331 to NC)	NC (8.509 to NC)	10.68 (3.285 to NC)	8.87 (5.125 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9877		0.5643	
Hazard ratio (95% CI) vs Pd	-	0.99 (0.50 to 1.97)		1.26 (0.57 to 2.82)	
P-value	-	0.9877		0.5652	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (22.9)	24 (27.0)	17 (20.5)	14 (21.5)	0.7678
Number (%) of patients censored	54 (77.1)	65 (73.0)	66 (79.5)	51 (78.5)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (1.938 to NC)	5.16 (1.971 to NC)	NC (2.530 to NC)	NC (1.544 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6876		0.9576	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.60 to 2.14)		0.98 (0.48 to 1.99)	
P-value	-	0.6878		0.9577	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (34.3)	47 (52.8)	44 (53.0)	41 (63.1)	0.3479
Number (%) of patients censored	46 (65.7)	42 (47.2)	39 (47.0)	24 (36.9)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	4.99 (2.168 to 7.885)	2.99 (1.971 to 4.140)	2.10 (1.281 to 2.891)	1.68 (1.018 to 2.825)	
Median (95% CI)	15.08 (7.885 to NC)	7.00 (4.797 to NC)	6.70 (3.055 to 12.057)	4.93 (2.957 to 8.115)	
75% quantile (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (12.057 to NC)	NC (8.608 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0420		0.3905	
Hazard ratio (95% CI) vs Pd	-	1.66 (1.01 to 2.71)		1.20 (0.79 to 1.84)	
P-value	-	0.0442		0.3912	
Hazard ratio inverted (95% CI) vs IPd		-		0.83 (0.54 to 1.27)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (10.0)	15 (16.9)	10 (12.0)	9 (13.8)	0.4954
Number (%) of patients censored	63 (90.0)	74 (83.1)	73 (88.0)	56 (86.2)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	15.74 (8.641 to NC)	NC (10.973 to NC)	NC (9.856 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.737 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.737 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3062		0.9236	
Hazard ratio (95% CI) vs Pd	-	1.59 (0.65 to 3.91)		1.05 (0.42 to 2.58)	
P-value	-	0.3106		0.9235	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (12.9)	20 (22.5)	17 (20.5)	12 (18.5)	0.1672
Number (%) of patients censored	61 (87.1)	69 (77.5)	66 (79.5)	53 (81.5)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (9.561 to NC)	10.02 (7.261 to NC)	10.74 (4.862 to NC)	NC (6.899 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1984		0.5053	
Hazard ratio (95% CI) vs Pd	-	1.67 (0.76 to 3.66)		0.78 (0.37 to 1.63)	
P-value	-	0.2034		0.5064	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (23.0)	31 (26.3)	4 (21.1)	4 (16.7)	0.6692
Number (%) of patients censored	97 (77.0)	87 (73.7)	15 (78.9)	20 (83.3)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	6.24 (2.530 to NC)	5.72 (1.971 to NC)	NC (0.953 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8209		0.6996	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.64 to 1.76)		0.76 (0.19 to 3.05)	
P-value	-	0.8210		0.7005	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	56 (44.4)	70 (59.3)	10 (52.6)	15 (62.5)	0.8468
Number (%) of patients censored	70 (55.6)	48 (40.7)	9 (47.4)	9 (37.5)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	2.89 (2.103 to 3.778)	2.63 (1.906 to 3.318)	2.10 (1.150 to 7.655)	1.10 (0.986 to 3.877)	
Median (95% CI)	10.68 (6.144 to NC)	5.75 (4.140 to 8.608)	15.08 (2.103 to 15.080)	4.93 (1.117 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	15.08 (NC to NC)	NC (5.684 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1081		0.2252	
Hazard ratio (95% CI) vs Pd	-	1.33 (0.94 to 1.89)		1.66 (0.73 to 3.80)	
P-value	-	0.1093		0.2301	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (12.7)	21 (17.8)	1 (5.3)	1 (4.2)	0.7278
Number (%) of patients censored	110 (87.3)	97 (82.2)	18 (94.7)	23 (95.8)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	15.74 (9.856 to NC)	NC (0.953 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.737 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4913		0.8534	
Hazard ratio (95% CI) vs Pd	-	1.26 (0.65 to 2.41)		0.77 (0.05 to 12.32)	
P-value	-	0.4922		0.8538	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (19.0)	25 (21.2)	1 (5.3)	6 (25.0)	0.1477
Number (%) of patients censored	102 (81.0)	93 (78.8)	18 (94.7)	18 (75.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (6.735 to NC)	NC (7.918 to NC)	NC (1.708 to NC)	9.40 (1.314 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.396 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9281		0.0936	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.56 to 1.71)		5.08 (0.61 to 42.20)	
P-value	-	0.9281		0.1323	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (50.0)	32 (23.9)	31 (23.8)	0.9818
Number (%) of patients censored	3 (100.0)	2 (50.0)	102 (76.1)	99 (76.2)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	3.24 (1.314 to NC)	6.24 (2.004 to NC)	9.86 (2.037 to NC)	
Median (95% CI)	NC (NC to NC)	NC (1.314 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.314 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3621		0.8094	
Hazard ratio (95% CI) vs Pd	-			0.94 (0.57 to 1.54)	
P-value	-	0.9981		0.8094	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	2 (50.0)	61 (45.5)	79 (60.8)	0.5454
Number (%) of patients censored	2 (66.7)	2 (50.0)	73 (54.5)	51 (39.2)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	5.31 (3.055 to NC)	2.83 (2.103 to 3.778)	2.10 (1.511 to 3.187)	
Median (95% CI)	NC (1.281 to NC)	NC (3.055 to NC)	10.68 (6.538 to NC)	5.62 (4.041 to 7.721)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (3.055 to NC)	NC (15.080 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7741		0.0506	
Hazard ratio (95% CI) vs Pd	-	0.70 (0.06 to 7.92)		1.39 (1.00 to 1.95)	
P-value	-	0.7751		0.0517	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_detl_ethn_de_i_t_x.rtf (08APR2021 14:50)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (50.0)	16 (11.9)	20 (15.4)	0.9868
Number (%) of patients censored	3 (100.0)	2 (50.0)	118 (88.1)	110 (84.6)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	4.76 (4.370 to NC)	NC (NC to NC)	15.74 (14.554 to NC)	
Median (95% CI)	NC (NC to NC)	NC (4.370 to NC)	NC (NC to NC)	NC (15.737 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (4.370 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4452		0.6365	
Hazard ratio (95% CI) vs Pd	-			1.17 (0.61 to 2.27)	
P-value	-	0.9982		0.6369	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	0 (0.0)	22 (16.4)	30 (23.1)	0.9815
Number (%) of patients censored	2 (66.7)	4 (100.0)	112 (83.6)	100 (76.9)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (NC to NC)	NC (9.561 to NC)	10.02 (7.261 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.3596	
Hazard ratio (95% CI) vs Pd	-			1.29 (0.75 to 2.24)	
P-value	-	0.9990		0.3609	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	12 (15.8)	13 (23.6)	6 (30.0)	4 (14.3)	0 (0.0)	1 (14.3)	2 (13.3)	3 (14.3)	13 (35.1)	17 (39.5)	0.6588
Number (%) of patients censored	64 (84.2)	42 (76.4)	14 (70.0)	24 (85.7)	5 (100.0)	6 (85.7)	13 (86.7)	18 (85.7)	24 (64.9)	26 (60.5)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (1.971 to NC)	5.72 (1.643 to NC)	5.75 (0.953 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (5.158 to NC)	NC (1.117 to NC)	NC (1.084 to NC)	2.53 (0.986 to NC)	1.91 (1.117 to 6.505)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.749 to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.158 to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.990 to NC)	NC (5.060 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.3910		0.1649		0.3980		0.9313		0.8431	
Hazard ratio (95% CI) vs Pd	-	1.41 (0.64 to 3.08)		0.42 (0.12 to 1.49)				1.08 (0.18 to 6.48)		1.08 (0.52 to 2.22)	
P-value	-	0.3933		0.1782		0.9984		0.9313		0.8438	
Improvement probability (95% CI)[b]											
2 Months	0.155 (0.083 to 0.249)	0.167 (0.083 to 0.278)	0.105 (0.018 to 0.284)	0.143 (0.045 to 0.295)			0.133 (0.022 to 0.346)	0.048 (0.003 to 0.197)	0.224 (0.105 to 0.370)	0.289 (0.161 to 0.429)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	25 (32.9)	26 (47.3)	12 (60.0)	19 (67.9)	1 (20.0)	5 (71.4)	8 (53.3)	13 (61.9)	22 (59.5)	25 (58.1)	0.2052
Number (%) of patients censored	51 (67.1)	29 (52.7)	8 (40.0)	9 (32.1)	4 (80.0)	2 (28.6)	7 (46.7)	8 (38.1)	15 (40.5)	18 (41.9)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	4.44 (2.464 to 7.655)	2.10 (1.051 to 4.731)	1.02 (0.986 to 4.665)	2.07 (0.986 to 4.041)	NC (6.012 to NC)	2.79 (2.628 to 4.698)	2.10 (1.150 to 5.421)	1.08 (0.986 to 2.037)	2.14 (1.708 to 3.055)	2.96 (1.873 to 4.271)	
Median (95% CI)	NC (10.678 to NC)	6.70 (3.877 to NC)	7.49 (1.018 to NC)	4.93 (3.318 to 11.795)	NC (6.012 to NC)	4.70 (2.628 to NC)	15.08 (2.004 to 15.080)	4.80 (1.084 to NC)	3.78 (2.168 to 9.298)	7.49 (3.778 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.491 to NC)	11.79 (5.618 to NC)	NC (6.012 to NC)	NC (3.055 to NC)	15.08 (NC to NC)	NC (4.797 to NC)	NC (6.801 to NC)	NC (8.608 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.0871		0.7162		0.0796		0.2319		0.2302	
Hazard ratio (95% CI) vs Pd	-	1.61 (0.93 to 2.79)		1.15 (0.55 to 2.38)		5.59 (0.65 to 48.41)		1.74 (0.69 to 4.37)		0.70 (0.39 to 1.25)	
P-value	-	0.0901		0.7164		0.1183		0.2379		0.2325	
Deterioration probability (95% CI)[b]											
2 Months	0.887 (0.786 to 0.942)	0.758 (0.620 to 0.852)	0.684 (0.428 to 0.844)	0.750 (0.546 to 0.872)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.867 (0.564 to 0.965)	0.619 (0.381 to 0.788)	0.801 (0.628 to 0.900)	0.856 (0.707 to 0.933)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	8 (10.5)	7 (12.7)	3 (15.0)	2 (7.1)	0 (0.0)	1 (14.3)	0 (0.0)	1 (4.8)	6 (16.2)	13 (30.2)	0.8001
Number (%) of patients censored	68 (89.5)	48 (87.3)	17 (85.0)	26 (92.9)	5 (100.0)	6 (85.7)	15 (100.0)	20 (95.2)	31 (83.8)	30 (69.8)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (NC to NC)	NC (5.717 to NC)	NC (2.793 to NC)	NC (3.745 to NC)	NC (NC to NC)	NC (5.158 to NC)	NC (NC to NC)	NC (1.084 to NC)	NC (1.938 to NC)	9.86 (1.906 to 15.737)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.973 to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.158 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	15.74 (14.554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.737 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.7881		0.4192		0.3980		0.3980		0.3007	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.42 to 3.17)		0.49 (0.08 to 2.91)						1.66 (0.63 to 4.38)	
P-value	-	0.7883		0.4291		0.9984		0.9984		0.3059	
Improvement probability (95% CI)[b]											
2 Months	0.070 (0.026 to 0.144)	0.093 (0.034 to 0.187)		0.036 (0.003 to 0.154)				0.048 (0.003 to 0.197)	0.112 (0.035 to 0.238)	0.120 (0.044 to 0.238)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_imppl_greg_de_i_t_x.rtf (08APR2021 14:51)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Number (%) of events	10 (13.2)	11 (20.0)	5 (25.0)	7 (25.0)	0 (0.0)	1 (14.3)	0 (0.0)	5 (23.8)	11 (29.7)	8 (18.6)	0.5066
Number (%) of patients censored	66 (86.8)	44 (80.0)	15 (75.0)	21 (75.0)	5 (100.0)	6 (85.7)	15 (100.0)	16 (76.2)	26 (70.3)	35 (81.4)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (8.378 to NC)	NC (5.585 to NC)	9.33 (0.986 to NC)	8.87 (1.971 to NC)	NC (NC to NC)	NC (2.628 to NC)	NC (NC to NC)	9.40 (1.314 to NC)	6.80 (1.938 to NC)	NC (7.261 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.331 to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.628 to NC)	NC (NC to NC)	NC (9.396 to NC)	NC (9.561 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.3849		0.9005		0.3980		0.0439		0.0807	
Hazard ratio (95% CI) vs Pd	-	1.46 (0.62 to 3.44)		0.93 (0.29 to 2.93)						0.45 (0.18 to 1.13)	
P-value	-	0.3877		0.9006		0.9984		0.9964		0.0886	
Deterioration probability (95% CI)[b]											
2 Months	0.972 (0.892 to 0.993)	0.963 (0.859 to 0.991)	0.947 (0.681 to 0.992)	0.929 (0.743 to 0.982)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.952 (0.707 to 0.993)	0.886 (0.725 to 0.956)	0.976 (0.843 to 0.997)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (15.5)	20 (26.0)	18 (32.1)	18 (23.4)	0.0858
Number (%) of patients censored	82 (84.5)	57 (74.0)	38 (67.9)	59 (76.6)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (2.661 to NC)	5.65 (1.971 to NC)	3.38 (1.446 to NC)	NC (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1735		0.2689	
Hazard ratio (95% CI) vs Pd	-	1.59 (0.81 to 3.10)		0.69 (0.36 to 1.33)	
P-value	-	0.1773		0.2715	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (38.1)	37 (48.1)	31 (55.4)	51 (66.2)	0.8288
Number (%) of patients censored	60 (61.9)	40 (51.9)	25 (44.6)	26 (33.8)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	3.15 (2.136 to 6.045)	2.63 (1.216 to 3.680)	2.10 (1.150 to 3.318)	2.04 (1.117 to 3.680)	
Median (95% CI)	NC (6.702 to NC)	7.66 (4.698 to NC)	7.49 (2.825 to NC)	5.55 (3.844 to 7.721)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (8.444 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2530		0.3654	
Hazard ratio (95% CI) vs Pd	-	1.30 (0.83 to 2.06)		1.23 (0.79 to 1.92)	
P-value	-	0.2544		0.3662	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (10.3)	12 (15.6)	7 (12.5)	12 (15.6)	0.8145
Number (%) of patients censored	87 (89.7)	65 (84.4)	49 (87.5)	65 (84.4)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	NC (5.717 to NC)	NC (10.973 to NC)	15.74 (10.480 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.737 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.737 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4109		0.7414	
Hazard ratio (95% CI) vs Pd	-	1.42 (0.61 to 3.29)		1.17 (0.46 to 2.98)	
P-value	-	0.4133		0.7417	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (15.5)	15 (19.5)	11 (19.6)	17 (22.1)	0.8946
Number (%) of patients censored	82 (84.5)	62 (80.5)	45 (80.4)	60 (77.9)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (6.735 to NC)	NC (6.571 to NC)	NC (4.665 to NC)	NC (7.688 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7300		0.8825	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.55 to 2.32)		1.06 (0.50 to 2.26)	
P-value	-	0.7295		0.8831	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (19.7)	34 (24.6)	6 (37.5)	4 (25.0)	0.3986
Number (%) of patients censored	110 (80.3)	104 (75.4)	10 (62.5)	12 (75.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (3.384 to NC)	9.86 (2.037 to NC)	1.97 (0.953 to NC)	5.16 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.873 to NC)	NC (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5052		0.4965	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.72 to 1.97)		0.65 (0.18 to 2.30)	
P-value	-	0.5058		0.4998	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	62 (45.3)	81 (58.7)	6 (37.5)	7 (43.8)	0.9263
Number (%) of patients censored	75 (54.7)	57 (41.3)	10 (62.5)	9 (56.3)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	2.96 (2.103 to 3.844)	2.40 (1.840 to 3.680)	1.28 (0.986 to NC)	2.63 (0.986 to 3.515)	
Median (95% CI)	10.68 (6.538 to NC)	6.67 (4.731 to 8.444)	NC (1.150 to NC)	3.52 (1.314 to NC)	
75% quantile (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.055 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1014		0.6811	
Hazard ratio (95% CI) vs Pd	-	1.32 (0.95 to 1.83)		1.26 (0.42 to 3.75)	
P-value	-	0.1025		0.6818	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (10.2)	20 (14.5)	3 (18.8)	4 (25.0)	0.9926
Number (%) of patients censored	123 (89.8)	118 (85.5)	13 (81.3)	12 (75.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	15.74 (14.554 to NC)	9.33 (0.953 to NC)	5.16 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.737 to NC)	NC (9.331 to NC)	NC (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4406		0.6024	
Hazard ratio (95% CI) vs Pd	-	1.31 (0.66 to 2.59)		1.49 (0.33 to 6.66)	
P-value	-	0.4420		0.6048	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (16.1)	28 (20.3)	4 (25.0)	4 (25.0)	0.8298
Number (%) of patients censored	115 (83.9)	110 (79.7)	12 (75.0)	12 (75.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (9.561 to NC)	NC (8.115 to NC)	2.79 (0.986 to NC)	8.71 (1.314 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.281 to NC)	NC (3.515 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6606		0.9337	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.65 to 1.98)		0.94 (0.23 to 3.78)	
P-value	-	0.6608		0.9337	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (25.5)	11 (17.2)	12 (21.4)	15 (28.3)	8 (18.6)	11 (32.4)	0.2320
Number (%) of patients censored	38 (74.5)	53 (82.8)	44 (78.6)	38 (71.7)	35 (81.4)	23 (67.6)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	4.73 (1.807 to NC)	NC (5.060 to NC)	NC (1.938 to NC)	5.65 (1.906 to NC)	NC (1.117 to NC)	1.91 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.858 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2730		0.5320		0.2303	
Hazard ratio (95% CI) vs Pd	-	0.64 (0.29 to 1.43)		1.27 (0.60 to 2.72)		1.73 (0.70 to 4.31)	
P-value	-	0.2770		0.5330		0.2362	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (45.1)	38 (59.4)	24 (42.9)	29 (54.7)	18 (41.9)	20 (58.8)	0.5558
Number (%) of patients censored	28 (54.9)	26 (40.6)	32 (57.1)	24 (45.3)	25 (58.1)	14 (41.2)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	3.75 (2.103 to 7.491)	2.83 (1.873 to 3.778)	2.83 (1.906 to 5.618)	1.91 (1.084 to 2.990)	2.10 (1.084 to 3.778)	1.97 (0.986 to 6.702)	
Median (95% CI)	15.08 (6.801 to NC)	4.93 (3.844 to NC)	NC (4.994 to NC)	5.75 (2.990 to NC)	6.05 (2.825 to NC)	7.72 (4.928 to 9.495)	
75% quantile (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.795 to NC)	NC (6.702 to NC)	NC (8.115 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0669		0.2196		0.9537	
Hazard ratio (95% CI) vs Pd	-	1.62 (0.96 to 2.72)		1.40 (0.82 to 2.41)		1.02 (0.53 to 1.94)	
P-value	-	0.0695		0.2217		0.9537	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (11.8)	7 (10.9)	7 (12.5)	7 (13.2)	4 (9.3)	9 (26.5)	0.3242
Number (%) of patients censored	45 (88.2)	57 (89.1)	49 (87.5)	46 (86.8)	39 (90.7)	25 (73.5)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	NC (9.331 to NC)	NC (14.554 to NC)	NC (10.973 to NC)	15.74 (15.737 to NC)	NC (3.745 to NC)	8.64 (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.737 to NC)	NC (NC to NC)	NC (10.480 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.737 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8946		0.8555		0.0831	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.31 to 2.76)		0.91 (0.31 to 2.62)		2.72 (0.84 to 8.83)	
P-value	-	0.8942		0.8554		0.0963	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (11.8)	10 (15.6)	9 (16.1)	11 (20.8)	9 (20.9)	11 (32.4)	0.9505
Number (%) of patients censored	45 (88.2)	54 (84.4)	47 (83.9)	42 (79.2)	34 (79.1)	23 (67.6)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	NC (10.743 to NC)	NC (8.115 to NC)	NC (4.862 to NC)	NC (5.979 to NC)	8.38 (3.285 to NC)	7.69 (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.378 to NC)	NC (8.115 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5039		0.7059		0.7765	
Hazard ratio (95% CI) vs Pd	-	1.41 (0.51 to 3.88)		1.18 (0.49 to 2.86)		1.14 (0.47 to 2.75)	
P-value	-	0.5060		0.7062		0.7767	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (22.6)	9 (23.1)	22 (22.4)	25 (25.3)	4 (16.7)	4 (25.0)	0.9381
Number (%) of patients censored	24 (77.4)	30 (76.9)	76 (77.6)	74 (74.7)	20 (83.3)	12 (75.0)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	NC (1.084 to NC)	NC (1.643 to NC)	NC (1.971 to NC)	5.72 (1.938 to NC)	NC (0.953 to NC)	2.86 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.117 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9990		0.7478		0.6655	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.37 to 2.68)		1.10 (0.62 to 1.95)		1.36 (0.34 to 5.43)	
P-value	-	0.9990		0.7483		0.6667	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (38.7)	20 (51.3)	49 (50.0)	58 (58.6)	7 (29.2)	10 (62.5)	0.8694
Number (%) of patients censored	19 (61.3)	19 (48.7)	49 (50.0)	41 (41.4)	17 (70.8)	6 (37.5)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	5.42 (1.873 to 12.057)	3.68 (1.938 to 4.041)	2.50 (1.938 to 3.745)	2.10 (1.117 to 2.858)	2.00 (0.953 to NC)	1.31 (0.953 to 6.702)	
Median (95% CI)	NC (6.801 to NC)	8.44 (3.877 to NC)	9.30 (4.665 to NC)	5.55 (4.271 to 8.115)	NC (2.004 to NC)	7.26 (1.051 to 9.495)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (11.795 to NC)	NC (6.045 to NC)	9.49 (6.702 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2482		0.2341		0.4495	
Hazard ratio (95% CI) vs Pd	-	1.52 (0.74 to 3.12)		1.26 (0.86 to 1.84)		1.46 (0.54 to 3.96)	
P-value	-	0.2517		0.2355		0.4518	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (9.7)	6 (15.4)	11 (11.2)	14 (14.1)	3 (12.5)	4 (25.0)	0.8026
Number (%) of patients censored	28 (90.3)	33 (84.6)	87 (88.8)	85 (85.9)	21 (87.5)	12 (75.0)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	NC (9.331 to NC)	14.55 (7.786 to NC)	NC (NC to NC)	15.74 (15.737 to NC)	NC (0.953 to NC)	10.48 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (15.737 to NC)	NC (NC to NC)	NC (2.858 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.480 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5285		0.7204		0.4133	
Hazard ratio (95% CI) vs Pd	-	1.56 (0.39 to 6.25)		1.16 (0.52 to 2.56)		1.85 (0.41 to 8.28)	
P-value	-	0.5318		0.7206		0.4206	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (9.7)	4 (10.3)	19 (19.4)	23 (23.2)	4 (16.7)	5 (31.3)	0.9858
Number (%) of patients censored	28 (90.3)	35 (89.7)	79 (80.6)	76 (76.8)	20 (83.3)	11 (68.8)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	NC (6.801 to NC)	NC (8.115 to NC)	NC (6.735 to NC)	10.02 (6.669 to NC)	8.38 (1.281 to NC)	7.26 (1.314 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.285 to NC)	NC (5.585 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.378 to NC)	NC (8.608 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8896		0.7067		0.8082	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.25 to 4.97)		1.12 (0.61 to 2.06)		1.18 (0.31 to 4.42)	
P-value	-	0.8897		0.7078		0.8084	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (17.4)	1 (7.1)	19 (20.0)	30 (25.4)	0.3092
Number (%) of patients censored	19 (82.6)	13 (92.9)	76 (80.0)	88 (74.6)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (0.986 to NC)	NC (1.938 to NC)	NC (2.004 to NC)	5.72 (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3695		0.4947	
Hazard ratio (95% CI) vs Pd	-	0.38 (0.04 to 3.41)		1.22 (0.69 to 2.17)	
P-value	-	0.3878		0.4954	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (34.8)	8 (57.1)	45 (47.4)	71 (60.2)	0.6047
Number (%) of patients censored	15 (65.2)	6 (42.9)	50 (52.6)	47 (39.8)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	2.83 (1.281 to 4.501)	3.32 (1.051 to 4.698)	2.89 (1.938 to 4.665)	2.10 (1.216 to 2.957)	
Median (95% CI)	4.50 (2.825 to NC)	4.70 (1.840 to NC)	10.68 (6.012 to NC)	5.75 (3.877 to 8.115)	
75% quantile (95% CI)	NC (4.501 to NC)	5.62 (3.844 to NC)	15.08 (15.080 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3715		0.1133	
Hazard ratio (95% CI) vs Pd	-	1.56 (0.58 to 4.17)		1.35 (0.93 to 1.96)	
P-value	-	0.3753		0.1147	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (8.7)	0 (0.0)	11 (11.6)	20 (16.9)	0.9875
Number (%) of patients censored	21 (91.3)	14 (100.0)	84 (88.4)	98 (83.1)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (1.446 to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.480 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2636		0.4097	
Hazard ratio (95% CI) vs Pd	-			1.36 (0.65 to 2.85)	
P-value	-	0.9978		0.4116	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (13.0)	3 (21.4)	18 (18.9)	26 (22.0)	0.6081
Number (%) of patients censored	20 (87.0)	11 (78.6)	77 (81.1)	92 (78.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	9.56 (1.281 to NC)	6.67 (1.314 to NC)	NC (6.735 to NC)	NC (7.918 to NC)	
Median (95% CI)	NC (9.561 to NC)	NC (3.318 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5747		0.8775	
Hazard ratio (95% CI) vs Pd	-	1.58 (0.32 to 7.92)		1.05 (0.57 to 1.91)	
P-value	-	0.5779		0.8780	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (16.7)	4 (16.7)	16 (20.5)	26 (25.2)	0.7613
Number (%) of patients censored	30 (83.3)	20 (83.3)	62 (79.5)	77 (74.8)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (1.873 to NC)	NC (1.938 to NC)	NC (1.971 to NC)	9.86 (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (5.717 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9015		0.6089	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.26 to 3.27)		1.18 (0.63 to 2.19)	
P-value	-	0.9016		0.6093	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (41.7)	14 (58.3)	37 (47.4)	62 (60.2)	0.6596
Number (%) of patients censored	21 (58.3)	10 (41.7)	41 (52.6)	41 (39.8)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	2.83 (1.281 to 4.501)	1.84 (0.986 to 4.271)	2.96 (1.938 to 4.994)	2.10 (1.511 to 3.055)	
Median (95% CI)	7.49 (3.055 to NC)	4.70 (1.840 to 5.618)	10.68 (5.618 to NC)	6.67 (3.778 to 8.608)	
75% quantile (95% CI)	NC (NC to NC)	NC (4.698 to NC)	15.08 (15.080 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2341		0.1633	
Hazard ratio (95% CI) vs Pd	-	1.55 (0.75 to 3.22)		1.33 (0.89 to 2.01)	
P-value	-	0.2378		0.1648	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (8.3)	2 (8.3)	9 (11.5)	17 (16.5)	0.7743
Number (%) of patients censored	33 (91.7)	22 (91.7)	69 (88.5)	86 (83.5)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (4.731 to NC)	NC (2.858 to NC)	NC (NC to NC)	NC (10.480 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9648		0.4914	
Hazard ratio (95% CI) vs Pd	-	0.96 (0.16 to 5.76)		1.33 (0.59 to 2.99)	
P-value	-	0.9649		0.4929	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (16.7)	5 (20.8)	14 (17.9)	24 (23.3)	0.9381
Number (%) of patients censored	30 (83.3)	19 (79.2)	64 (82.1)	79 (76.7)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (2.924 to NC)	10.02 (1.314 to NC)	NC (6.735 to NC)	NC (7.261 to NC)	
Median (95% CI)	NC (NC to NC)	NC (10.021 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8705		0.6020	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.34 to 3.63)		1.19 (0.62 to 2.30)	
P-value	-	0.8706		0.6024	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (26.7)	21 (25.3)	9 (14.3)	17 (23.9)	0.3413
Number (%) of patients censored	66 (73.3)	62 (74.7)	54 (85.7)	54 (76.1)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	4.73 (1.938 to NC)	5.06 (1.906 to NC)	NC (2.825 to NC)	9.86 (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8409		0.3188	
Hazard ratio (95% CI) vs Pd	-	0.94 (0.52 to 1.69)		1.50 (0.67 to 3.38)	
P-value	-	0.8412		0.3222	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (44.4)	41 (49.4)	28 (44.4)	47 (66.2)	0.3227
Number (%) of patients censored	50 (55.6)	42 (50.6)	35 (55.6)	24 (33.8)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	3.06 (2.103 to 6.012)	3.32 (1.971 to 4.271)	2.17 (1.150 to 4.435)	1.31 (1.018 to 2.628)	
Median (95% CI)	12.06 (6.702 to NC)	8.11 (4.830 to NC)	9.30 (4.435 to NC)	4.73 (2.990 to 6.998)	
75% quantile (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.655 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5965		0.0762	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.73 to 1.74)		1.52 (0.95 to 2.43)	
P-value	-	0.5962		0.0783	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (14.4)	14 (16.9)	4 (6.3)	10 (14.1)	0.5116
Number (%) of patients censored	77 (85.6)	69 (83.1)	59 (93.7)	61 (85.9)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (10.973 to NC)	14.55 (7.786 to NC)	NC (NC to NC)	15.74 (9.856 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (15.737 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6760		0.2932	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.55 to 2.50)		1.85 (0.58 to 5.92)	
P-value	-	0.6760		0.3009	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (16.7)	14 (16.9)	11 (17.5)	18 (25.4)	0.6569
Number (%) of patients censored	75 (83.3)	69 (83.1)	52 (82.5)	53 (74.6)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (6.801 to NC)	NC (8.115 to NC)	NC (4.665 to NC)	8.71 (5.979 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9305		0.5866	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.47 to 2.01)		1.23 (0.58 to 2.61)	
P-value	-	0.9305		0.5872	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	0 (0.0)	31 (20.5)	38 (25.0)	0.9795
Number (%) of patients censored	0 (0.0)	2 (100.0)	120 (79.5)	114 (75.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	1.08 (1.084 to 1.938)	NC (NC to NC)	NC (2.990 to NC)	6.51 (2.037 to NC)	
Median (95% CI)	1.51 (1.084 to 1.938)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	1.94 (1.084 to 1.938)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.5147	
Hazard ratio (95% CI) vs Pd	-			1.17 (0.73 to 1.88)	
P-value	-	0.9991		0.5151	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (100.0)	68 (45.0)	86 (56.6)	0.9798
Number (%) of patients censored	2 (100.0)	0 (0.0)	83 (55.0)	66 (43.4)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	1.12 (1.117 to 2.037)	2.83 (2.103 to 3.745)	2.63 (1.873 to 3.318)	
Median (95% CI)	NC (NC to NC)	1.58 (1.117 to 2.037)	10.68 (6.144 to NC)	6.67 (4.731 to 8.608)	
75% quantile (95% CI)	NC (NC to NC)	2.04 (1.117 to 2.037)	NC (15.080 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.1367	
Hazard ratio (95% CI) vs Pd	-			1.27 (0.93 to 1.75)	
P-value	-	0.9991		0.1377	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	0 (0.0)	15 (9.9)	24 (15.8)	0.9886
Number (%) of patients censored	0 (0.0)	2 (100.0)	136 (90.1)	128 (84.2)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	1.94 (1.938 to 3.187)	NC (NC to NC)	NC (NC to NC)	15.74 (14.554 to NC)	
Median (95% CI)	2.56 (1.938 to 3.187)	NC (NC to NC)	NC (NC to NC)	NC (15.737 to NC)	
75% quantile (95% CI)	3.19 (1.938 to 3.187)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.2310	
Hazard ratio (95% CI) vs Pd	-			1.48 (0.78 to 2.82)	
P-value	-	0.9991		0.2340	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	26 (17.2)	31 (20.4)	0.9833
Number (%) of patients censored	2 (100.0)	1 (50.0)	125 (82.8)	121 (79.6)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	4.11 (4.107 to NC)	NC (9.331 to NC)	NC (8.115 to NC)	
Median (95% CI)	NC (NC to NC)	NC (4.107 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (4.107 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.8036	
Hazard ratio (95% CI) vs Pd	-			1.07 (0.63 to 1.80)	
P-value	-	0.9990		0.8041	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (22.8)	27 (26.0)	7 (17.1)	8 (24.2)	0.5976
Number (%) of patients censored	78 (77.2)	77 (74.0)	34 (82.9)	25 (75.8)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	6.24 (1.971 to NC)	6.51 (1.938 to NC)	NC (1.446 to NC)	2.20 (1.117 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8087		0.4735	
Hazard ratio (95% CI) vs Pd	-	1.07 (0.61 to 1.87)		1.45 (0.52 to 3.99)	
P-value	-	0.8091		0.4760	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (44.6)	61 (58.7)	19 (46.3)	17 (51.5)	0.5196
Number (%) of patients censored	56 (55.4)	43 (41.3)	22 (53.7)	16 (48.5)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	2.83 (2.103 to 3.778)	2.60 (1.840 to 3.515)	2.04 (1.117 to 6.012)	2.79 (1.084 to 4.928)	
Median (95% CI)	12.06 (6.045 to NC)	5.68 (4.140 to 8.444)	9.30 (4.994 to NC)	7.72 (2.957 to NC)	
75% quantile (95% CI)	NC (15.080 to NC)	NC (11.795 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1032		0.9361	
Hazard ratio (95% CI) vs Pd	-	1.38 (0.94 to 2.02)		1.03 (0.53 to 1.98)	
P-value	-	0.1047		0.9361	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (10.9)	17 (16.3)	4 (9.8)	5 (15.2)	0.6612
Number (%) of patients censored	90 (89.1)	87 (83.7)	37 (90.2)	28 (84.8)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (10.973 to NC)	15.74 (10.480 to NC)	NC (2.825 to NC)	NC (1.544 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.737 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4114		0.5948	
Hazard ratio (95% CI) vs Pd	-	1.37 (0.64 to 2.94)		1.43 (0.38 to 5.32)	
P-value	-	0.4133		0.5967	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (17.8)	22 (21.2)	6 (14.6)	5 (15.2)	0.8126
Number (%) of patients censored	83 (82.2)	82 (78.8)	35 (85.4)	28 (84.8)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (8.378 to NC)	NC (7.261 to NC)	NC (6.735 to NC)	NC (5.585 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8507		0.8988	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.57 to 1.98)		0.93 (0.28 to 3.04)	
P-value	-	0.8510		0.8990	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (23.0)	27 (26.5)	10 (19.2)	11 (21.6)	0.9776
Number (%) of patients censored	77 (77.0)	75 (73.5)	42 (80.8)	40 (78.4)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	6.24 (1.971 to NC)	5.72 (1.938 to NC)	NC (1.446 to NC)	NC (1.643 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7809		0.8756	
Hazard ratio (95% CI) vs Pd	-	1.08 (0.62 to 1.89)		1.07 (0.45 to 2.52)	
P-value	-	0.7814		0.8757	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (44.0)	59 (57.8)	23 (44.2)	28 (54.9)	0.7913
Number (%) of patients censored	56 (56.0)	43 (42.2)	29 (55.8)	23 (45.1)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	2.89 (2.103 to 3.844)	2.63 (1.873 to 3.745)	2.46 (1.150 to 6.012)	2.04 (1.084 to 3.877)	
Median (95% CI)	12.06 (6.045 to NC)	5.75 (4.271 to 8.444)	9.33 (5.421 to NC)	6.67 (3.680 to NC)	
75% quantile (95% CI)	NC (15.080 to NC)	NC (11.795 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1167		0.3983	
Hazard ratio (95% CI) vs Pd	-	1.37 (0.92 to 2.02)		1.27 (0.73 to 2.20)	
P-value	-	0.1182		0.3994	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (11.0)	17 (16.7)	6 (11.5)	7 (13.7)	0.6918
Number (%) of patients censored	89 (89.0)	85 (83.3)	46 (88.5)	44 (86.3)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (10.973 to NC)	15.74 (10.480 to NC)	NC (2.825 to NC)	NC (3.745 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.737 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3991		0.8744	
Hazard ratio (95% CI) vs Pd	-	1.39 (0.65 to 2.96)		1.09 (0.37 to 3.25)	
P-value	-	0.4012		0.8747	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_imppl_dghc_de_i_t_x.rtf (08APR2021 14:51)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (17.0)	20 (19.6)	8 (15.4)	11 (21.6)	0.6784
Number (%) of patients censored	83 (83.0)	82 (80.4)	44 (84.6)	40 (78.4)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (8.378 to NC)	NC (6.669 to NC)	NC (6.735 to NC)	NC (6.899 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9226		0.5574	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.54 to 1.97)		1.31 (0.53 to 3.26)	
P-value	-	0.9227		0.5586	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (30.0)	5 (35.7)	30 (21.0)	33 (23.6)	0.7752
Number (%) of patients censored	7 (70.0)	9 (64.3)	113 (79.0)	107 (76.4)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	2.66 (0.920 to NC)	1.91 (1.380 to NC)	NC (2.825 to NC)	9.86 (2.201 to NC)	
Median (95% CI)	NC (0.920 to NC)	NC (1.906 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8955		0.7404	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.22 to 3.82)		1.09 (0.66 to 1.78)	
P-value	-	0.8955		0.7407	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (30.0)	9 (64.3)	65 (45.5)	79 (56.4)	0.8049
Number (%) of patients censored	7 (70.0)	5 (35.7)	78 (54.5)	61 (43.6)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	3.06 (1.018 to NC)	1.31 (1.051 to 3.844)	2.83 (2.103 to 3.844)	2.63 (1.906 to 3.318)	
Median (95% CI)	NC (1.018 to NC)	3.99 (1.117 to NC)	10.68 (6.538 to NC)	6.67 (4.731 to 8.444)	
75% quantile (95% CI)	NC (3.055 to NC)	NC (3.844 to NC)	NC (15.080 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4756		0.1134	
Hazard ratio (95% CI) vs Pd	-	1.61 (0.43 to 6.03)		1.30 (0.94 to 1.81)	
P-value	-	0.4798		0.1149	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (20.0)	4 (28.6)	15 (10.5)	20 (14.3)	0.5772
Number (%) of patients censored	8 (80.0)	10 (71.4)	128 (89.5)	120 (85.7)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (0.920 to NC)	15.74 (1.544 to NC)	NC (NC to NC)	NC (14.554 to NC)	
Median (95% CI)	NC (0.920 to NC)	15.74 (3.581 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.737 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8150		0.4318	
Hazard ratio (95% CI) vs Pd	-	0.81 (0.13 to 4.85)		1.31 (0.67 to 2.55)	
P-value	-	0.8153		0.4331	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	3 (21.4)	25 (17.5)	29 (20.7)	0.9349
Number (%) of patients censored	9 (90.0)	11 (78.6)	118 (82.5)	111 (79.3)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (3.055 to NC)	NC (1.314 to NC)	NC (9.331 to NC)	NC (7.918 to NC)	
Median (95% CI)	NC (3.055 to NC)	NC (8.608 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8817		0.7258	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.12 to 12.17)		1.10 (0.64 to 1.88)	
P-value	-	0.8818		0.7264	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (22.9)	18 (20.7)	11 (22.4)	17 (30.9)	0.3480
Number (%) of patients censored	74 (77.1)	69 (79.3)	38 (77.6)	38 (69.1)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (2.004 to NC)	NC (4.172 to NC)	6.24 (1.873 to NC)	2.04 (1.347 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5522		0.4741	
Hazard ratio (95% CI) vs Pd	-	0.83 (0.44 to 1.54)		1.32 (0.62 to 2.81)	
P-value	-	0.5528		0.4755	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (42.7)	51 (58.6)	25 (51.0)	34 (61.8)	0.2220
Number (%) of patients censored	55 (57.3)	36 (41.4)	24 (49.0)	21 (38.2)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	2.89 (2.103 to 6.144)	2.10 (1.216 to 3.055)	2.46 (1.741 to 3.745)	2.60 (1.084 to 4.271)	
Median (95% CI)	15.08 (7.491 to NC)	4.93 (3.680 to 11.795)	5.62 (3.055 to NC)	7.49 (4.271 to 8.871)	
75% quantile (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (10.678 to NC)	NC (8.608 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0375		0.8876	
Hazard ratio (95% CI) vs Pd	-	1.54 (1.02 to 2.33)		1.04 (0.62 to 1.74)	
P-value	-	0.0390		0.8878	
Hazard ratio inverted (95% CI) vs IPd		-		0.96 (0.57 to 1.62)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (12.5)	11 (12.6)	5 (10.2)	11 (20.0)	0.3276
Number (%) of patients censored	84 (87.5)	76 (87.4)	44 (89.8)	44 (80.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (10.973 to NC)	NC (14.554 to NC)	NC (7.491 to NC)	15.74 (3.581 to 15.737)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	15.74 (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	15.74 (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8398		0.3563	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.40 to 2.09)		1.65 (0.56 to 4.83)	
P-value	-	0.8400		0.3613	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (12.5)	16 (18.4)	13 (26.5)	15 (27.3)	0.3974
Number (%) of patients censored	84 (87.5)	71 (81.6)	36 (73.5)	40 (72.7)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	NC (8.115 to NC)	6.74 (2.924 to NC)	8.61 (4.928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.743 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4245		0.6990	
Hazard ratio (95% CI) vs Pd	-	1.36 (0.64 to 2.86)		0.86 (0.41 to 1.82)	
P-value	-	0.4262		0.6992	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (100.0)	33 (21.9)	36 (23.7)	0.9861
Number (%) of patients censored	2 (100.0)	0 (0.0)	118 (78.1)	116 (76.3)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	1.91 (1.906 to 1.971)	NC (2.661 to NC)	9.86 (2.234 to NC)	
Median (95% CI)	NC (NC to NC)	1.94 (1.906 to 1.971)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	1.97 (1.906 to 1.971)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.9125	
Hazard ratio (95% CI) vs Pd	-			1.03 (0.64 to 1.65)	
P-value	-	0.9991		0.9125	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	1 (50.0)	66 (43.7)	87 (57.2)	0.0668
Number (%) of patients censored	0 (0.0)	1 (50.0)	85 (56.3)	65 (42.8)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	1.28 (1.281 to 2.103)	4.14 (4.140 to NC)	2.89 (2.103 to 3.844)	2.40 (1.840 to 3.187)	
Median (95% CI)	1.69 (1.281 to 2.103)	NC (4.140 to NC)	12.06 (6.702 to NC)	5.75 (4.698 to 8.444)	
75% quantile (95% CI)	2.10 (1.281 to 2.103)	NC (4.140 to NC)	NC (15.080 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.0564	
Hazard ratio (95% CI) vs Pd	-			1.36 (0.99 to 1.88)	
P-value	-	0.9985		0.0574	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	17 (11.3)	24 (15.8)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	134 (88.7)	128 (84.2)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	15.74 (14.554 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.737 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.3952	
Hazard ratio (95% CI) vs Pd	-			1.31 (0.70 to 2.44)	
P-value	-			0.3966	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	25 (16.6)	32 (21.1)	0.9851
Number (%) of patients censored	1 (50.0)	2 (100.0)	126 (83.4)	120 (78.9)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (NC to NC)	NC (9.561 to NC)	NC (8.115 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.5656	
Hazard ratio (95% CI) vs Pd	-			1.17 (0.69 to 1.97)	
P-value	-	0.9990		0.5660	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (21.7)	25 (21.2)	8 (21.1)	13 (36.1)	0.1653
Number (%) of patients censored	90 (78.3)	93 (78.8)	30 (78.9)	23 (63.9)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (1.938 to NC)	NC (1.971 to NC)	NC (2.530 to NC)	3.94 (1.314 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.158 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7012		0.1527	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.52 to 1.56)		1.88 (0.78 to 4.54)	
P-value	-	0.7007		0.1596	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (41.7)	69 (58.5)	20 (52.6)	19 (52.8)	0.5207
Number (%) of patients censored	67 (58.3)	49 (41.5)	18 (47.4)	17 (47.2)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	2.96 (1.938 to 4.435)	2.40 (1.314 to 3.318)	2.46 (1.281 to 6.144)	2.10 (1.084 to 4.271)	
Median (95% CI)	12.06 (6.045 to NC)	5.75 (4.731 to 8.608)	7.49 (3.055 to NC)	6.70 (3.055 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (8.444 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0640		0.7563	
Hazard ratio (95% CI) vs Pd	-	1.41 (0.98 to 2.04)		1.10 (0.59 to 2.07)	
P-value	-	0.0653		0.7558	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (13.0)	17 (14.4)	2 (5.3)	7 (19.4)	0.0921
Number (%) of patients censored	100 (87.0)	101 (85.6)	36 (94.7)	29 (80.6)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (10.973 to NC)	15.74 (14.554 to NC)	NC (NC to NC)	NC (3.581 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.737 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8900		0.0603	
Hazard ratio (95% CI) vs Pd	-	0.95 (0.47 to 1.91)		4.02 (0.84 to 19.37)	
P-value	-	0.8898		0.0827	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (15.7)	27 (22.9)	8 (21.1)	5 (13.9)	0.2570
Number (%) of patients censored	97 (84.3)	91 (77.1)	30 (78.9)	31 (86.1)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (9.561 to NC)	8.87 (6.899 to NC)	NC (2.464 to NC)	NC (8.115 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3838		0.4098	
Hazard ratio (95% CI) vs Pd	-	1.30 (0.72 to 2.37)		0.63 (0.21 to 1.92)	
P-value	-	0.3852		0.4140	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (21.5)	35 (23.8)	2 (22.2)	3 (42.9)	0.3919
Number (%) of patients censored	113 (78.5)	112 (76.2)	7 (77.8)	4 (57.1)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (2.530 to NC)	9.86 (2.234 to NC)	NC (0.986 to NC)	1.12 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (1.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.938 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8712		0.3859	
Hazard ratio (95% CI) vs Pd	-	1.04 (0.64 to 1.69)		2.17 (0.36 to 13.11)	
P-value	-	0.8713		0.3974	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	64 (44.4)	87 (59.2)	4 (44.4)	1 (14.3)	0.1620
Number (%) of patients censored	80 (55.6)	60 (40.8)	5 (55.6)	6 (85.7)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	2.83 (2.037 to 3.745)	2.10 (1.511 to 2.990)	6.05 (0.986 to NC)	NC (4.928 to NC)	
Median (95% CI)	12.06 (6.144 to NC)	5.62 (4.140 to 7.655)	NC (0.986 to NC)	NC (4.928 to NC)	
75% quantile (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (10.678 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0514		0.2629	
Hazard ratio (95% CI) vs Pd	-	1.38 (1.00 to 1.90)		0.31 (0.03 to 2.75)	
P-value	-	0.0524		0.2902	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (11.8)	22 (15.0)	0 (0.0)	2 (28.6)	0.9869
Number (%) of patients censored	127 (88.2)	125 (85.0)	9 (100.0)	5 (71.4)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	15.74 (14.554 to NC)	NC (NC to NC)	1.12 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.737 to NC)	NC (NC to NC)	NC (1.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6912		0.0954	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.60 to 2.15)			
P-value	-	0.6914		0.9977	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (16.0)	31 (21.1)	3 (33.3)	1 (14.3)	0.4011
Number (%) of patients censored	121 (84.0)	116 (78.9)	6 (66.7)	6 (85.7)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (9.331 to NC)	NC (8.115 to NC)	10.68 (3.450 to NC)	NC (4.928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.450 to NC)	NC (4.928 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.678 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5324		0.4734	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.69 to 2.04)		0.45 (0.05 to 4.30)	
P-value	-	0.5329		0.4851	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (22.7)	27 (29.0)	13 (20.0)	11 (18.0)	0.3592
Number (%) of patients censored	68 (77.3)	66 (71.0)	52 (80.0)	50 (82.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (1.938 to NC)	5.16 (1.971 to NC)	NC (2.661 to NC)	NC (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4004		0.6059	
Hazard ratio (95% CI) vs Pd	-	1.28 (0.72 to 2.28)		0.81 (0.36 to 1.81)	
P-value	-	0.4016		0.6071	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (52.3)	53 (57.0)	22 (33.8)	35 (57.4)	0.3191
Number (%) of patients censored	42 (47.7)	40 (43.0)	43 (66.2)	26 (42.6)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	2.79 (2.004 to 3.745)	2.10 (1.314 to 3.187)	3.15 (1.741 to 7.622)	2.63 (1.117 to 3.877)	
Median (95% CI)	7.49 (4.435 to NC)	5.68 (3.877 to 8.444)	NC (7.622 to NC)	7.26 (4.140 to NC)	
75% quantile (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4411		0.0676	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.79 to 1.73)		1.64 (0.96 to 2.79)	
P-value	-	0.4422		0.0704	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_detl_llen_de_i_t_x.rtf (08APR2021 14:50)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (12.5)	16 (17.2)	6 (9.2)	8 (13.1)	0.9024
Number (%) of patients censored	77 (87.5)	77 (82.8)	59 (90.8)	53 (86.9)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	14.55 (9.856 to NC)	NC (10.973 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	15.74 (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.737 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4609		0.6215	
Hazard ratio (95% CI) vs Pd	-	1.33 (0.62 to 2.88)		1.30 (0.45 to 3.76)	
P-value	-	0.4624		0.6225	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_imppl_llen_de_i_t_x.rtf (08APR2021 14:51)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Appetite loss
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (20.5)	16 (17.2)	8 (12.3)	16 (26.2)	0.1361
Number (%) of patients censored	70 (79.5)	77 (82.8)	57 (87.7)	45 (73.8)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	10.74 (6.735 to NC)	NC (8.509 to NC)	NC (6.735 to NC)	8.71 (5.125 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5126		0.1733	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.41 to 1.57)		1.79 (0.77 to 4.18)	
P-value	-	0.5127		0.1794	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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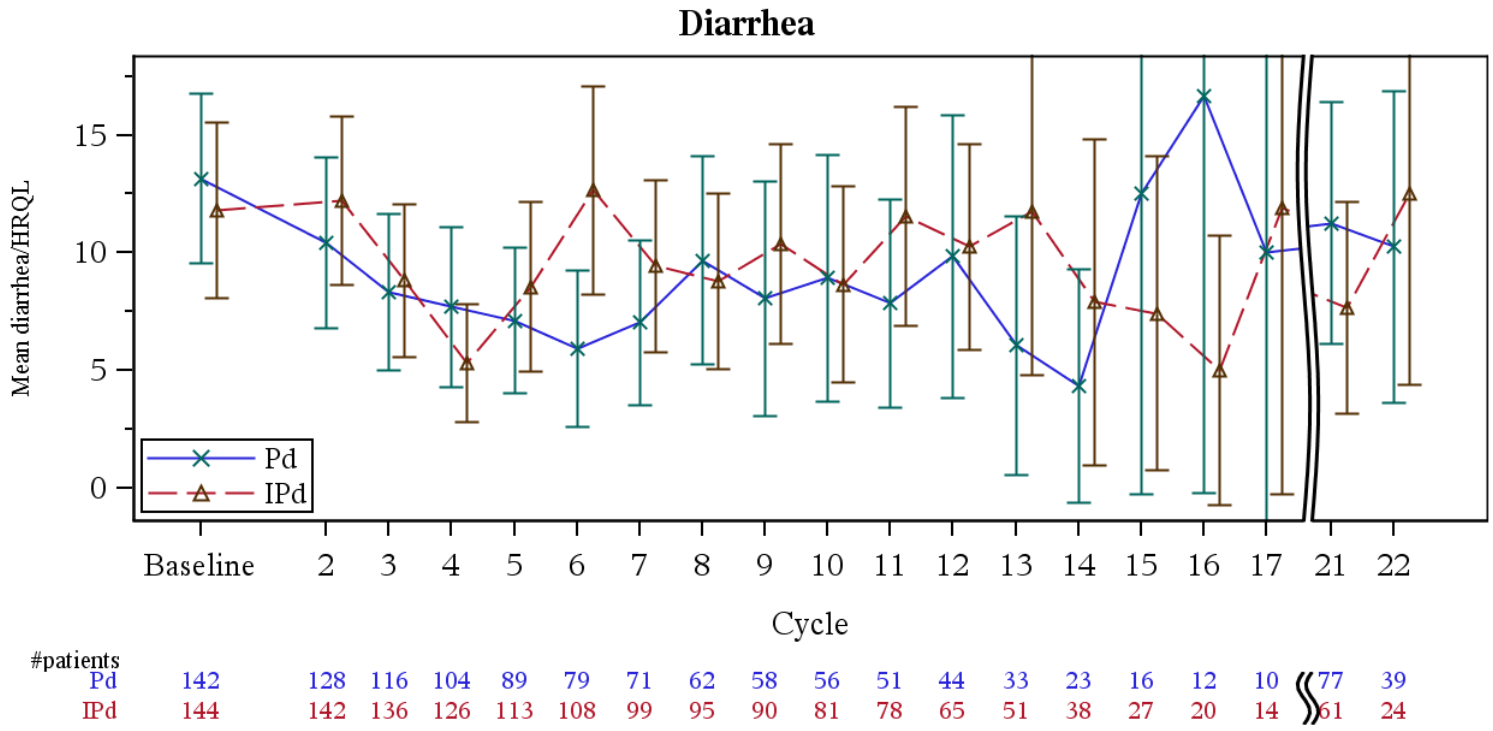
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Diarrhea
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-C30 - Mean and 95% CI for diarrhea score over time (LOCF) - ITT population



A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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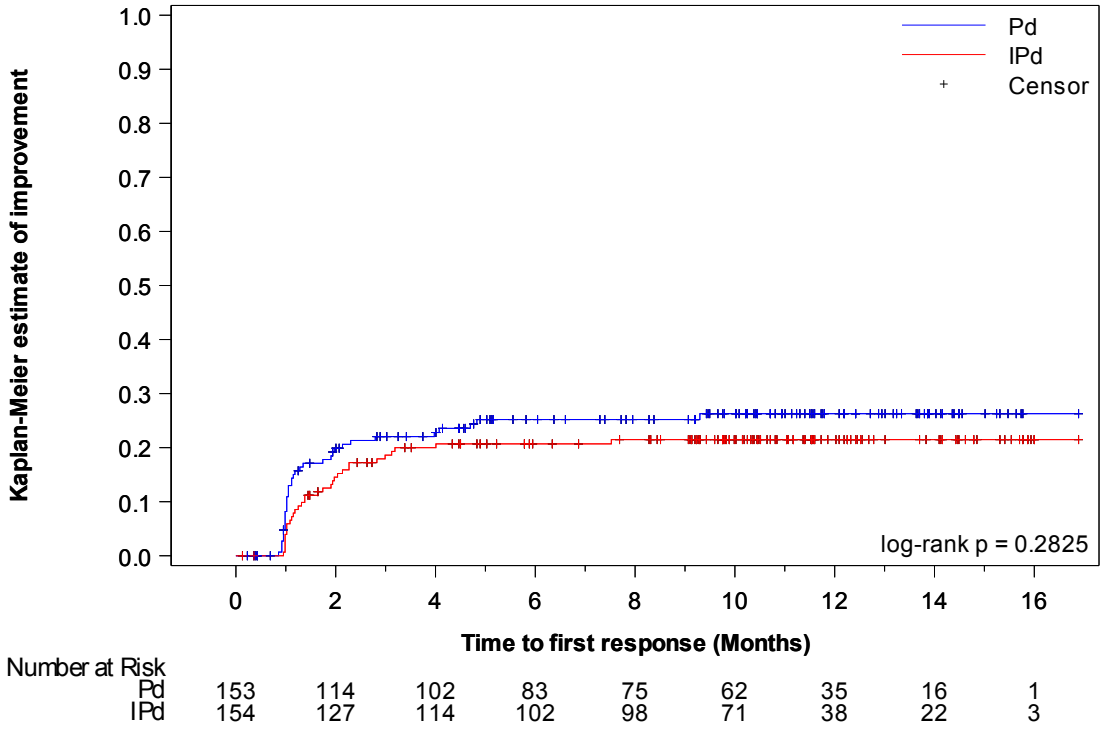
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Diarrhea
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-C30 - Time to first improvement by 15 pt in diarrhea (LOCF) - ITT population

First improvement 15 points Diarrhea (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	37 (24.2)	32 (20.8)
Number (%) of patients censored	116 (75.8)	122 (79.2)
Kaplan-Meier estimates of diarrhea in months		
25% quantile (95% CI)	4.83 (1.741 to NC)	NC (2.825 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2825
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.77 (0.48 to 1.24)
P-value	-	0.2838
Probability (95% CI)[c]		
2 Months	0.20 (0.139 to 0.267)	0.15 (0.095 to 0.206)
4 Months	0.23 (0.163 to 0.299)	0.20 (0.140 to 0.267)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_imp15l_de_i_t_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Diarrhea
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-C30 - Time to first improvement by 15 pt in diarrhea - Kaplan-Meier curve (LOCF) - ITT population



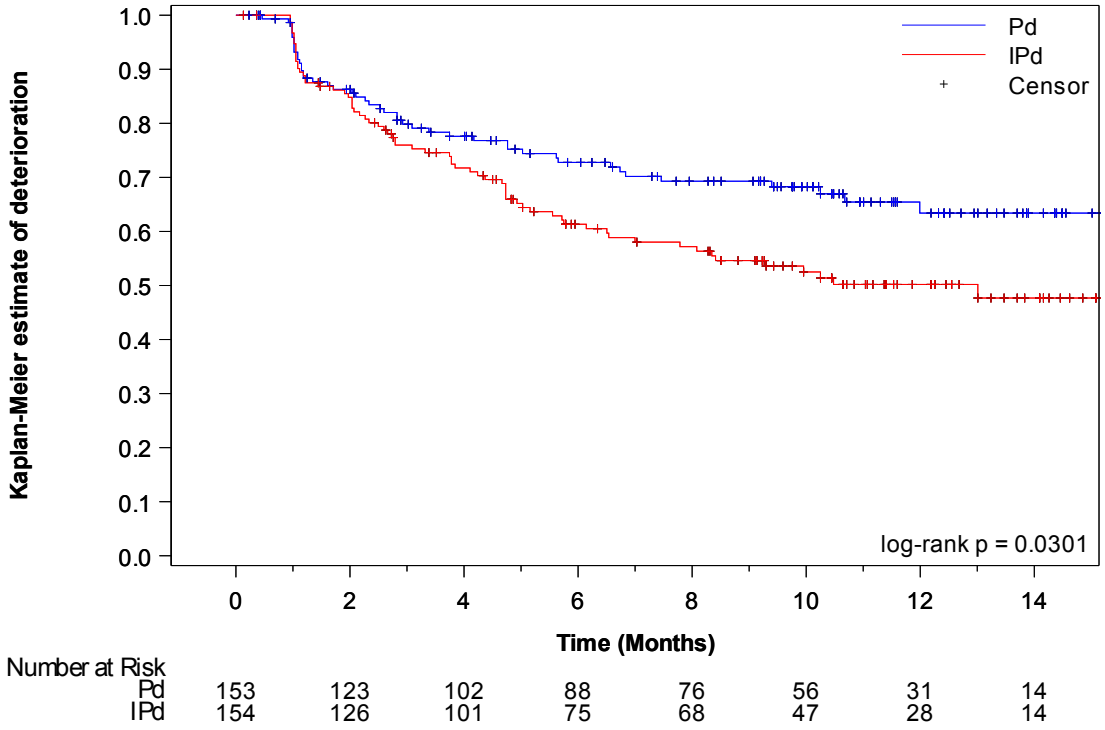
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_imp15l_de_i_f_x.rtf (08APR2021 15:33)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Diarrhea
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-C30 - Time to first deterioration by 15 pt in diarrhea (LOCF) - ITT population

First deterioration 15 points Diarrhea (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	46 (30.1)	69 (44.8)
Number (%) of patients censored	107 (69.9)	85 (55.2)
Kaplan-Meier estimates of diarrhea in months		
25% quantile (95% CI)	5.03 (2.595 to 10.251)	3.32 (2.168 to 4.731)
Median (95% CI)	NC (NC to NC)	13.01 (6.998 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0301
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.51 (1.04 to 2.20)
P-value	-	0.0312
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.0312	-
Probability (95% CI)[c]		
2 Months	0.86 (0.796 to 0.909)	0.85 (0.780 to 0.896)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_det15l_de_i_t_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Diarrhea
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-C30 - Time to first deterioration by 15 pt in diarrhea - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_det15l_de_i_f_x.rtf (08APR2021 15:33)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Diarrhea
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in diarrhea (LOCF) - ITT population

First permanent improvement 15 points Diarrhea (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	25 (16.3)	23 (14.9)
Number (%) of patients censored	128 (83.7)	131 (85.1)
Kaplan-Meier estimates of diarrhea in months		
25% quantile (95% CI)	NC (9.429 to NC)	NC (11.828 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5454
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.84 (0.48 to 1.48)
P-value	-	0.5454
Probability (95% CI)[c]		
2 Months	0.10 (0.060 to 0.158)	0.07 (0.034 to 0.113)
4 Months	0.13 (0.083 to 0.192)	0.09 (0.054 to 0.147)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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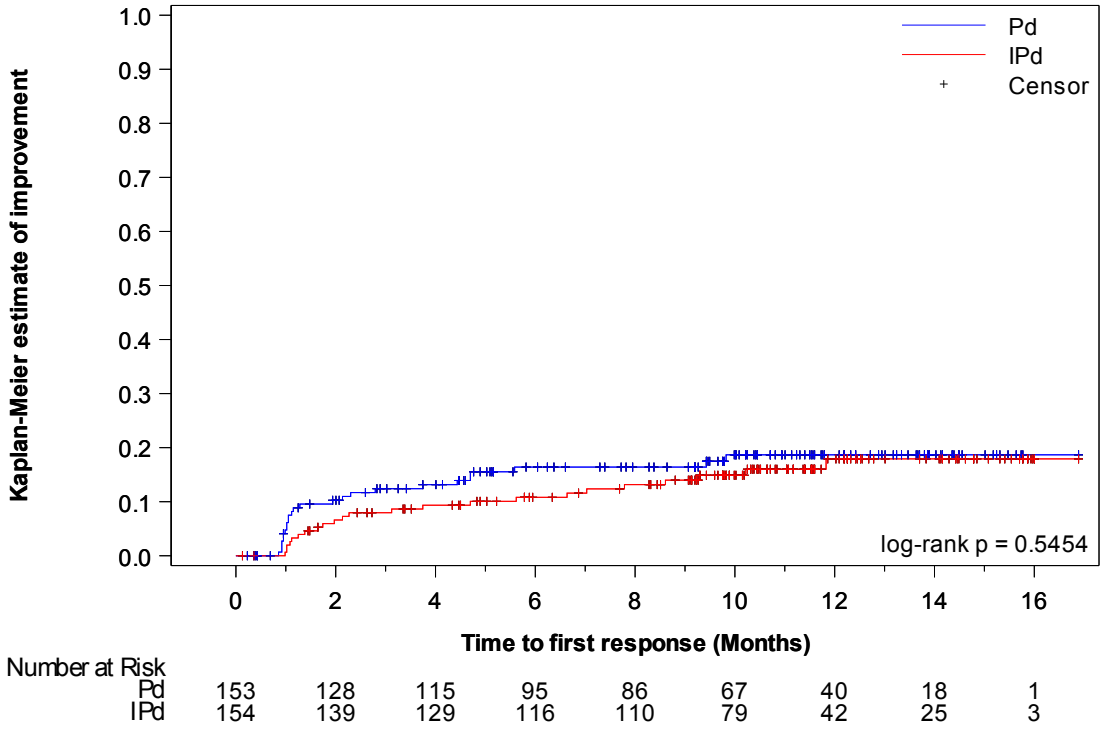
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Diarrhea
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-C30 - Time until permanent improvement by 15 pt in diarrhea - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_imp15pl_de_i_f_x.rtf (08APR2021 15:33)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Diarrhea
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in diarrhea (LOCF) - ITT population

First permanent deterioration 15 points Diarrhea (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	19 (12.4)	9 (5.8)
Number (%) of patients censored	134 (87.6)	145 (94.2)
Kaplan-Meier estimates of diarrhea in months		
25% quantile (95% CI)	NC (11.992 to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0222
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.41 (0.18 to 0.90)
P-value	-	0.0269
Probability (95% CI)[c]		
2 Months	0.95 (0.902 to 0.977)	1.00 (1.000 to 1.000)
4 Months	0.94 (0.883 to 0.967)	0.98 (0.937 to 0.993)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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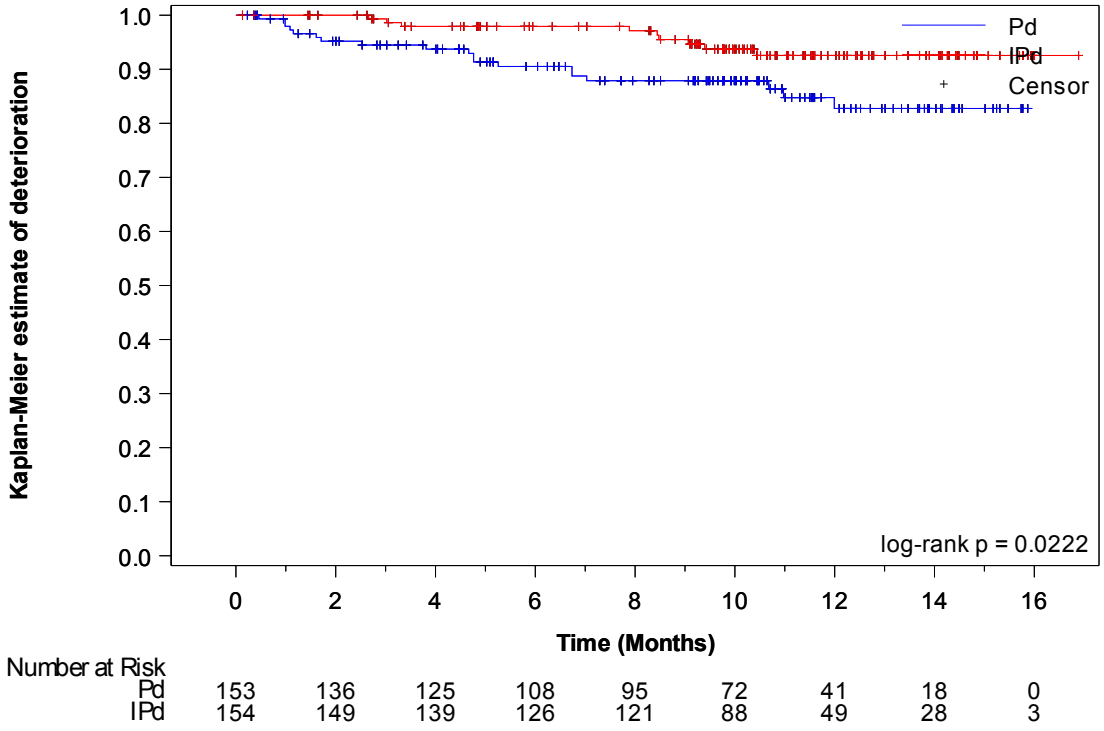
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Diarrhea
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-C30 - Time until permanent deterioration by 15 pt in diarrhea - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_det15pl_de_i_f_x.rtf (08APR2021 15:33)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (24.3)	17 (31.5)	12 (22.2)	6 (8.8)	8 (27.6)	9 (28.1)	0.1086
Number (%) of patients censored	53 (75.7)	37 (68.5)	42 (77.8)	62 (91.2)	21 (72.4)	23 (71.9)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	4.83 (1.051 to NC)	1.94 (1.018 to NC)	NC (1.741 to NC)	NC (NC to NC)	1.97 (0.986 to NC)	2.99 (1.248 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.975 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5129		0.0299		0.7882	
Hazard ratio (95% CI) vs Pd	-	1.25 (0.64 to 2.45)		0.35 (0.13 to 0.94)		0.88 (0.34 to 2.28)	
P-value	-	0.5138		0.0378		0.7884	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (30.0)	22 (40.7)	15 (27.8)	33 (48.5)	10 (34.5)	14 (43.8)	0.4485
Number (%) of patients censored	49 (70.0)	32 (59.3)	39 (72.2)	35 (51.5)	19 (65.5)	18 (56.3)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	5.03 (1.150 to NC)	3.84 (1.117 to 8.345)	7.46 (2.595 to NC)	2.79 (1.971 to 4.731)	2.53 (1.018 to NC)	3.32 (1.216 to 5.717)	
Median (95% CI)	NC (NC to NC)	13.01 (8.082 to NC)	NC (11.992 to NC)	8.41 (4.731 to NC)	NC (3.088 to NC)	NC (4.370 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3101		0.0211		0.8565	
Hazard ratio (95% CI) vs Pd	-	1.36 (0.75 to 2.48)		2.02 (1.10 to 3.73)		1.08 (0.48 to 2.43)	
P-value	-	0.3120		0.0239		0.8565	
Hazard ratio inverted (95% CI) vs IPd		-		0.49 (0.27 to 0.91)		0.93 (0.41 to 2.09)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_detl_age_de_i_t_x.rtf (08APR2021 14:54)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (17.1)	14 (25.9)	8 (14.8)	4 (5.9)	5 (17.2)	5 (15.6)	0.1582
Number (%) of patients censored	58 (82.9)	40 (74.1)	46 (85.2)	64 (94.1)	24 (82.8)	27 (84.4)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	NC (4.698 to NC)	8.61 (2.136 to NC)	NC (5.585 to NC)	NC (NC to NC)	NC (1.018 to NC)	NC (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.828 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3902		0.0800		0.6894	
Hazard ratio (95% CI) vs Pd	-	1.40 (0.65 to 3.03)		0.36 (0.11 to 1.19)		0.78 (0.22 to 2.70)	
P-value	-	0.3924		0.0937		0.6901	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_imppl_age_de_i_t_x.rtf (08APR2021 14:55)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (8.6)	4 (7.4)	7 (13.0)	2 (2.9)	6 (20.7)	3 (9.4)	0.3691
Number (%) of patients censored	64 (91.4)	50 (92.6)	47 (87.0)	66 (97.1)	23 (79.3)	29 (90.6)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	NC (NC to NC)	NC (10.448 to NC)	NC (7.031 to NC)	NC (NC to NC)	10.97 (2.530 to NC)	NC (8.476 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.973 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7367		0.0259		0.1232	
Hazard ratio (95% CI) vs Pd	-	0.81 (0.23 to 2.85)		0.20 (0.04 to 0.96)		0.35 (0.09 to 1.41)	
P-value	-	0.7372		0.0449		0.1401	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (24.8)	23 (22.5)	12 (23.1)	9 (17.3)	0.6312
Number (%) of patients censored	76 (75.2)	79 (77.5)	40 (76.9)	43 (82.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	4.83 (1.183 to NC)	NC (1.971 to NC)	4.70 (1.051 to NC)	NC (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5527		0.3448	
Hazard ratio (95% CI) vs Pd	-	0.84 (0.48 to 1.48)		0.66 (0.28 to 1.57)	
P-value	-	0.5526		0.3483	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	28 (27.7)	45 (44.1)	18 (34.6)	24 (46.2)	0.6031
Number (%) of patients censored	73 (72.3)	57 (55.9)	34 (65.4)	28 (53.8)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	5.62 (2.333 to NC)	3.75 (2.267 to 4.731)	4.76 (1.084 to 10.678)	2.79 (1.051 to 5.552)	
Median (95% CI)	NC (NC to NC)	10.48 (6.144 to NC)	NC (10.251 to NC)	13.01 (5.027 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0387		0.3729	
Hazard ratio (95% CI) vs Pd	-	1.64 (1.02 to 2.63)		1.32 (0.72 to 2.43)	
P-value	-	0.0407		0.3745	
Hazard ratio inverted (95% CI) vs IPd		-		0.76 (0.41 to 1.40)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	18 (17.8)	17 (16.7)	7 (13.5)	6 (11.5)	0.8279
Number (%) of patients censored	83 (82.2)	85 (83.3)	45 (86.5)	46 (88.5)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (4.698 to NC)	NC (8.608 to NC)	NC (4.698 to NC)	NC (11.828 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6440		0.6134	
Hazard ratio (95% CI) vs Pd	-	0.86 (0.44 to 1.66)		0.76 (0.25 to 2.25)	
P-value	-	0.6437		0.6146	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_imppl_plne_de_i_t_x.rtf (08APR2021 14:55)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (8.9)	6 (5.9)	10 (19.2)	3 (5.8)	0.2853
Number (%) of patients censored	92 (91.1)	96 (94.1)	42 (80.8)	49 (94.2)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	10.97 (4.764 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3252		0.0218	
Hazard ratio (95% CI) vs Pd	-	0.60 (0.21 to 1.68)		0.25 (0.07 to 0.90)	
P-value	-	0.3305		0.0341	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_detpl_plne_de_i_t_x.rtf (08APR2021 14:55)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (27.1)	19 (21.3)	18 (21.7)	13 (20.0)	0.6749
Number (%) of patients censored	51 (72.9)	70 (78.7)	65 (78.3)	52 (80.0)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	3.98 (1.051 to NC)	NC (2.037 to NC)	NC (1.183 to NC)	NC (1.380 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2737		0.6739	
Hazard ratio (95% CI) vs Pd	-	0.70 (0.37 to 1.33)		0.86 (0.42 to 1.75)	
P-value	-	0.2762		0.6742	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_impl_sex_de_i_t_x.rtf (08APR2021 14:54)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (35.7)	44 (49.4)	21 (25.3)	25 (38.5)	0.9776
Number (%) of patients censored	45 (64.3)	45 (50.6)	62 (74.7)	40 (61.5)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	4.76 (2.037 to 7.458)	3.09 (1.708 to 4.731)	6.57 (2.103 to NC)	3.75 (2.037 to 5.749)	
Median (95% CI)	NC (10.251 to NC)	9.30 (5.158 to NC)	NC (NC to NC)	NC (6.538 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1083		0.1799	
Hazard ratio (95% CI) vs Pd	-	1.49 (0.91 to 2.44)		1.48 (0.83 to 2.65)	
P-value	-	0.1107		0.1827	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (14.3)	15 (16.9)	15 (18.1)	8 (12.3)	0.2745
Number (%) of patients censored	60 (85.7)	74 (83.1)	68 (81.9)	57 (87.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (4.698 to NC)	NC (7.786 to NC)	NC (4.435 to NC)	NC (11.828 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8153		0.1904	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.49 to 2.45)		0.57 (0.24 to 1.34)	
P-value	-	0.8153		0.1963	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_imppl_sex_de_i_t_x.rtf (08APR2021 14:55)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (14.3)	6 (6.7)	9 (10.8)	3 (4.6)	0.7944
Number (%) of patients censored	60 (85.7)	83 (93.3)	74 (89.2)	62 (95.4)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (7.031 to NC)	NC (NC to NC)	NC (10.678 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0982		0.0927	
Hazard ratio (95% CI) vs Pd	-	0.44 (0.16 to 1.20)		0.34 (0.09 to 1.27)	
P-value	-	0.1080		0.1086	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (21.4)	27 (22.9)	9 (47.4)	4 (16.7)	0.0494
Number (%) of patients censored	99 (78.6)	91 (77.1)	10 (52.6)	20 (83.3)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (2.136 to NC)	NC (2.037 to NC)	1.12 (0.953 to 2.300)	NC (1.248 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.117 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9780		0.0181	
Hazard ratio (95% CI) vs Pd	-	0.99 (0.58 to 1.69)		0.27 (0.08 to 0.86)	
P-value	-	0.9780		0.0277	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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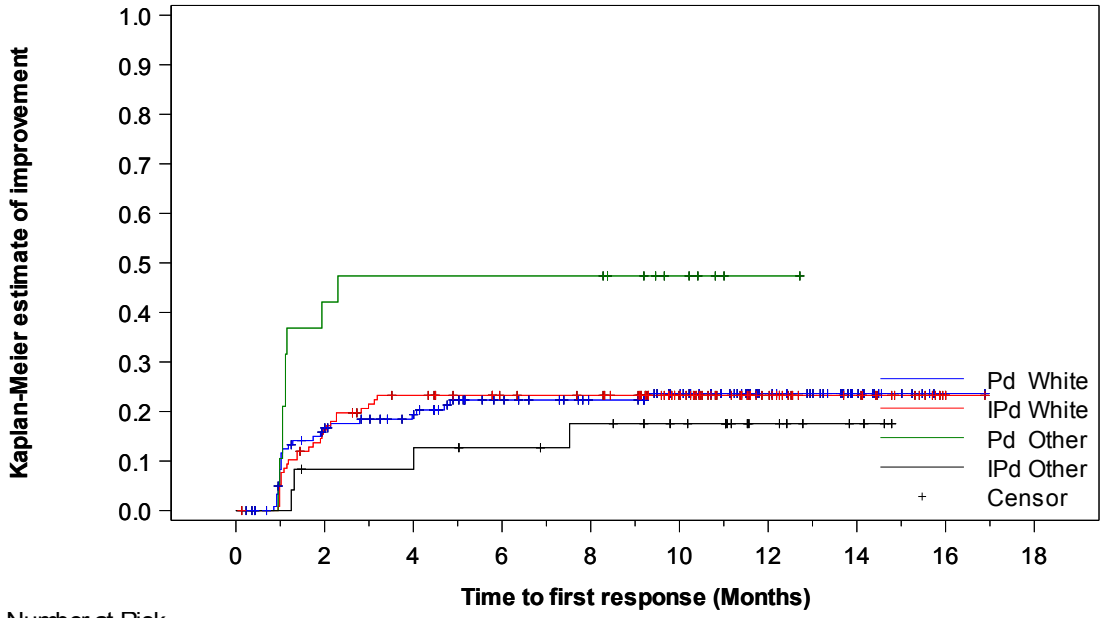
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to race (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd White	126	92	70	62	32	6	0
IPd White	118	89	79	74	28	11	0
Pd Other	19	10	10	8	1	0	0
IPd Other	24	21	19	16	7	0	0

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_impl_race_de_i_f_x.rtf (08APR2021 14:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (29.4)	54 (45.8)	5 (26.3)	13 (54.2)	0.4947
Number (%) of patients censored	89 (70.6)	64 (54.2)	14 (73.7)	11 (45.8)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	5.03 (2.825 to 10.678)	3.32 (2.037 to 4.731)	10.25 (1.117 to NC)	3.09 (0.986 to 7.786)	
Median (95% CI)	NC (NC to NC)	13.01 (5.749 to NC)	NC (10.251 to NC)	9.95 (3.844 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.251 to NC)	NC (9.955 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0301		0.1222	
Hazard ratio (95% CI) vs Pd	-	1.58 (1.04 to 2.41)		2.22 (0.79 to 6.29)	
P-value	-	0.0316		0.1318	
Hazard ratio inverted (95% CI) vs IPd		-		0.45 (0.16 to 1.27)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (14.3)	20 (16.9)	7 (36.8)	2 (8.3)	0.0383
Number (%) of patients censored	108 (85.7)	98 (83.1)	12 (63.2)	22 (91.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (9.823 to NC)	NC (9.298 to NC)	1.15 (0.953 to NC)	NC (1.248 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.150 to NC)	NC (11.828 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8704		0.0124	
Hazard ratio (95% CI) vs Pd	-	1.05 (0.56 to 1.99)		0.17 (0.03 to 0.81)	
P-value	-	0.8705		0.0269	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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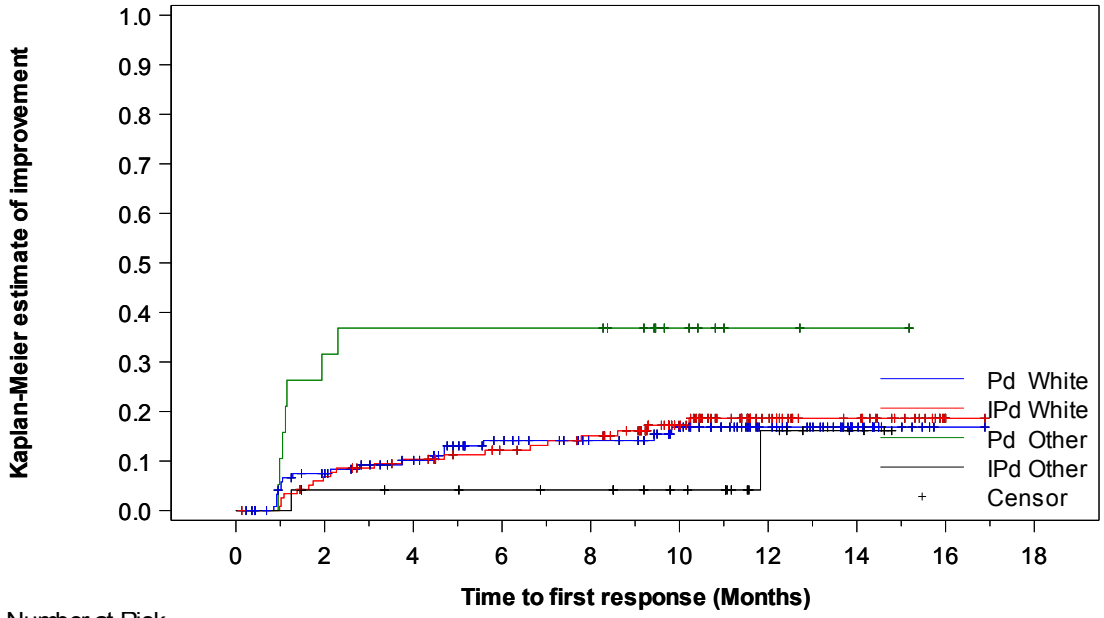
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.7 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to race (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd White	126	102	79	69	36	6	0
IPd White	118	104	92	82	32	13	0
Pd Other	19	12	12	10	2	1	0
IPd Other	24	22	20	17	7	0	0

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_imppl_race_de_i_f_x.rtf (08APR2021 14:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.8 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (11.9)	7 (5.9)	1 (5.3)	2 (8.3)	0.3575
Number (%) of patients censored	111 (88.1)	111 (94.1)	18 (94.7)	22 (91.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (11.992 to NC)	NC (NC to NC)	NC (1.708 to NC)	NC (2.661 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0549		0.7097	
Hazard ratio (95% CI) vs Pd	-	0.43 (0.17 to 1.05)		1.57 (0.14 to 17.34)	
P-value	-	0.0625		0.7121	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (66.7)	0 (0.0)	30 (22.4)	29 (22.3)	0.9864
Number (%) of patients censored	1 (33.3)	4 (100.0)	104 (77.6)	101 (77.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	1.28 (1.281 to 1.347)	NC (NC to NC)	NC (1.938 to NC)	NC (2.267 to NC)	
Median (95% CI)	1.31 (1.281 to 1.347)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	1.35 (1.281 to 1.347)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0177		0.7474	
Hazard ratio (95% CI) vs Pd	-			0.92 (0.55 to 1.53)	
P-value	-	0.9988		0.7473	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	2 (50.0)	40 (29.9)	61 (46.9)	0.3725
Number (%) of patients censored	2 (66.7)	2 (50.0)	94 (70.1)	69 (53.1)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	2.27 (2.267 to NC)	3.83 (2.497 to NC)	5.03 (2.825 to 10.678)	3.09 (2.037 to 4.665)	
Median (95% CI)	NC (2.267 to NC)	NC (2.497 to NC)	NC (NC to NC)	10.48 (6.505 to NC)	
75% quantile (95% CI)	NC (2.267 to NC)	NC (2.497 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4504		0.0164	
Hazard ratio (95% CI) vs Pd	-	0.35 (0.02 to 5.89)		1.62 (1.09 to 2.42)	
P-value	-	0.4689		0.0174	
Hazard ratio inverted (95% CI) vs IPd		-		0.62 (0.41 to 0.92)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	0 (0.0)	20 (14.9)	20 (15.4)	0.9892
Number (%) of patients censored	2 (66.7)	4 (100.0)	114 (85.1)	110 (84.6)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (NC to NC)	NC (9.823 to NC)	NC (11.828 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.8312	
Hazard ratio (95% CI) vs Pd	-			0.93 (0.50 to 1.74)	
P-value	-	0.9990		0.8311	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	0 (0.0)	15 (11.2)	9 (6.9)	0.9891
Number (%) of patients censored	2 (66.7)	4 (100.0)	119 (88.8)	121 (93.1)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	5.26 (NC to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (NC to NC)	
Median (95% CI)	5.26 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	5.26 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0455		0.1377	
Hazard ratio (95% CI) vs Pd	-			0.54 (0.24 to 1.23)	
P-value	-	1.0000		0.1439	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	17 (22.4)	14 (25.5)	4 (20.0)	3 (10.7)	3 (60.0)	3 (42.9)	7 (46.7)	3 (14.3)	6 (16.2)	9 (20.9)	0.2802
Number (%) of patients censored	59 (77.6)	41 (74.5)	16 (80.0)	25 (89.3)	2 (40.0)	4 (57.1)	8 (53.3)	18 (85.7)	31 (83.8)	34 (79.1)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	9.30 (1.906 to NC)	3.12 (1.643 to NC)	NC (0.986 to NC)	NC (1.018 to NC)	1.12 (0.953 to NC)	1.25 (1.084 to NC)	1.12 (0.986 to 2.300)	NC (1.314 to NC)	NC (1.018 to NC)	NC (1.380 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	1.35 (0.953 to NC)	NC (1.084 to NC)	NC (1.051 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (1.938 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.8433		0.3461		0.4814		0.0212		0.6784	
Hazard ratio (95% CI) vs Pd	-	1.07 (0.53 to 2.18)		0.49 (0.11 to 2.21)		0.57 (0.11 to 2.82)		0.23 (0.06 to 0.90)		1.24 (0.44 to 3.49)	
P-value	-	0.8427		0.3561		0.4871		0.0345		0.6790	
Improvement probability (95% CI)[b]											
2 Months	0.169 (0.093 to 0.264)	0.149 (0.069 to 0.256)	0.158 (0.039 to 0.349)	0.107 (0.027 to 0.251)	0.600 (0.126 to 0.882)	0.429 (0.098 to 0.734)	0.400 (0.165 to 0.628)	0.048 (0.003 to 0.197)	0.140 (0.051 to 0.272)	0.168 (0.074 to 0.295)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_impl_greg_de_i_t_x.rtf (08APR2021 14:54)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	21 (27.6)	19 (34.5)	4 (20.0)	11 (39.3)	2 (40.0)	3 (42.9)	4 (26.7)	11 (52.4)	15 (40.5)	25 (58.1)	0.8401
Number (%) of patients censored	55 (72.4)	36 (65.5)	16 (80.0)	17 (60.7)	3 (60.0)	4 (57.1)	11 (73.3)	10 (47.6)	22 (59.5)	18 (41.9)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	5.62 (2.103 to NC)	4.73 (1.216 to 8.345)	11.99 (0.986 to NC)	3.32 (1.051 to 6.538)	2.60 (2.267 to NC)	3.78 (2.793 to NC)	10.25 (1.117 to NC)	3.84 (0.986 to 8.082)	2.04 (1.018 to 6.571)	2.17 (1.084 to 4.665)	
Median (95% CI)	NC (NC to NC)	NC (6.144 to NC)	NC (11.992 to NC)	NC (3.745 to NC)	NC (2.267 to NC)	NC (2.793 to NC)	10.25 (6.834 to NC)	9.95 (3.844 to NC)	NC (2.825 to NC)	5.55 (4.107 to 13.010)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.267 to NC)	NC (5.158 to NC)	NC (10.251 to NC)	NC (9.955 to NC)	NC (NC to NC)	NC (10.251 to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.4842		0.1576		0.8431		0.2055		0.3242	
Hazard ratio (95% CI) vs Pd	-	1.25 (0.67 to 2.32)		2.25 (0.71 to 7.11)		0.83 (0.14 to 5.03)		2.08 (0.65 to 6.66)		1.38 (0.73 to 2.62)	
P-value	-	0.4851		0.1686		0.8434		0.2151		0.3262	
Deterioration probability (95% CI)[b]											

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	14 (18.4)	9 (16.4)	2 (10.0)	3 (10.7)	1 (20.0)	3 (42.9)	5 (33.3)	1 (4.8)	3 (8.1)	7 (16.3)	0.2483
Number (%) of patients censored	62 (81.6)	46 (83.6)	18 (90.0)	25 (89.3)	4 (80.0)	4 (57.1)	10 (66.7)	20 (95.2)	34 (91.9)	36 (83.7)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (3.745 to NC)	NC (3.745 to NC)	NC (1.051 to NC)	NC (1.018 to NC)	NC (1.117 to NC)	1.25 (1.084 to NC)	1.94 (0.986 to NC)	NC (11.828 to NC)	NC (4.698 to NC)	NC (7.786 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.117 to NC)	NC (1.084 to NC)	NC (1.150 to NC)	NC (11.828 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.117 to NC)	NC (5.618 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.6115		0.9203		0.4693		0.0089		0.4985	
Hazard ratio (95% CI) vs Pd	-	0.81 (0.35 to 1.86)		1.10 (0.18 to 6.56)		2.26 (0.23 to 21.73)		0.08 (0.01 to 0.80)		1.59 (0.41 to 6.19)	
P-value	-	0.6122		0.9203		0.4813		0.0308		0.5024	
Improvement probability (95% CI)[b]											
2 Months	0.112 (0.052 to 0.197)	0.056 (0.015 to 0.140)	0.053 (0.004 to 0.214)	0.107 (0.027 to 0.251)	0.200 (0.008 to 0.582)	0.286 (0.041 to 0.612)	0.267 (0.083 to 0.496)		0.028 (0.002 to 0.124)	0.048 (0.009 to 0.144)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	8 (10.5)	2 (3.6)	3 (15.0)	2 (7.1)	1 (20.0)	0 (0.0)	0 (0.0)	2 (9.5)	7 (18.9)	3 (7.0)	0.9943
Number (%) of patients censored	68 (89.5)	53 (96.4)	17 (85.0)	26 (92.9)	4 (80.0)	7 (100.0)	15 (100.0)	19 (90.5)	30 (81.1)	40 (93.0)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (10.678 to NC)	NC (NC to NC)	NC (4.665 to NC)	NC (7.885 to NC)	NC (5.257 to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.661 to NC)	NC (2.530 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (NC to NC)	NC (5.257 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.257 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.1216		0.4970		0.2367		0.2233		0.0536	
Hazard ratio (95% CI) vs Pd	-	0.31 (0.07 to 1.48)		0.54 (0.09 to 3.28)						0.28 (0.07 to 1.11)	
P-value	-	0.1429		0.5034		0.9984		0.9978		0.0700	
Deterioration probability (95% CI)[b]											

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (25.8)	21 (27.3)	12 (21.4)	11 (14.3)	0.3591
Number (%) of patients censored	72 (74.2)	56 (72.7)	44 (78.6)	66 (85.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	4.70 (1.281 to NC)	2.83 (1.741 to NC)	NC (1.117 to NC)	NC (7.524 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9335		0.2316	
Hazard ratio (95% CI) vs Pd	-	0.98 (0.55 to 1.74)		0.61 (0.27 to 1.38)	
P-value	-	0.9335		0.2363	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (30.9)	29 (37.7)	16 (28.6)	40 (51.9)	0.1552
Number (%) of patients censored	67 (69.1)	48 (62.3)	40 (71.4)	37 (48.1)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	4.76 (2.103 to 7.458)	4.37 (2.037 to 6.144)	9.40 (2.037 to NC)	2.79 (1.906 to 4.238)	
Median (95% CI)	NC (NC to NC)	NC (8.345 to NC)	NC (11.992 to NC)	8.08 (4.731 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5636		0.0140	
Hazard ratio (95% CI) vs Pd	-	1.16 (0.70 to 1.94)		2.04 (1.14 to 3.64)	
P-value	-	0.5640		0.0161	
Hazard ratio inverted (95% CI) vs IPd		-		0.49 (0.27 to 0.88)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (17.5)	15 (19.5)	8 (14.3)	8 (10.4)	0.5092
Number (%) of patients censored	80 (82.5)	62 (80.5)	48 (85.7)	69 (89.6)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (4.435 to NC)	NC (4.698 to NC)	NC (4.698 to NC)	NC (11.828 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9890		0.4091	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.50 to 1.99)		0.66 (0.25 to 1.77)	
P-value	-	0.9890		0.4123	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (12.4)	3 (3.9)	7 (12.5)	6 (7.8)	0.3898
Number (%) of patients censored	85 (87.6)	74 (96.1)	49 (87.5)	71 (92.2)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (10.678 to NC)	NC (NC to NC)	NC (10.973 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0304		0.2995	
Hazard ratio (95% CI) vs Pd	-	0.27 (0.08 to 0.96)		0.57 (0.19 to 1.68)	
P-value	-	0.0435		0.3060	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_detpl_rreg_de_i_t_x.rtf (08APR2021 14:55)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (22.6)	30 (21.7)	6 (37.5)	2 (12.5)	0.2170
Number (%) of patients censored	106 (77.4)	108 (78.3)	10 (62.5)	14 (87.5)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (1.741 to NC)	NC (2.267 to NC)	1.94 (0.953 to NC)	NC (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.281 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5949		0.1264	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.53 to 1.44)		0.31 (0.06 to 1.52)	
P-value	-	0.5944		0.1489	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (30.7)	63 (45.7)	4 (25.0)	6 (37.5)	0.8096
Number (%) of patients censored	95 (69.3)	75 (54.3)	12 (75.0)	10 (62.5)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	5.03 (2.595 to 10.251)	3.32 (2.037 to 4.731)	4.17 (0.986 to NC)	2.76 (1.084 to 6.144)	
Median (95% CI)	NC (NC to NC)	13.01 (6.998 to NC)	NC (2.530 to NC)	6.14 (2.661 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.144 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0389		0.3873	
Hazard ratio (95% CI) vs Pd	-	1.50 (1.02 to 2.22)		1.74 (0.49 to 6.21)	
P-value	-	0.0403		0.3932	
Hazard ratio inverted (95% CI) vs IPd		-		0.57 (0.16 to 2.05)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (15.3)	23 (16.7)	4 (25.0)	0 (0.0)	0.9840
Number (%) of patients censored	116 (84.7)	115 (83.3)	12 (75.0)	16 (100.0)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (9.823 to NC)	NC (10.218 to NC)	2.30 (0.953 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.938 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9387		0.0379	
Hazard ratio (95% CI) vs Pd	-	0.98 (0.54 to 1.77)			
P-value	-	0.9386		0.9968	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (12.4)	8 (5.8)	2 (12.5)	1 (6.3)	0.8777
Number (%) of patients censored	120 (87.6)	130 (94.2)	14 (87.5)	15 (93.8)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (11.992 to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (2.661 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0267		0.5781	
Hazard ratio (95% CI) vs Pd	-	0.40 (0.17 to 0.93)		0.51 (0.05 to 5.65)	
P-value	-	0.0323		0.5852	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (27.5)	10 (15.6)	12 (21.4)	10 (18.9)	10 (23.3)	11 (32.4)	0.3307
Number (%) of patients censored	37 (72.5)	54 (84.4)	44 (78.6)	43 (81.1)	33 (76.7)	23 (67.6)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	4.07 (1.051 to NC)	NC (3.187 to NC)	NC (1.051 to NC)	NC (1.971 to NC)	4.83 (1.018 to NC)	2.27 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.008 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1172		0.6241		0.5667	
Hazard ratio (95% CI) vs Pd	-	0.53 (0.23 to 1.19)		0.81 (0.35 to 1.88)		1.28 (0.54 to 3.02)	
P-value	-	0.1235		0.6247		0.5677	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (27.5)	25 (39.1)	20 (35.7)	29 (54.7)	10 (23.3)	14 (41.2)	0.9941
Number (%) of patients censored	37 (72.5)	39 (60.9)	36 (64.3)	24 (45.3)	33 (76.7)	20 (58.8)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	9.40 (2.595 to NC)	4.11 (1.708 to 6.998)	3.75 (1.150 to 6.571)	2.79 (2.070 to 4.731)	6.83 (1.018 to NC)	2.17 (1.051 to 4.731)	
Median (95% CI)	NC (NC to NC)	NC (7.786 to NC)	NC (6.571 to NC)	8.34 (4.665 to 13.010)	NC (11.992 to NC)	NC (2.661 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.251 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1281		0.0999		0.2416	
Hazard ratio (95% CI) vs Pd	-	1.65 (0.86 to 3.19)		1.61 (0.91 to 2.85)		1.62 (0.72 to 3.64)	
P-value	-	0.1322		0.1031		0.2461	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (17.6)	7 (10.9)	9 (16.1)	7 (13.2)	7 (16.3)	8 (23.5)	0.6954
Number (%) of patients censored	42 (82.4)	57 (89.1)	47 (83.9)	46 (86.8)	36 (83.7)	26 (76.5)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	NC (2.300 to NC)	NC (10.218 to NC)	NC (4.698 to NC)	NC (9.298 to NC)	NC (1.281 to NC)	11.83 (2.267 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.828 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3320		0.5715		0.8623	
Hazard ratio (95% CI) vs Pd	-	0.62 (0.23 to 1.66)		0.75 (0.28 to 2.02)		1.09 (0.39 to 3.03)	
P-value	-	0.3367		0.5727		0.8625	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (7.8)	5 (7.8)	10 (17.9)	3 (5.7)	3 (7.0)	1 (2.9)	0.3221
Number (%) of patients censored	47 (92.2)	59 (92.2)	46 (82.1)	50 (94.3)	40 (93.0)	33 (97.1)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	10.97 (5.257 to NC)	NC (NC to NC)	NC (4.665 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9518		0.0312		0.3259	
Hazard ratio (95% CI) vs Pd	-	1.04 (0.28 to 3.88)		0.27 (0.07 to 0.97)		0.34 (0.04 to 3.26)	
P-value	-	0.9519		0.0448		0.3491	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (25.8)	9 (23.1)	26 (26.5)	17 (17.2)	3 (12.5)	6 (37.5)	0.0880
Number (%) of patients censored	23 (74.2)	30 (76.9)	72 (73.5)	82 (82.8)	21 (87.5)	10 (62.5)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	9.30 (1.018 to NC)	NC (1.643 to NC)	3.98 (1.150 to NC)	NC (3.121 to NC)	NC (1.018 to NC)	1.31 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7720		0.0759		0.0968	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.34 to 2.25)		0.58 (0.31 to 1.07)		3.05 (0.76 to 12.21)	
P-value	-	0.7722		0.0796		0.1147	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (32.3)	16 (41.0)	32 (32.7)	49 (49.5)	4 (16.7)	4 (25.0)	0.8484
Number (%) of patients censored	21 (67.7)	23 (59.0)	66 (67.3)	50 (50.5)	20 (83.3)	12 (75.0)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	6.74 (1.610 to NC)	4.73 (1.051 to 7.786)	3.75 (2.037 to 10.678)	2.79 (1.906 to 4.370)	6.83 (0.986 to NC)	2.66 (0.953 to NC)	
Median (95% CI)	NC (9.396 to NC)	NC (6.538 to NC)	NC (11.992 to NC)	9.30 (5.027 to NC)	NC (6.834 to NC)	NC (2.037 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3750		0.0288		0.7235	
Hazard ratio (95% CI) vs Pd	-	1.43 (0.65 to 3.15)		1.64 (1.05 to 2.56)		1.28 (0.32 to 5.16)	
P-value	-	0.3776		0.0304		0.7242	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (12.9)	6 (15.4)	18 (18.4)	13 (13.1)	3 (12.5)	4 (25.0)	0.4744
Number (%) of patients censored	27 (87.1)	33 (84.6)	80 (81.6)	86 (86.9)	21 (87.5)	12 (75.0)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	NC (1.938 to NC)	NC (6.637 to NC)	NC (4.698 to NC)	NC (11.828 to NC)	NC (1.018 to NC)	8.61 (2.267 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.698 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7505		0.2264		0.7391	
Hazard ratio (95% CI) vs Pd	-	1.23 (0.35 to 4.35)		0.65 (0.32 to 1.32)		1.29 (0.29 to 5.83)	
P-value	-	0.7509		0.2301		0.7398	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (6.5)	3 (7.7)	16 (16.3)	5 (5.1)	1 (4.2)	1 (6.3)	0.2974
Number (%) of patients censored	29 (93.5)	36 (92.3)	82 (83.7)	94 (94.9)	23 (95.8)	15 (93.8)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	NC (NC to NC)	NC (10.448 to NC)	NC (10.678 to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (2.661 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8454		0.0069		0.8861	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.20 to 7.15)		0.27 (0.10 to 0.75)		1.22 (0.08 to 19.70)	
P-value	-	0.8456		0.0117		0.8863	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (17.4)	3 (21.4)	26 (27.4)	26 (22.0)	0.5151
Number (%) of patients censored	19 (82.6)	11 (78.6)	69 (72.6)	92 (78.0)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (1.018 to NC)	NC (0.986 to NC)	3.98 (1.051 to NC)	NC (2.267 to NC)	
Median (95% CI)	NC (NC to NC)	NC (1.938 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7942		0.2412	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.27 to 5.46)		0.72 (0.42 to 1.25)	
P-value	-	0.7946		0.2432	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (21.7)	6 (42.9)	31 (32.6)	53 (44.9)	0.5639
Number (%) of patients censored	18 (78.3)	8 (57.1)	64 (67.4)	65 (55.1)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	6.57 (1.018 to NC)	3.32 (1.051 to 8.345)	4.17 (1.708 to 10.251)	3.84 (2.037 to 5.027)	
Median (95% CI)	NC (6.571 to NC)	8.34 (2.070 to NC)	NC (NC to NC)	13.01 (6.538 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (3.778 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2679		0.1496	
Hazard ratio (95% CI) vs Pd	-	1.93 (0.59 to 6.34)		1.38 (0.89 to 2.16)	
P-value	-	0.2766		0.1514	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (13.0)	1 (7.1)	16 (16.8)	19 (16.1)	0.6640
Number (%) of patients censored	20 (87.0)	13 (92.9)	79 (83.2)	99 (83.9)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (1.018 to NC)	NC (5.618 to NC)	NC (4.698 to NC)	NC (10.218 to NC)	
Median (95% CI)	NC (4.435 to NC)	NC (5.618 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4605		0.6462	
Hazard ratio (95% CI) vs Pd	-	0.44 (0.05 to 4.21)		0.86 (0.44 to 1.66)	
P-value	-	0.4730		0.6465	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (8.7)	2 (14.3)	14 (14.7)	6 (5.1)	0.1331
Number (%) of patients censored	21 (91.3)	12 (85.7)	81 (85.3)	112 (94.9)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (3.811 to NC)	NC (2.661 to NC)	NC (10.678 to NC)	NC (NC to NC)	
Median (95% CI)	NC (6.735 to NC)	NC (3.318 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6352		0.0079	
Hazard ratio (95% CI) vs Pd	-	1.60 (0.23 to 11.37)		0.29 (0.11 to 0.77)	
P-value	-	0.6383		0.0124	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (25.0)	6 (25.0)	18 (23.1)	23 (22.3)	0.8476
Number (%) of patients censored	27 (75.0)	18 (75.0)	60 (76.9)	80 (77.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	2.79 (1.150 to NC)	2.27 (0.986 to NC)	NC (1.117 to NC)	NC (2.267 to NC)	
Median (95% CI)	NC (NC to NC)	NC (2.267 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9962		0.6920	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.35 to 2.80)		0.88 (0.48 to 1.64)	
P-value	-	0.9962		0.6922	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (25.0)	12 (50.0)	26 (33.3)	46 (44.7)	0.2795
Number (%) of patients censored	27 (75.0)	12 (50.0)	52 (66.7)	57 (55.3)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	4.76 (1.183 to NC)	2.33 (0.986 to 3.778)	4.17 (1.610 to 10.251)	4.11 (2.037 to 5.158)	
Median (95% CI)	NC (6.571 to NC)	8.34 (2.333 to NC)	NC (10.678 to NC)	13.01 (6.538 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (8.345 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0674		0.2593	
Hazard ratio (95% CI) vs Pd	-	2.20 (0.92 to 5.22)		1.32 (0.81 to 2.13)	
P-value	-	0.0746		0.2609	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (19.4)	3 (12.5)	10 (12.8)	17 (16.5)	0.3413
Number (%) of patients censored	29 (80.6)	21 (87.5)	68 (87.2)	86 (83.5)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (1.150 to NC)	NC (3.745 to NC)	NC (NC to NC)	NC (10.218 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3496		0.6661	
Hazard ratio (95% CI) vs Pd	-	0.53 (0.14 to 2.05)		1.19 (0.54 to 2.59)	
P-value	-	0.3577		0.6665	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (13.9)	3 (12.5)	10 (12.8)	5 (4.9)	0.3265
Number (%) of patients censored	31 (86.1)	21 (87.5)	68 (87.2)	98 (95.1)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (4.764 to NC)	NC (2.661 to NC)	NC (10.678 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7430		0.0319	
Hazard ratio (95% CI) vs Pd	-	0.79 (0.19 to 3.30)		0.33 (0.11 to 0.96)	
P-value	-	0.7436		0.0415	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (25.6)	19 (22.9)	14 (22.2)	13 (18.3)	0.6783
Number (%) of patients censored	67 (74.4)	64 (77.1)	49 (77.8)	58 (81.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	4.70 (1.117 to NC)	NC (1.741 to NC)	9.30 (1.183 to NC)	NC (2.990 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6132		0.3452	
Hazard ratio (95% CI) vs Pd	-	0.86 (0.47 to 1.57)		0.70 (0.33 to 1.48)	
P-value	-	0.6135		0.3478	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_impl_auto_de_i_t_x.rtf (08APR2021 14:54)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (31.1)	35 (42.2)	18 (28.6)	34 (47.9)	0.8352
Number (%) of patients censored	62 (68.9)	48 (57.8)	45 (71.4)	37 (52.1)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	5.03 (2.267 to 10.678)	2.79 (1.708 to 4.928)	5.62 (2.037 to NC)	4.24 (2.037 to 5.158)	
Median (95% CI)	NC (NC to NC)	NC (6.538 to NC)	NC (11.992 to NC)	10.25 (5.717 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1324		0.1036	
Hazard ratio (95% CI) vs Pd	-	1.46 (0.89 to 2.40)		1.60 (0.90 to 2.84)	
P-value	-	0.1347		0.1068	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (17.8)	14 (16.9)	9 (14.3)	9 (12.7)	0.7616
Number (%) of patients censored	74 (82.2)	69 (83.1)	54 (85.7)	62 (87.3)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (4.698 to NC)	NC (7.031 to NC)	NC (4.698 to NC)	NC (11.828 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7522		0.5112	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.43 to 1.83)		0.73 (0.29 to 1.85)	
P-value	-	0.7527		0.5129	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (13.3)	6 (7.2)	7 (11.1)	3 (4.2)	0.5200
Number (%) of patients censored	78 (86.7)	77 (92.8)	56 (88.9)	68 (95.8)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (10.678 to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1665		0.0685	
Hazard ratio (95% CI) vs Pd	-	0.51 (0.19 to 1.35)		0.30 (0.08 to 1.18)	
P-value	-	0.1748		0.0855	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	36 (23.8)	32 (21.1)	0.9821
Number (%) of patients censored	1 (50.0)	2 (100.0)	115 (76.2)	120 (78.9)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	4.70 (4.698 to NC)	NC (NC to NC)	9.30 (1.741 to NC)	NC (2.825 to NC)	
Median (95% CI)	NC (4.698 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (4.698 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.3636	
Hazard ratio (95% CI) vs Pd	-			0.80 (0.50 to 1.29)	
P-value	-	0.9990		0.3638	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	2 (100.0)	45 (29.8)	67 (44.1)	0.9751
Number (%) of patients censored	1 (50.0)	0 (0.0)	106 (70.2)	85 (55.9)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	1.02 (1.018 to NC)	5.03 (5.027 to 7.786)	5.03 (2.825 to 10.251)	3.09 (2.070 to 4.731)	
Median (95% CI)	NC (1.018 to NC)	6.41 (5.027 to 7.786)	NC (NC to NC)	13.01 (6.998 to NC)	
75% quantile (95% CI)	NC (1.018 to NC)	7.79 (5.027 to 7.786)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6949		0.0282	
Hazard ratio (95% CI) vs Pd	-	1.62 (0.14 to 18.31)		1.52 (1.04 to 2.22)	
P-value	-	0.6975		0.0294	
Hazard ratio inverted (95% CI) vs IPd		-		0.66 (0.45 to 0.96)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	24 (15.9)	23 (15.1)	0.9850
Number (%) of patients censored	1 (50.0)	2 (100.0)	127 (84.1)	129 (84.9)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	4.70 (4.698 to NC)	NC (NC to NC)	NC (9.823 to NC)	NC (11.828 to NC)	
Median (95% CI)	NC (4.698 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (4.698 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.5881	
Hazard ratio (95% CI) vs Pd	-			0.85 (0.48 to 1.51)	
P-value	-	0.9990		0.5876	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	19 (12.6)	9 (5.9)	0.9997
Number (%) of patients censored	2 (100.0)	2 (100.0)	132 (87.4)	143 (94.1)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0222	
Hazard ratio (95% CI) vs Pd	-			0.41 (0.18 to 0.90)	
P-value	-			0.0270	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_detpl_allt_de_i_t_x.rtf (08APR2021 14:54)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (25.7)	16 (15.4)	10 (24.4)	8 (24.2)	0.0657
Number (%) of patients censored	75 (74.3)	88 (84.6)	31 (75.6)	25 (75.8)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	4.70 (1.117 to NC)	NC (NC to NC)	4.07 (0.986 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0360		0.8684	
Hazard ratio (95% CI) vs Pd	-	0.52 (0.28 to 0.97)		0.92 (0.36 to 2.34)	
P-value	-	0.0394		0.8688	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (35.6)	47 (45.2)	6 (14.6)	16 (48.5)	0.0842
Number (%) of patients censored	65 (64.4)	57 (54.8)	35 (85.4)	17 (51.5)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	3.38 (1.347 to 6.834)	3.75 (2.037 to 5.158)	NC (2.267 to NC)	2.66 (1.906 to 4.731)	
Median (95% CI)	NC (10.251 to NC)	10.48 (6.538 to NC)	NC (NC to NC)	7.79 (3.844 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3063		0.0038	
Hazard ratio (95% CI) vs Pd	-	1.25 (0.81 to 1.94)		3.66 (1.43 to 9.35)	
P-value	-	0.3073		0.0068	
Hazard ratio inverted (95% CI) vs IPd		-		0.27 (0.11 to 0.70)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (18.8)	11 (10.6)	6 (14.6)	5 (15.2)	0.6512
Number (%) of patients censored	82 (81.2)	93 (89.4)	35 (85.4)	28 (84.8)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (4.698 to NC)	NC (11.828 to NC)	NC (2.300 to NC)	NC (3.121 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0527		0.9188	
Hazard ratio (95% CI) vs Pd	-	0.49 (0.23 to 1.02)		0.94 (0.29 to 3.08)	
P-value	-	0.0579		0.9190	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (12.9)	7 (6.7)	4 (9.8)	2 (6.1)	0.9862
Number (%) of patients censored	88 (87.1)	97 (93.3)	37 (90.2)	31 (93.9)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (10.973 to NC)	NC (NC to NC)	NC (5.257 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0785		0.4756	
Hazard ratio (95% CI) vs Pd	-	0.45 (0.18 to 1.12)		0.54 (0.10 to 2.98)	
P-value	-	0.0867		0.4824	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (26.0)	16 (15.7)	11 (21.2)	16 (31.4)	0.0407
Number (%) of patients censored	74 (74.0)	86 (84.3)	41 (78.8)	35 (68.6)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	4.70 (1.117 to NC)	NC (7.524 to NC)	NC (1.347 to NC)	2.27 (1.183 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0386		0.3135	
Hazard ratio (95% CI) vs Pd	-	0.52 (0.28 to 0.98)		1.48 (0.69 to 3.19)	
P-value	-	0.0421		0.3166	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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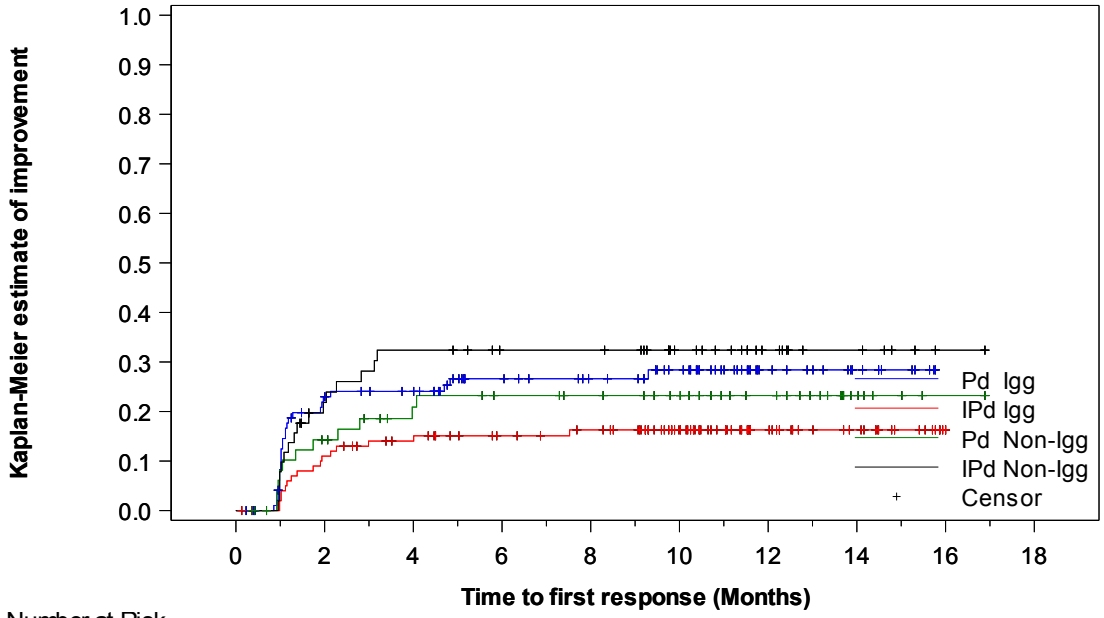
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to MM type at initial diagnosis (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd Igg	100	69	51	44	17	5	0
IPd Igg	102	83	73	66	27	9	0
Pd Non-Igg	52	37	31	28	17	3	0
IPd Non-Igg	51	34	28	27	11	3	0

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (36.0)	45 (44.1)	10 (19.2)	23 (45.1)	0.0702
Number (%) of patients censored	64 (64.0)	57 (55.9)	42 (80.8)	28 (54.9)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	3.38 (1.347 to 6.834)	3.75 (2.070 to 5.552)	NC (2.530 to NC)	2.79 (1.906 to 4.731)	
Median (95% CI)	NC (10.251 to NC)	13.01 (6.998 to NC)	NC (NC to NC)	NC (4.731 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4256		0.0098	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.77 to 1.85)		2.57 (1.22 to 5.40)	
P-value	-	0.4262		0.0128	
Hazard ratio inverted (95% CI) vs IPd		-		0.39 (0.19 to 0.82)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (19.0)	11 (10.8)	6 (11.5)	12 (23.5)	0.0262
Number (%) of patients censored	81 (81.0)	91 (89.2)	46 (88.5)	39 (76.5)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (4.698 to NC)	NC (11.828 to NC)	NC (9.823 to NC)	9.30 (2.267 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0554		0.1640	
Hazard ratio (95% CI) vs Pd	-	0.49 (0.23 to 1.03)		1.98 (0.74 to 5.27)	
P-value	-	0.0606		0.1722	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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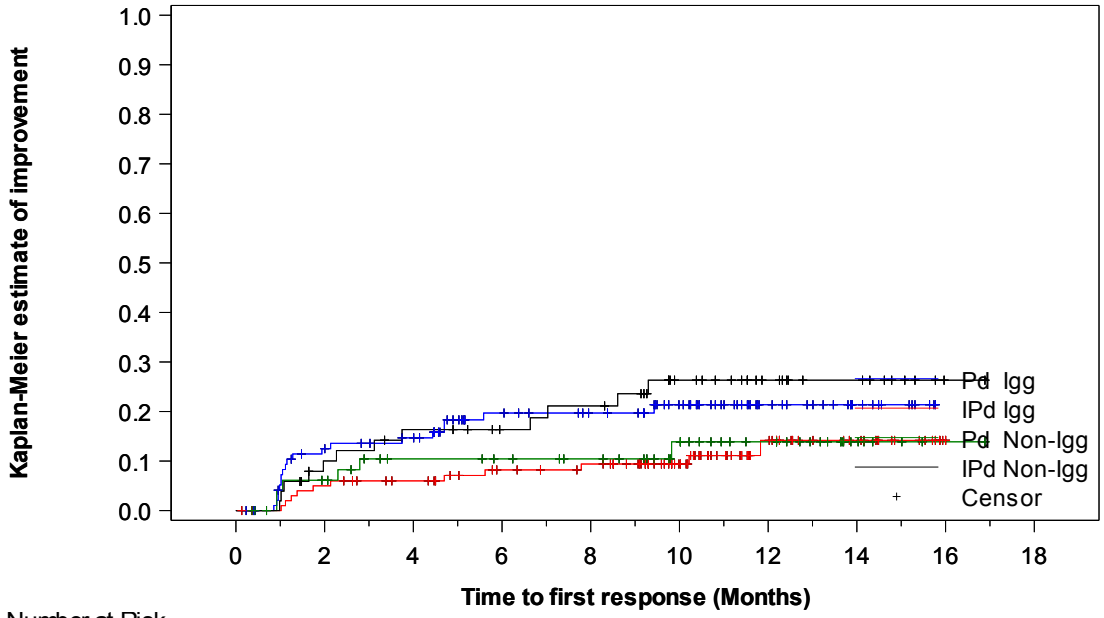
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.7 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to MM type at initial diagnosis (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd Igg	100	79	58	51	22	6	0
IPd Igg	102	91	80	71	28	9	0
Pd Non-Igg	52	40	36	31	17	3	0
IPd Non-Igg	51	42	35	31	14	5	0

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.8 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (13.0)	7 (6.9)	6 (11.5)	2 (3.9)	0.6519
Number (%) of patients censored	87 (87.0)	95 (93.1)	46 (88.5)	49 (96.1)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (10.973 to NC)	NC (NC to NC)	NC (5.257 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0808		0.1181	
Hazard ratio (95% CI) vs Pd	-	0.45 (0.18 to 1.13)		0.30 (0.06 to 1.49)	
P-value	-	0.0890		0.1409	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (30.0)	3 (21.4)	34 (23.8)	29 (20.7)	0.5564
Number (%) of patients censored	7 (70.0)	11 (78.6)	109 (76.2)	111 (79.3)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	1.74 (0.920 to NC)	NC (1.314 to NC)	9.30 (1.938 to NC)	NC (2.825 to NC)	
Median (95% CI)	NC (0.920 to NC)	NC (1.380 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5002		0.3947	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.12 to 2.88)		0.81 (0.49 to 1.32)	
P-value	-	0.5054		0.3960	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	6 (42.9)	45 (31.5)	63 (45.0)	0.4703
Number (%) of patients censored	9 (90.0)	8 (57.1)	98 (68.5)	77 (55.0)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (2.825 to NC)	6.54 (0.986 to 13.010)	4.76 (2.333 to 9.396)	2.79 (2.037 to 4.665)	
Median (95% CI)	NC (2.825 to NC)	13.01 (5.027 to NC)	NC (NC to NC)	10.48 (6.144 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.251 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3222		0.0377	
Hazard ratio (95% CI) vs Pd	-	2.80 (0.33 to 23.49)		1.50 (1.02 to 2.19)	
P-value	-	0.3429		0.0390	
Hazard ratio inverted (95% CI) vs IPd		-		0.67 (0.46 to 0.98)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (20.0)	2 (14.3)	23 (16.1)	21 (15.0)	0.5002
Number (%) of patients censored	8 (80.0)	12 (85.7)	120 (83.9)	119 (85.0)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (0.920 to NC)	NC (1.380 to NC)	NC (9.823 to NC)	NC (11.828 to NC)	
Median (95% CI)	NC (0.920 to NC)	NC (8.608 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3773		0.6057	
Hazard ratio (95% CI) vs Pd	-	0.40 (0.05 to 3.21)		0.86 (0.47 to 1.55)	
P-value	-	0.3908		0.6059	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (14.3)	19 (13.3)	7 (5.0)	0.9874
Number (%) of patients censored	10 (100.0)	12 (85.7)	124 (86.7)	133 (95.0)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (NC to NC)	NC (2.661 to NC)	NC (11.992 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (7.885 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4054		0.0092	
Hazard ratio (95% CI) vs Pd	-			0.33 (0.14 to 0.79)	
P-value	-	0.9972		0.0131	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_detpl_mri_de_i_t_x.rtf (08APR2021 14:54)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (24.0)	13 (14.9)	13 (26.5)	18 (32.7)	0.1475
Number (%) of patients censored	73 (76.0)	74 (85.1)	36 (73.5)	37 (67.3)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	9.30 (1.150 to NC)	NC (7.524 to NC)	3.98 (1.018 to NC)	1.91 (1.183 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0846		0.6830	
Hazard ratio (95% CI) vs Pd	-	0.55 (0.28 to 1.09)		1.16 (0.57 to 2.37)	
P-value	-	0.0891		0.6833	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_impl_crcl_de_i_t_x.rtf (08APR2021 14:54)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (30.2)	43 (49.4)	13 (26.5)	24 (43.6)	0.9429
Number (%) of patients censored	67 (69.8)	44 (50.6)	36 (73.5)	31 (56.4)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	4.76 (2.333 to NC)	3.78 (1.906 to 4.928)	6.83 (2.530 to NC)	2.66 (2.037 to 4.731)	
Median (95% CI)	NC (NC to NC)	9.95 (5.717 to NC)	NC (10.678 to NC)	NC (4.665 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0319		0.1326	
Hazard ratio (95% CI) vs Pd	-	1.67 (1.04 to 2.67)		1.67 (0.85 to 3.28)	
P-value	-	0.0338		0.1369	
Hazard ratio inverted (95% CI) vs IPd		-		0.60 (0.30 to 1.18)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_detl_crcl_de_i_t_x.rtf (08APR2021 14:54)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (17.7)	8 (9.2)	8 (16.3)	14 (25.5)	0.0688
Number (%) of patients censored	79 (82.3)	79 (90.8)	41 (83.7)	41 (74.5)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (4.698 to NC)	NC (NC to NC)	NC (3.745 to NC)	10.22 (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0597		0.4599	
Hazard ratio (95% CI) vs Pd	-	0.46 (0.20 to 1.06)		1.39 (0.58 to 3.31)	
P-value	-	0.0665		0.4619	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (8.3)	7 (8.0)	8 (16.3)	2 (3.6)	0.0936
Number (%) of patients censored	88 (91.7)	80 (92.0)	41 (83.7)	53 (96.4)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	11.99 (4.665 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7593		0.0146	
Hazard ratio (95% CI) vs Pd	-	0.85 (0.31 to 2.36)		0.18 (0.04 to 0.85)	
P-value	-	0.7598		0.0302	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	36 (23.8)	31 (20.4)	0.9410
Number (%) of patients censored	1 (50.0)	1 (50.0)	115 (76.2)	121 (79.6)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	1.97 (1.971 to NC)	9.30 (1.906 to NC)	NC (2.990 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (1.971 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (1.971 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.3052	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		0.78 (0.48 to 1.26)	
P-value	-	0.8092		0.3059	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	46 (30.5)	68 (44.7)	0.9800
Number (%) of patients censored	2 (100.0)	1 (50.0)	105 (69.5)	84 (55.3)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (NC to NC)	0.99 (0.986 to NC)	4.76 (2.595 to 10.251)	3.32 (2.168 to 4.731)	
Median (95% CI)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	13.01 (6.998 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.0311	
Hazard ratio (95% CI) vs Pd	-			1.51 (1.04 to 2.19)	
P-value	-	0.9990		0.0323	
Hazard ratio inverted (95% CI) vs IPd		-		0.66 (0.46 to 0.97)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_detl_prmab_de_i_t_x.rtf (08APR2021 14:54)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	24 (15.9)	22 (14.5)	0.9655
Number (%) of patients censored	1 (50.0)	1 (50.0)	127 (84.1)	130 (85.5)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	1.97 (1.971 to NC)	NC (9.823 to NC)	NC (11.828 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (1.971 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (1.971 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.4924	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		0.82 (0.46 to 1.46)	
P-value	-	0.8092		0.4932	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_imppl_prmab_de_i_t_x.rtf (08APR2021 14:55)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	19 (12.6)	9 (5.9)	0.9997
Number (%) of patients censored	2 (100.0)	2 (100.0)	132 (87.4)	143 (94.1)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0241	
Hazard ratio (95% CI) vs Pd	-			0.41 (0.19 to 0.91)	
P-value	-			0.0290	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (22.6)	21 (17.8)	11 (28.9)	11 (30.6)	0.4079
Number (%) of patients censored	89 (77.4)	97 (82.2)	27 (71.1)	25 (69.4)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (1.741 to NC)	NC (3.187 to NC)	4.83 (1.051 to NC)	2.99 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.524 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2197		0.8872	
Hazard ratio (95% CI) vs Pd	-	0.70 (0.39 to 1.24)		1.06 (0.46 to 2.45)	
P-value	-	0.2222		0.8871	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (29.6)	53 (44.9)	12 (31.6)	16 (44.4)	0.8744
Number (%) of patients censored	81 (70.4)	65 (55.1)	26 (68.4)	20 (55.6)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	5.03 (2.595 to 10.678)	3.75 (2.070 to 4.731)	7.46 (1.183 to NC)	2.50 (1.183 to 5.158)	
Median (95% CI)	NC (NC to NC)	13.01 (6.538 to NC)	NC (10.251 to NC)	8.41 (3.778 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0606		0.2144	
Hazard ratio (95% CI) vs Pd	-	1.51 (0.98 to 2.32)		1.60 (0.76 to 3.40)	
P-value	-	0.0624		0.2185	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_detl_refr4_de_i_t_x.rtf (08APR2021 14:54)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (16.5)	16 (13.6)	6 (15.8)	7 (19.4)	0.4417
Number (%) of patients censored	96 (83.5)	102 (86.4)	32 (84.2)	29 (80.6)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (5.585 to NC)	NC (11.828 to NC)	NC (1.281 to NC)	NC (3.745 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3294		0.7797	
Hazard ratio (95% CI) vs Pd	-	0.72 (0.37 to 1.40)		1.17 (0.39 to 3.48)	
P-value	-	0.3316		0.7803	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (13.0)	5 (4.2)	4 (10.5)	4 (11.1)	0.1263
Number (%) of patients censored	100 (87.0)	113 (95.8)	34 (89.5)	32 (88.9)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (10.973 to NC)	NC (NC to NC)	NC (7.031 to NC)	NC (9.101 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0069		0.9888	
Hazard ratio (95% CI) vs Pd	-	0.27 (0.10 to 0.75)		1.01 (0.25 to 4.04)	
P-value	-	0.0118		0.9888	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (24.3)	31 (21.1)	2 (22.2)	1 (14.3)	0.8826
Number (%) of patients censored	109 (75.7)	116 (78.9)	7 (77.8)	6 (85.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	4.83 (1.741 to NC)	NC (2.825 to NC)	NC (0.986 to NC)	NC (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3193		0.7236	
Hazard ratio (95% CI) vs Pd	-	0.78 (0.48 to 1.27)		0.65 (0.06 to 7.18)	
P-value	-	0.3205		0.7257	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (30.6)	63 (42.9)	2 (22.2)	6 (85.7)	0.0473
Number (%) of patients censored	100 (69.4)	84 (57.1)	7 (77.8)	1 (14.3)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	4.76 (2.333 to 7.458)	3.78 (2.267 to 4.731)	10.68 (9.396 to NC)	1.05 (1.018 to 3.088)	
Median (95% CI)	NC (NC to NC)	NC (6.998 to NC)	NC (9.396 to NC)	3.09 (1.018 to 10.480)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	10.48 (2.037 to 10.480)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0972		0.0005	
Hazard ratio (95% CI) vs Pd	-	1.38 (0.94 to 2.03)		20.35 (2.27 to 182.26)	
P-value	-	0.0986		0.0071	
Hazard ratio inverted (95% CI) vs IPd		-		0.05 (0.01 to 0.44)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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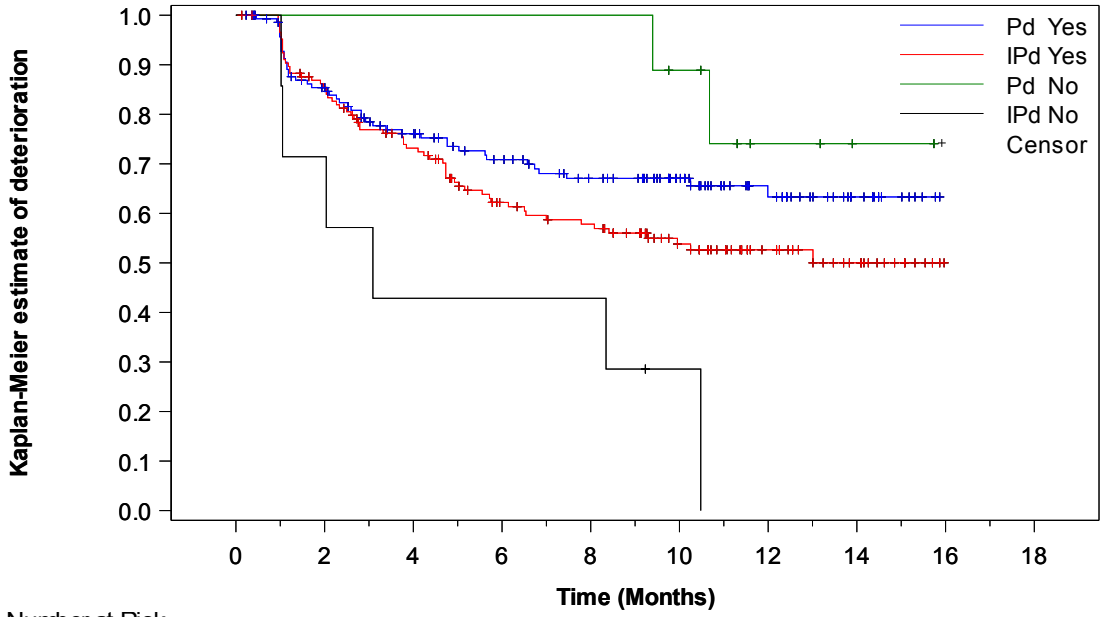
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to refractory to IMID status (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd Yes	144	100	79	64	28	6	0
IPd Yes	147	105	72	58	28	7	0
Pd No	9	9	9	9	3	1	0
IPd No	7	4	3	2	0	0	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (16.0)	23 (15.6)	2 (22.2)	0 (0.0)	0.9886
Number (%) of patients censored	121 (84.0)	124 (84.4)	7 (77.8)	7 (100.0)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (9.429 to NC)	NC (11.828 to NC)	NC (0.986 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6443		0.1987	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.49 to 1.56)			
P-value	-	0.6436		0.9977	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.7 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (12.5)	8 (5.4)	1 (11.1)	1 (14.3)	0.3362
Number (%) of patients censored	126 (87.5)	139 (94.6)	8 (88.9)	6 (85.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (11.992 to NC)	NC (NC to NC)	NC (10.678 to NC)	NC (10.448 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.678 to NC)	NC (10.448 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.448 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0156		0.5770	
Hazard ratio (95% CI) vs Pd	-	0.37 (0.16 to 0.86)		2.16 (0.13 to 34.61)	
P-value	-	0.0202		0.5863	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (23.9)	21 (22.6)	16 (24.6)	11 (18.0)	0.4380
Number (%) of patients censored	67 (76.1)	72 (77.4)	49 (75.4)	50 (82.0)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	9.30 (1.183 to NC)	NC (1.938 to NC)	3.98 (1.117 to NC)	NC (2.267 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7434		0.2145	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.49 to 1.65)		0.62 (0.29 to 1.33)	
P-value	-	0.7431		0.2189	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (33.0)	41 (44.1)	17 (26.2)	28 (45.9)	0.5591
Number (%) of patients censored	59 (67.0)	52 (55.9)	48 (73.8)	33 (54.1)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	4.17 (2.037 to 7.458)	3.78 (2.267 to 4.731)	9.40 (2.267 to NC)	3.09 (1.216 to 5.552)	
Median (95% CI)	NC (10.251 to NC)	10.25 (5.717 to NC)	NC (11.992 to NC)	13.01 (5.552 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1649		0.0657	
Hazard ratio (95% CI) vs Pd	-	1.40 (0.87 to 2.25)		1.75 (0.96 to 3.20)	
P-value	-	0.1669		0.0692	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (18.2)	14 (15.1)	9 (13.8)	9 (14.8)	0.7698
Number (%) of patients censored	72 (81.8)	79 (84.9)	56 (86.2)	52 (85.2)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (4.435 to NC)	NC (9.298 to NC)	NC (5.585 to NC)	NC (6.637 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4705		0.8468	
Hazard ratio (95% CI) vs Pd	-	0.77 (0.38 to 1.57)		0.91 (0.36 to 2.30)	
P-value	-	0.4718		0.8467	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Diarrhea
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (9.1)	5 (5.4)	11 (16.9)	4 (6.6)	0.4606
Number (%) of patients censored	80 (90.9)	88 (94.6)	54 (83.1)	57 (93.4)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	11.99 (5.257 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2994		0.0282	
Hazard ratio (95% CI) vs Pd	-	0.56 (0.18 to 1.71)		0.30 (0.09 to 0.94)	
P-value	-	0.3063		0.0387	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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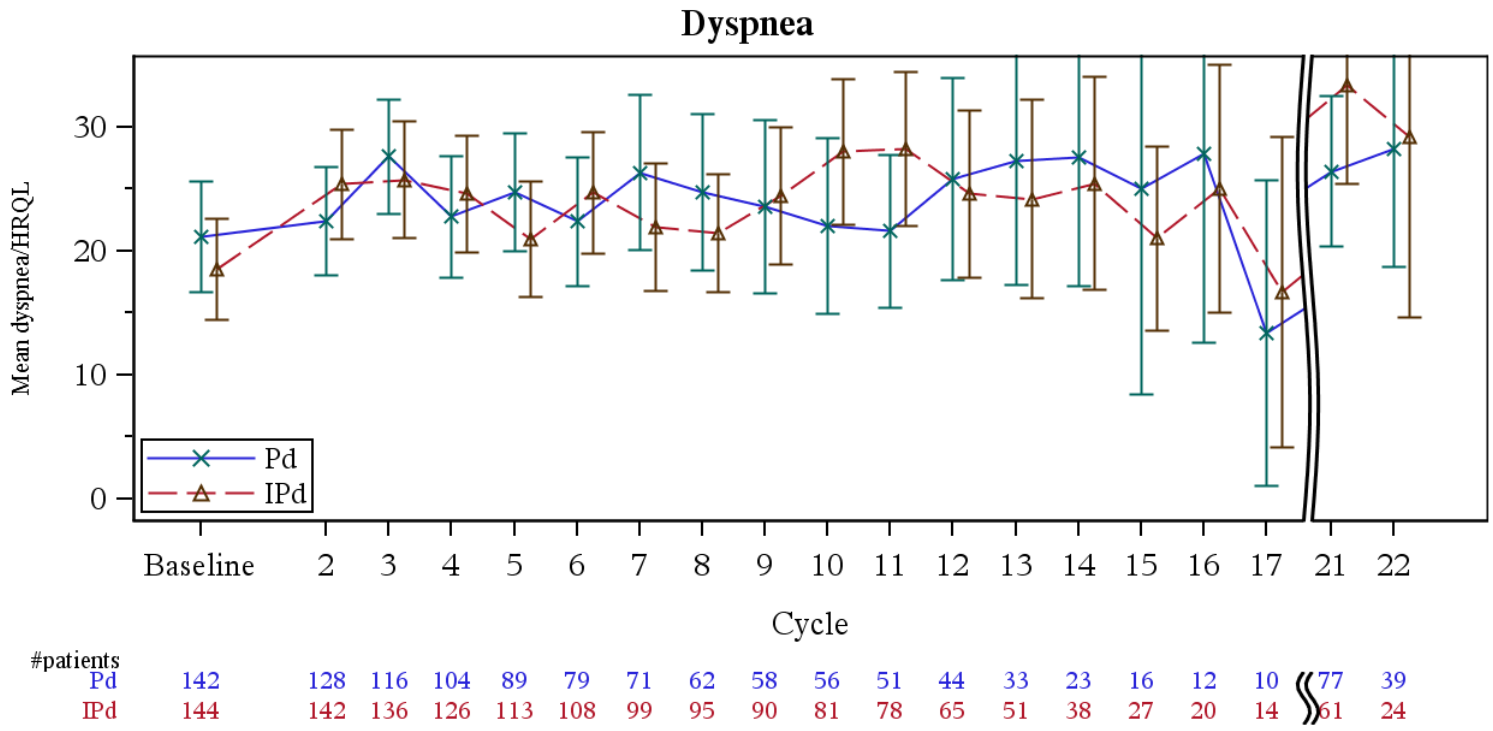
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Dyspnea
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-C30 - Mean and 95% CI for dyspnea score over time (LOCF) - ITT population



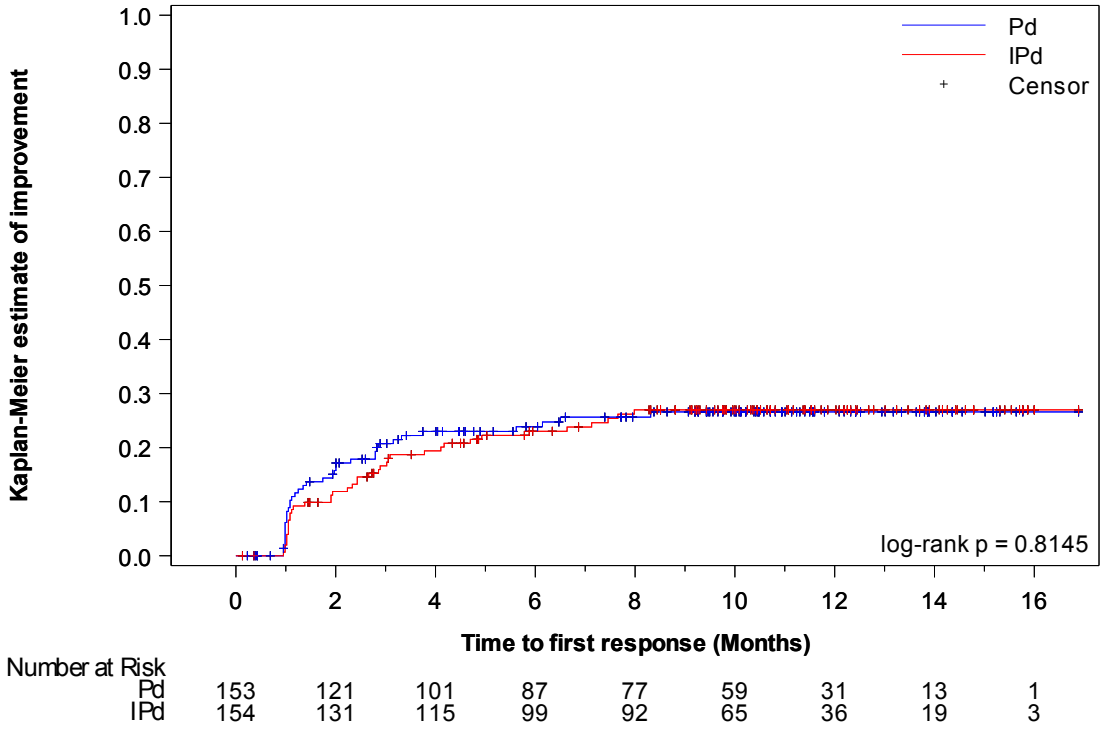
A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_line_i_f.sas OUT=REPORT/OUTPUT/eff_qlq_line_c30_dys_de_i_f_x.rtf (12FEB2021 17:15)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Dyspnea
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-C30 - Time to first improvement by 15 pt in dyspnea (LOCF) - ITT population

First improvement 15 points Dyspnea (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	37 (24.2)	39 (25.3)
Number (%) of patients censored	116 (75.8)	115 (74.7)
Kaplan-Meier estimates of dyspnea in months		
25% quantile (95% CI)	6.51 (2.300 to NC)	7.46 (3.055 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8145
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.95 (0.60 to 1.49)
P-value	-	0.8144
Probability (95% CI)[c]		
2 Months	0.16 (0.104 to 0.221)	0.12 (0.073 to 0.176)
4 Months	0.23 (0.165 to 0.302)	0.19 (0.135 to 0.261)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_imp15l_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Dyspnea
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-C30 - Time to first improvement by 15 pt in dyspnea - Kaplan-Meier curve (LOCF) - ITT population



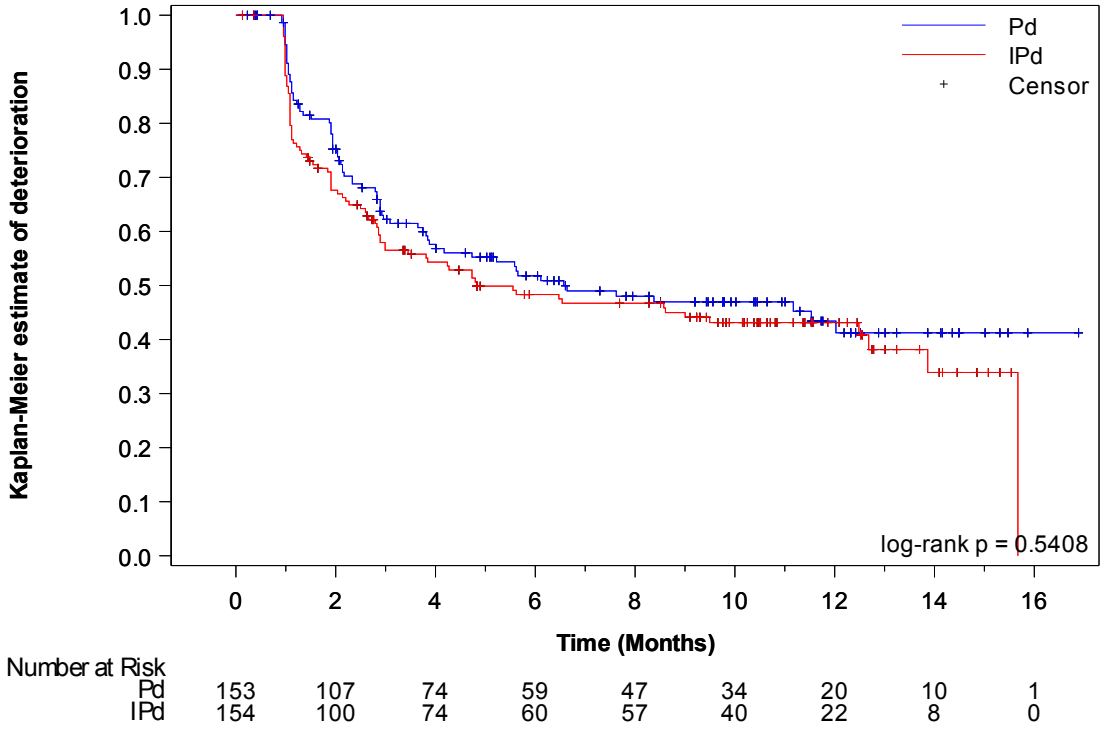
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_imp15l_de_i_f_x.rtf (08APR2021 15:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Dyspnea
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-C30 - Time to first deterioration by 15 pt in dyspnea (LOCF) - ITT population

First deterioration 15 points Dyspnea (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	75 (49.0)	86 (55.8)
Number (%) of patients censored	78 (51.0)	68 (44.2)
Kaplan-Meier estimates of dyspnea in months		
25% quantile (95% CI)	2.04 (1.281 to 2.793)	1.30 (1.084 to 1.906)
Median (95% CI)	6.57 (3.844 to NC)	4.83 (2.891 to 12.485)
75% quantile (95% CI)	NC (NC to NC)	15.67 (13.864 to 15.671)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5408
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.10 (0.81 to 1.51)
P-value	-	0.5414
Probability (95% CI)[c]		
2 Months	0.75 (0.674 to 0.815)	0.68 (0.595 to 0.744)
4 Months	0.58 (0.490 to 0.653)	0.54 (0.459 to 0.620)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_det15l_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Dyspnea
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-C30 - Time to first deterioration by 15 pt in dyspnea - Kaplan-Meier curve (LOCF) - ITT population



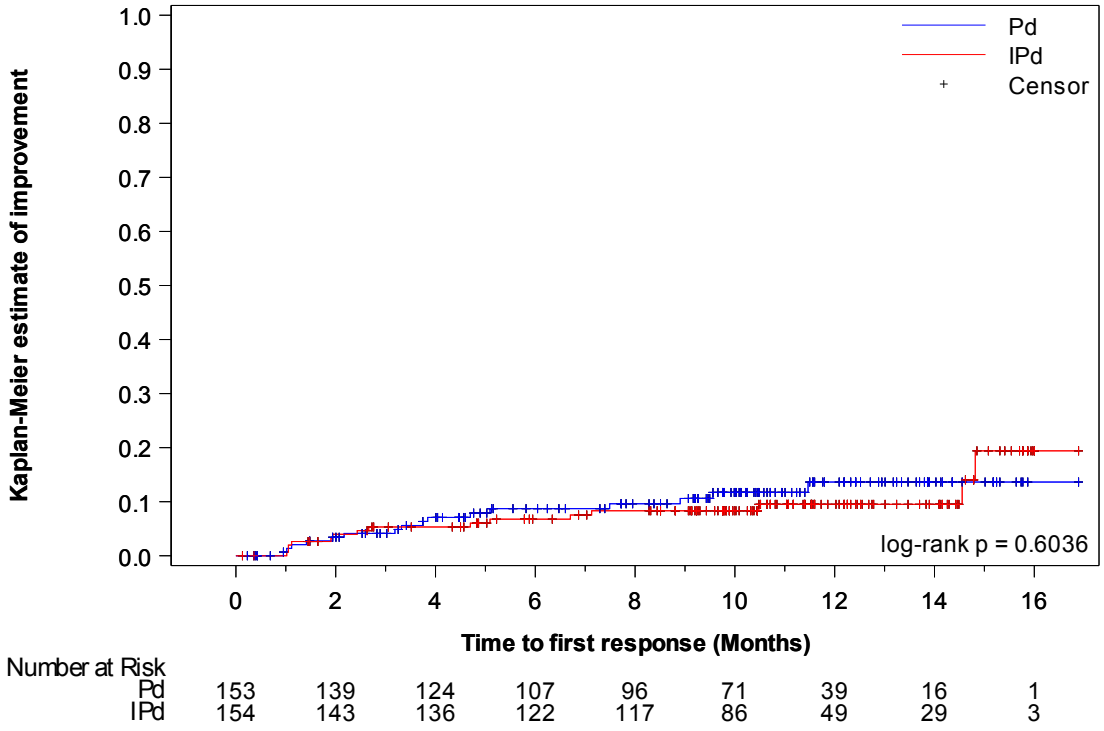
A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_det15l_de_i_f_x.rtf (08APR2021 15:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Dyspnea
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in dyspnea (LOCF) - ITT population

First permanent improvement 15 points Dyspnea (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	16 (10.5)	15 (9.7)
Number (%) of patients censored	137 (89.5)	139 (90.3)
Kaplan-Meier estimates of dyspnea in months		
25% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6036
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.83 (0.41 to 1.68)
P-value	-	0.6041
Probability (95% CI)[c]		
2 Months	0.03 (0.013 to 0.073)	0.04 (0.016 to 0.080)
4 Months	0.07 (0.036 to 0.121)	0.05 (0.025 to 0.097)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_imp15pl_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Dyspnea
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-C30 - Time until permanent improvement by 15 pt in dyspnea - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_imp15pl_de_i_f_x.rtf (08APR2021 15:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Dyspnea
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in dyspnea (LOCF) - ITT population

First permanent deterioration 15 points Dyspnea (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	38 (24.8)	44 (28.6)
Number (%) of patients censored	115 (75.2)	110 (71.4)
Kaplan-Meier estimates of dyspnea in months		
25% quantile (95% CI)	8.38 (4.205 to NC)	8.61 (5.552 to 15.671)
Median (95% CI)	NC (14.686 to NC)	NC (15.671 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9080
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.03 (0.66 to 1.59)
P-value	-	0.9081
Probability (95% CI)[c]		
2 Months	0.89 (0.827 to 0.931)	0.89 (0.833 to 0.934)
4 Months	0.82 (0.751 to 0.878)	0.85 (0.785 to 0.901)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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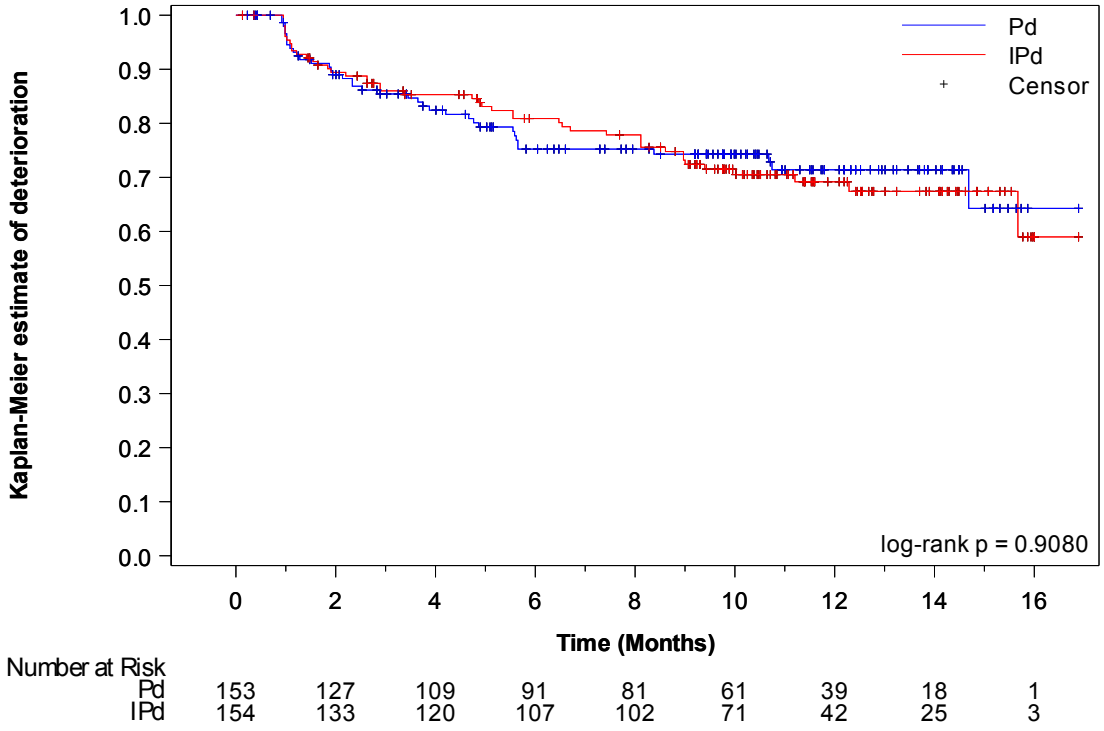
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Dyspnea
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-C30 - Time until permanent deterioration by 15 pt in dyspnea - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_det15pl_de_i_f_x.rtf (08APR2021 15:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (17.1)	16 (29.6)	16 (29.6)	12 (17.6)	9 (31.0)	11 (34.4)	0.0824
Number (%) of patients censored	58 (82.9)	38 (70.4)	38 (70.4)	56 (82.4)	20 (69.0)	21 (65.6)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	NC (3.745 to NC)	4.93 (1.380 to NC)	3.15 (1.741 to NC)	NC (4.107 to NC)	1.18 (0.986 to NC)	2.66 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.971 to NC)	NC (5.881 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1456		0.0720		0.8720	
Hazard ratio (95% CI) vs Pd	-	1.73 (0.82 to 3.66)		0.51 (0.24 to 1.08)		0.93 (0.38 to 2.25)	
P-value	-	0.1506		0.0775		0.8714	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_impl_age_de_i_t_x.rtf (08APR2021 14:47)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (51.4)	31 (57.4)	22 (40.7)	38 (55.9)	17 (58.6)	17 (53.1)	0.2285
Number (%) of patients censored	34 (48.6)	23 (42.6)	32 (59.3)	30 (44.1)	12 (41.4)	15 (46.9)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	1.91 (1.117 to 2.825)	1.31 (1.084 to 2.595)	2.33 (1.216 to 4.172)	1.08 (1.018 to 1.906)	1.94 (0.986 to 2.891)	2.20 (0.986 to 4.797)	
Median (95% CI)	5.65 (2.825 to NC)	2.99 (2.595 to 15.671)	NC (4.008 to NC)	4.73 (2.037 to NC)	5.59 (2.037 to 11.532)	8.61 (3.811 to NC)	
75% quantile (95% CI)	NC (NC to NC)	15.67 (13.864 to 15.671)	NC (NC to NC)	NC (12.682 to NC)	11.53 (5.618 to NC)	NC (9.002 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6326		0.0946		0.2967	
Hazard ratio (95% CI) vs Pd	-	1.12 (0.70 to 1.82)		1.56 (0.92 to 2.64)		0.69 (0.35 to 1.38)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (7.1)	6 (11.1)	9 (16.7)	4 (5.9)	2 (6.9)	5 (15.6)	0.0889
Number (%) of patients censored	65 (92.9)	48 (88.9)	45 (83.3)	64 (94.1)	27 (93.1)	27 (84.4)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	NC (11.466 to NC)	14.82 (14.817 to NC)	NC (5.092 to NC)	NC (14.554 to NC)	NC (2.168 to NC)	NC (1.117 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5517		0.0240		0.3341	
Hazard ratio (95% CI) vs Pd	-	1.43 (0.44 to 4.70)		0.28 (0.09 to 0.91)		2.20 (0.43 to 11.33)	
P-value	-	0.5538		0.0345		0.3465	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (25.7)	20 (37.0)	9 (16.7)	18 (26.5)	11 (37.9)	6 (18.8)	0.0363
Number (%) of patients censored	52 (74.3)	34 (63.0)	45 (83.3)	50 (73.5)	18 (62.1)	26 (81.3)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	10.68 (3.450 to NC)	2.89 (1.413 to 15.671)	NC (4.205 to NC)	9.40 (5.552 to NC)	3.75 (1.018 to 8.378)	11.20 (5.125 to NC)	
Median (95% CI)	NC (14.686 to NC)	15.67 (7.425 to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.665 to NC)	NC (11.203 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.671 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2583		0.3486		0.0214	
Hazard ratio (95% CI) vs Pd	-	1.44 (0.76 to 2.74)		1.46 (0.66 to 3.26)		0.33 (0.12 to 0.89)	
P-value	-	0.2609		0.3515		0.0286	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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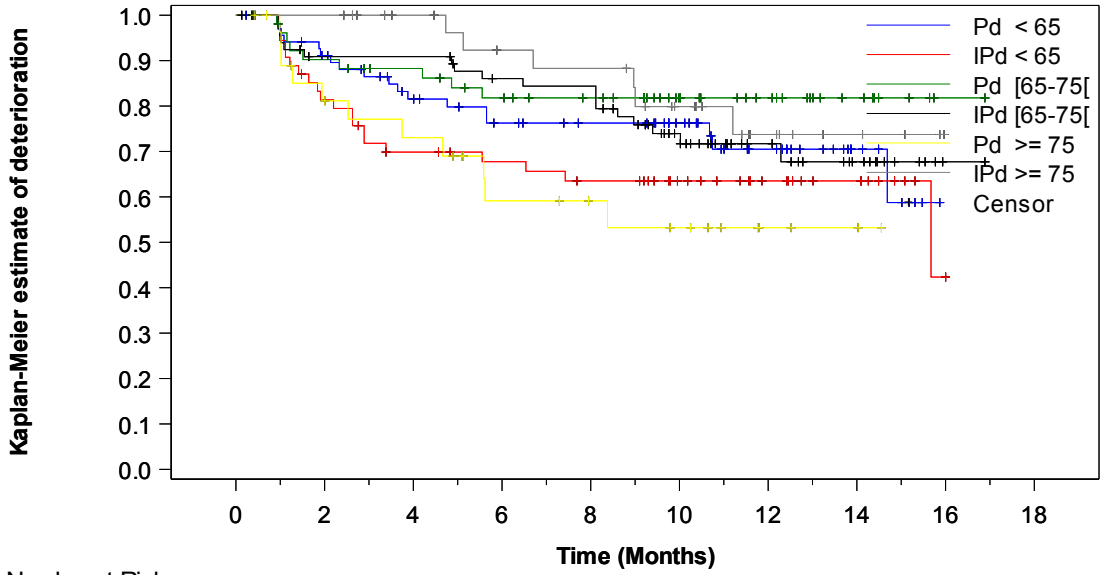
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.7 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to age (IRT) (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd < 65	70	55	42	38	20	5	0
IPd < 65	54	37	32	29	15	5	0
Pd [65-75[	54	43	37	31	16	4	0
IPd [65-75[	68	58	52	43	19	5	0
Pd >= 75	29	19	12	9	3	0	0
IPd >= 75	32	29	23	20	8	3	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_detpl_age_de_i_f_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	24 (23.8)	22 (21.6)	13 (25.0)	17 (32.7)	0.3864
Number (%) of patients censored	77 (76.2)	80 (78.4)	39 (75.0)	35 (67.3)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	6.51 (2.004 to NC)	NC (3.778 to NC)	5.62 (1.084 to NC)	3.09 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5155		0.5735	
Hazard ratio (95% CI) vs Pd	-	0.83 (0.46 to 1.47)		1.23 (0.60 to 2.53)	
P-value	-	0.5154		0.5741	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_impl_plne_de_i_t_x.rtf (08APR2021 14:47)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (45.5)	56 (54.9)	29 (55.8)	30 (57.7)	0.3043
Number (%) of patients censored	55 (54.5)	46 (45.1)	23 (44.2)	22 (42.3)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.94 (1.281 to 2.825)	1.45 (1.051 to 2.201)	2.33 (1.018 to 2.924)	1.22 (1.084 to 2.891)	
Median (95% CI)	11.17 (3.877 to NC)	4.27 (2.793 to 12.682)	5.65 (2.891 to 12.025)	8.61 (2.891 to 13.864)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.622 to NC)	15.67 (12.485 to 15.671)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2068		0.5799	
Hazard ratio (95% CI) vs Pd	-	1.28 (0.87 to 1.90)		0.86 (0.51 to 1.45)	
P-value	-	0.2080		0.5802	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	13 (12.9)	10 (9.8)	3 (5.8)	5 (9.6)	0.3508
Number (%) of patients censored	88 (87.1)	92 (90.2)	49 (94.2)	47 (90.4)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (9.561 to NC)	NC (14.554 to NC)	NC (11.466 to NC)	NC (10.480 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3519		0.5791	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.30 to 1.55)		1.50 (0.36 to 6.27)	
P-value	-	0.3553		0.5817	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (19.8)	31 (30.4)	18 (34.6)	13 (25.0)	0.0396
Number (%) of patients censored	81 (80.2)	71 (69.6)	34 (65.4)	39 (75.0)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	14.69 (4.665 to NC)	8.11 (4.731 to 12.287)	4.25 (1.150 to 8.378)	10.02 (3.384 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (5.651 to NC)	15.67 (15.671 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.671 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1611		0.1172	
Hazard ratio (95% CI) vs Pd	-	1.49 (0.85 to 2.62)		0.57 (0.28 to 1.16)	
P-value	-	0.1639		0.1220	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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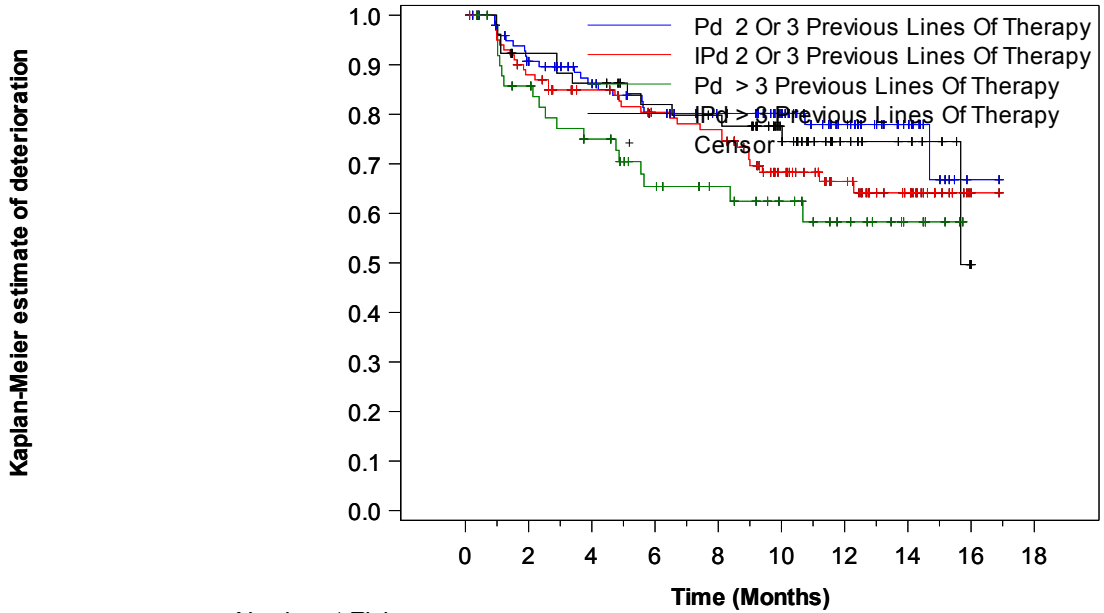
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.7 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to nb of prior lines (IRT) (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd 2 Or 3 Previous Lines Of Therapy	101	81	65	58	28	6	0
IPd 2 Or 3 Previous Lines Of Therapy	102	80	69	57	31	8	0
Pd > 3 Previous Lines Of Therapy	52	36	26	20	11	3	0
IPd > 3 Previous Lines Of Therapy	52	44	38	35	11	5	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_detpl_plne_de_i_f_x.rtf (08APR2021 14:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (21.4)	23 (25.8)	22 (26.5)	16 (24.6)	0.4196
Number (%) of patients censored	55 (78.6)	66 (74.2)	61 (73.5)	49 (75.4)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (2.004 to NC)	4.93 (2.661 to NC)	3.75 (1.413 to NC)	7.98 (2.431 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6400		0.4982	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.61 to 2.24)		0.80 (0.42 to 1.53)	
P-value	-	0.6403		0.4991	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_impl_sex_de_i_t_x.rtf (08APR2021 14:47)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (50.0)	49 (55.1)	40 (48.2)	37 (56.9)	0.9554
Number (%) of patients censored	35 (50.0)	40 (44.9)	43 (51.8)	28 (43.1)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.94 (1.347 to 2.957)	1.30 (1.084 to 2.136)	2.04 (1.117 to 2.825)	1.25 (0.986 to 2.595)	
Median (95% CI)	5.62 (3.647 to NC)	4.83 (2.661 to 13.864)	6.64 (2.891 to NC)	6.47 (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	15.67 (13.864 to 15.671)	NC (NC to NC)	NC (12.682 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4369		0.5922	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.77 to 1.83)		1.13 (0.72 to 1.77)	
P-value	-	0.4375		0.5924	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (7.1)	9 (10.1)	11 (13.3)	6 (9.2)	0.2928
Number (%) of patients censored	65 (92.9)	80 (89.9)	72 (86.7)	59 (90.8)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (8.903 to NC)	NC (14.817 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6288		0.2895	
Hazard ratio (95% CI) vs Pd	-	1.31 (0.44 to 3.92)		0.59 (0.22 to 1.59)	
P-value	-	0.6298		0.2952	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (28.6)	20 (22.5)	18 (21.7)	24 (36.9)	0.0675
Number (%) of patients censored	50 (71.4)	69 (77.5)	65 (78.3)	41 (63.1)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	5.55 (2.136 to NC)	15.67 (5.552 to NC)	10.74 (4.205 to NC)	6.54 (1.906 to 8.969)	
Median (95% CI)	NC (NC to NC)	NC (15.671 to NC)	NC (14.686 to NC)	NC (11.203 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2570		0.1642	
Hazard ratio (95% CI) vs Pd	-	0.70 (0.38 to 1.30)		1.54 (0.83 to 2.84)	
P-value	-	0.2595		0.1674	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (25.4)	29 (24.6)	4 (21.1)	6 (25.0)	0.6735
Number (%) of patients censored	94 (74.6)	89 (75.4)	15 (78.9)	18 (75.0)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	6.14 (2.004 to NC)	7.98 (3.055 to NC)	NC (0.986 to NC)	7.13 (2.234 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.129 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5665		0.8025	
Hazard ratio (95% CI) vs Pd	-	0.86 (0.52 to 1.43)		1.18 (0.33 to 4.17)	
P-value	-	0.5668		0.8027	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	62 (49.2)	67 (56.8)	11 (57.9)	15 (62.5)	0.9569
Number (%) of patients censored	64 (50.8)	51 (43.2)	8 (42.1)	9 (37.5)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	2.04 (1.511 to 2.793)	1.41 (1.084 to 2.136)	1.12 (1.018 to 2.891)	1.10 (0.986 to 1.906)	
Median (95% CI)	6.57 (3.844 to NC)	5.55 (2.858 to 12.682)	2.89 (1.117 to NC)	3.84 (1.117 to NC)	
75% quantile (95% CI)	NC (NC to NC)	15.67 (13.864 to 15.671)	NC (2.891 to NC)	NC (4.731 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4080		0.7043	
Hazard ratio (95% CI) vs Pd	-	1.16 (0.82 to 1.63)		1.16 (0.53 to 2.53)	
P-value	-	0.4081		0.7046	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_detl_race_de_i_t_x.rtf (08APR2021 14:47)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (11.9)	11 (9.3)	0 (0.0)	2 (8.3)	0.9910
Number (%) of patients censored	111 (88.1)	107 (90.7)	19 (100.0)	22 (91.7)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (11.466 to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (2.661 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3016		0.1890	
Hazard ratio (95% CI) vs Pd	-	0.66 (0.30 to 1.45)			
P-value	-	0.3049		0.9977	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_imppl_race_de_i_t_x.rtf (08APR2021 14:47)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (27.0)	35 (29.7)	3 (15.8)	8 (33.3)	0.2727
Number (%) of patients censored	92 (73.0)	83 (70.3)	16 (84.2)	16 (66.7)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	5.62 (3.647 to NC)	8.97 (4.862 to 15.671)	NC (1.018 to NC)	6.70 (1.117 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (15.671 to NC)	NC (NC to NC)	NC (6.702 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9063		0.2302	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.61 to 1.56)		2.21 (0.59 to 8.34)	
P-value	-	0.9063		0.2423	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_detpl_race_de_i_t_x.rtf (08APR2021 14:47)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (25.0)	33 (24.6)	32 (24.6)	0.9827
Number (%) of patients censored	3 (100.0)	3 (75.0)	101 (75.4)	98 (75.4)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (NC to NC)	NC (3.055 to NC)	6.51 (2.004 to NC)	7.66 (3.088 to NC)	
Median (95% CI)	NC (NC to NC)	NC (3.055 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (3.055 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.7041	
Hazard ratio (95% CI) vs Pd	-			0.91 (0.56 to 1.48)	
P-value	-	0.9985		0.7040	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_impl_ethn_de_i_t_x.rtf (08APR2021 14:47)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (66.7)	2 (50.0)	66 (49.3)	75 (57.7)	0.0763
Number (%) of patients censored	1 (33.3)	2 (50.0)	68 (50.7)	55 (42.3)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.28 (1.281 to 1.347)	2.55 (2.497 to NC)	1.94 (1.150 to 2.825)	1.15 (1.084 to 1.906)	
Median (95% CI)	1.31 (1.281 to 1.347)	NC (2.497 to NC)	6.57 (3.811 to NC)	4.83 (2.858 to 12.485)	
75% quantile (95% CI)	1.35 (1.281 to 1.347)	NC (2.497 to NC)	NC (NC to NC)	15.67 (13.864 to 15.671)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0177		0.3102	
Hazard ratio (95% CI) vs Pd	-			1.19 (0.85 to 1.65)	
P-value	-	0.9982		0.3111	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	13 (9.7)	13 (10.0)	1.0000
Number (%) of patients censored	3 (100.0)	4 (100.0)	121 (90.3)	117 (90.0)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.8141	
Hazard ratio (95% CI) vs Pd	-			0.91 (0.42 to 1.97)	
P-value	-			0.8139	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	1 (25.0)	33 (24.6)	38 (29.2)	0.3551
Number (%) of patients censored	2 (66.7)	3 (75.0)	101 (75.4)	92 (70.8)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (9.396 to NC)	10.68 (3.877 to NC)	8.11 (5.125 to 15.671)	
Median (95% CI)	NC (1.281 to NC)	NC (9.396 to NC)	NC (14.686 to NC)	NC (15.671 to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (9.396 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.8062	
Hazard ratio (95% CI) vs Pd	-			1.06 (0.66 to 1.69)	
P-value	-	0.9985		0.8065	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	21 (27.6)	11 (20.0)	4 (20.0)	6 (21.4)	1 (20.0)	2 (28.6)	3 (20.0)	5 (23.8)	8 (21.6)	15 (34.9)	0.5717
Number (%) of patients censored	55 (72.4)	44 (80.0)	16 (80.0)	22 (78.6)	4 (80.0)	5 (71.4)	12 (80.0)	16 (76.2)	29 (78.4)	28 (65.1)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	2.79 (1.183 to NC)	NC (2.431 to NC)	NC (0.986 to NC)	NC (1.018 to NC)	NC (0.953 to NC)	7.46 (3.055 to NC)	NC (0.986 to NC)	7.13 (2.234 to NC)	5.62 (1.938 to NC)	2.89 (1.117 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (3.055 to NC)	NC (3.154 to NC)	NC (7.129 to NC)	NC (NC to NC)	NC (6.637 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (7.458 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.2174		0.9793		0.7913		0.8012		0.2721	
Hazard ratio (95% CI) vs Pd	-	0.63 (0.31 to 1.32)		1.02 (0.29 to 3.60)		1.38 (0.12 to 15.32)		1.20 (0.29 to 5.03)		1.61 (0.68 to 3.80)	
P-value	-	0.2214		0.9794		0.7922		0.8015		0.2766	
Improvement probability (95% CI)[b]											
2 Months	0.197 (0.114 to 0.296)	0.111 (0.045 to 0.211)	0.158 (0.039 to 0.349)	0.179 (0.065 to 0.337)	0.200 (0.008 to 0.582)		0.067 (0.004 to 0.260)		0.113 (0.036 to 0.240)	0.167 (0.074 to 0.294)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	30 (39.5)	29 (52.7)	9 (45.0)	12 (42.9)	4 (80.0)	5 (71.4)	9 (60.0)	13 (61.9)	23 (62.2)	27 (62.8)	0.3240
Number (%) of patients censored	46 (60.5)	26 (47.3)	11 (55.0)	16 (57.1)	1 (20.0)	2 (28.6)	6 (40.0)	8 (38.1)	14 (37.8)	16 (37.2)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	2.89 (1.938 to 5.585)	1.22 (0.986 to 1.906)	1.22 (0.986 to 7.622)	2.25 (0.953 to 12.682)	0.99 (0.986 to 2.037)	1.91 (0.953 to 4.731)	1.12 (1.018 to 2.891)	1.12 (0.986 to 1.906)	1.94 (1.051 to 2.333)	1.91 (1.051 to 2.891)	
Median (95% CI)	12.02 (5.618 to NC)	2.99 (1.906 to NC)	7.62 (1.216 to NC)	12.68 (2.825 to NC)	1.35 (0.986 to NC)	4.73 (0.953 to NC)	2.89 (1.084 to NC)	3.84 (1.117 to NC)	2.92 (2.136 to 5.651)	5.62 (2.858 to 13.864)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.622 to NC)	NC (12.682 to NC)	2.04 (0.986 to NC)	NC (3.450 to NC)	NC (2.891 to NC)	NC (3.844 to NC)	NC (4.008 to NC)	15.67 (9.495 to 15.671)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_detl_greg_de_i_t_x.rtf (08APR2021 14:47)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.0700		0.8453		0.3808		0.8786		0.5102	
Hazard ratio (95% CI) vs Pd	-	1.60 (0.96 to 2.67)		0.92 (0.39 to 2.18)		0.55 (0.14 to 2.13)		1.07 (0.46 to 2.50)		0.83 (0.47 to 1.45)	
P-value	-	0.0725		0.8454		0.3868		0.8792		0.5108	
Deterioration probability (95% CI)[b]											
2 Months	0.830 (0.720 to 0.900)	0.629 (0.485 to 0.742)	0.684 (0.428 to 0.844)	0.750 (0.546 to 0.872)	0.400 (0.052 to 0.753)	0.714 (0.258 to 0.920)	0.600 (0.318 to 0.797)	0.567 (0.333 to 0.747)	0.746 (0.568 to 0.859)	0.737 (0.576 to 0.845)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_detl_greg_de_i_t_x.rtf (08APR2021 14:47)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	11 (14.5)	5 (9.1)	0 (0.0)	3 (10.7)	1 (20.0)	0 (0.0)	0 (0.0)	2 (9.5)	4 (10.8)	5 (11.6)	0.9942
Number (%) of patients censored	65 (85.5)	50 (90.9)	20 (100.0)	25 (89.3)	4 (80.0)	7 (100.0)	15 (100.0)	19 (90.5)	33 (89.2)	38 (88.4)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (7.491 to NC)	14.82 (14.817 to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (0.953 to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.661 to NC)	NC (3.745 to NC)	NC (10.480 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.2910		0.1461		0.2367		0.2084		0.7488	
Hazard ratio (95% CI) vs Pd	-	0.57 (0.20 to 1.64)								0.81 (0.21 to 3.04)	
P-value	-	0.2975		0.9958		0.9984		0.9978		0.7492	
Improvement probability (95% CI)[b]											
2 Months	0.042 (0.011 to 0.108)	0.037 (0.007 to 0.114)		0.107 (0.027 to 0.251)	0.200 (0.008 to 0.582)				0.029 (0.002 to 0.127)	0.024 (0.002 to 0.108)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	15 (19.7)	18 (32.7)	4 (20.0)	7 (25.0)	2 (40.0)	3 (42.9)	3 (20.0)	6 (28.6)	14 (37.8)	10 (23.3)	0.1924
Number (%) of patients censored	61 (80.3)	37 (67.3)	16 (80.0)	21 (75.0)	3 (60.0)	4 (57.1)	12 (80.0)	15 (71.4)	23 (62.2)	33 (76.7)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	10.68 (4.862 to NC)	2.20 (1.084 to NC)	NC (0.986 to NC)	11.20 (4.928 to NC)	4.21 (0.986 to NC)	4.73 (2.628 to NC)	NC (1.018 to NC)	8.11 (1.117 to NC)	3.65 (1.511 to 10.743)	12.29 (6.538 to NC)	
Median (95% CI)	NC (NC to NC)	NC (9.396 to NC)	NC (NC to NC)	NC (11.203 to NC)	NC (0.986 to NC)	NC (2.628 to NC)	NC (2.891 to NC)	NC (8.115 to NC)	14.69 (5.651 to NC)	NC (15.671 to NC)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (8.969 to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.1042		0.8157		0.9180		0.6133		0.0479	
Hazard ratio (95% CI) vs Pd	-	1.75 (0.88 to 3.48)		1.16 (0.34 to 3.99)		0.91 (0.15 to 5.47)		1.43 (0.36 to 5.71)		0.45 (0.20 to 1.01)	
P-value	-	0.1087		0.8158		0.9181		0.6152		0.0539	
Deterioration probability (95% CI)[b]											

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (25.8)	19 (24.7)	12 (21.4)	20 (26.0)	0.4449
Number (%) of patients censored	72 (74.2)	58 (75.3)	44 (78.6)	57 (74.0)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	5.62 (1.741 to NC)	7.46 (3.023 to NC)	NC (2.300 to NC)	7.66 (2.431 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5648		0.6158	
Hazard ratio (95% CI) vs Pd	-	0.84 (0.46 to 1.52)		1.20 (0.59 to 2.46)	
P-value	-	0.5653		0.6163	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (46.4)	44 (57.1)	30 (53.6)	42 (54.5)	0.3740
Number (%) of patients censored	52 (53.6)	33 (42.9)	26 (46.4)	35 (45.5)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	2.14 (1.511 to 3.088)	1.35 (1.084 to 2.037)	1.91 (1.051 to 2.333)	1.22 (1.084 to 2.793)	
Median (95% CI)	11.17 (4.172 to NC)	4.80 (2.201 to 15.671)	4.01 (2.333 to NC)	6.47 (2.858 to 13.864)	
75% quantile (95% CI)	NC (NC to NC)	15.67 (NC to NC)	NC (NC to NC)	NC (12.682 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2097		0.9170	
Hazard ratio (95% CI) vs Pd	-	1.30 (0.86 to 1.98)		0.98 (0.61 to 1.56)	
P-value	-	0.2111		0.9168	
Deterioration probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (13.4)	6 (7.8)	3 (5.4)	9 (11.7)	0.0793
Number (%) of patients censored	84 (86.6)	71 (92.2)	53 (94.6)	68 (88.3)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (11.466 to NC)	NC (14.817 to NC)	NC (NC to NC)	NC (14.554 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1473		0.2575	
Hazard ratio (95% CI) vs Pd	-	0.50 (0.19 to 1.31)		2.09 (0.57 to 7.74)	
P-value	-	0.1557		0.2683	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (24.7)	26 (33.8)	14 (25.0)	18 (23.4)	0.3383
Number (%) of patients censored	73 (75.3)	51 (66.2)	42 (75.0)	59 (76.6)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	5.65 (3.877 to NC)	4.86 (1.643 to 10.021)	10.74 (2.333 to NC)	11.20 (7.425 to NC)	
Median (95% CI)	NC (NC to NC)	15.67 (15.671 to NC)	NC (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.671 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3683		0.5802	
Hazard ratio (95% CI) vs Pd	-	1.29 (0.74 to 2.25)		0.82 (0.41 to 1.65)	
P-value	-	0.3696		0.5808	
Deterioration probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (22.6)	35 (25.4)	6 (37.5)	4 (25.0)	0.4450
Number (%) of patients censored	106 (77.4)	103 (74.6)	10 (62.5)	12 (75.0)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (2.793 to NC)	7.66 (3.088 to NC)	2.00 (0.953 to NC)	3.06 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.413 to NC)	NC (2.661 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9140		0.4352	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.63 to 1.67)		0.61 (0.17 to 2.15)	
P-value	-	0.9141		0.4399	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	68 (49.6)	80 (58.0)	7 (43.8)	6 (37.5)	0.8874
Number (%) of patients censored	69 (50.4)	58 (42.0)	9 (56.3)	10 (62.5)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	2.04 (1.281 to 2.793)	1.41 (1.084 to 2.037)	1.87 (0.986 to 4.172)	1.08 (0.953 to NC)	
Median (95% CI)	6.57 (3.844 to NC)	4.83 (2.891 to 12.485)	NC (1.281 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	15.67 (13.864 to 15.671)	NC (4.172 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3414		0.9253	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.85 to 1.62)		1.05 (0.35 to 3.15)	
P-value	-	0.3430		0.9251	
Deterioration probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (8.8)	12 (8.7)	4 (25.0)	3 (18.8)	0.6168
Number (%) of patients censored	125 (91.2)	126 (91.3)	12 (75.0)	13 (81.3)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	5.09 (1.413 to NC)	14.82 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.844 to NC)	14.82 (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7948		0.4059	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.40 to 2.00)		0.49 (0.09 to 2.70)	
P-value	-	0.7946		0.4156	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_imppl_ecog_de_i_t_x.rtf (08APR2021 14:47)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (23.4)	40 (29.0)	6 (37.5)	4 (25.0)	0.3955
Number (%) of patients censored	105 (76.6)	98 (71.0)	10 (62.5)	12 (75.0)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	10.68 (4.764 to NC)	8.61 (5.552 to 15.671)	1.87 (0.986 to NC)	12.29 (0.986 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (15.671 to NC)	NC (1.281 to NC)	NC (2.628 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.287 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6518		0.4997	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.70 to 1.77)		0.65 (0.18 to 2.30)	
P-value	-	0.6532		0.5030	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (23.5)	15 (23.4)	14 (25.0)	11 (20.8)	11 (25.6)	12 (35.3)	0.6840
Number (%) of patients censored	39 (76.5)	49 (76.6)	42 (75.0)	42 (79.2)	32 (74.4)	22 (64.7)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	NC (2.300 to NC)	NC (3.088 to NC)	3.75 (1.248 to NC)	NC (2.431 to NC)	3.32 (0.986 to NC)	2.86 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.312 to NC)	NC (4.698 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9740		0.4481		0.6586	
Hazard ratio (95% CI) vs Pd	-	1.01 (0.47 to 2.16)		0.74 (0.33 to 1.62)		1.20 (0.53 to 2.73)	
P-value	-	0.9741		0.4499		0.6585	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (62.7)	35 (54.7)	26 (46.4)	31 (58.5)	15 (34.9)	18 (52.9)	0.5408
Number (%) of patients censored	19 (37.3)	29 (45.3)	30 (53.6)	22 (41.5)	28 (65.1)	16 (47.1)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	2.04 (1.281 to 2.825)	1.31 (1.084 to 2.595)	2.14 (1.018 to 3.745)	1.22 (1.051 to 2.267)	1.91 (1.018 to 5.585)	1.84 (0.986 to 4.271)	
Median (95% CI)	4.17 (2.825 to 12.025)	4.80 (2.628 to 15.671)	11.17 (3.647 to NC)	4.73 (2.201 to 13.864)	NC (2.168 to NC)	9.00 (2.136 to NC)	
75% quantile (95% CI)	NC (11.532 to NC)	15.67 (NC to NC)	NC (NC to NC)	13.86 (12.682 to NC)	NC (NC to NC)	NC (9.495 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8896		0.2342		0.4608	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.60 to 1.56)		1.37 (0.81 to 2.31)		1.30 (0.65 to 2.58)	
P-value	-	0.8895		0.2361		0.4622	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (7.8)	3 (4.7)	8 (14.3)	5 (9.4)	4 (9.3)	7 (20.6)	0.3906
Number (%) of patients censored	47 (92.2)	61 (95.3)	48 (85.7)	48 (90.6)	39 (90.7)	27 (79.4)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (7.491 to NC)	NC (NC to NC)	NC (3.318 to NC)	14.82 (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5534		0.3697		0.3837	
Hazard ratio (95% CI) vs Pd	-	0.64 (0.14 to 2.85)		0.60 (0.20 to 1.84)		1.73 (0.50 to 6.00)	
P-value	-	0.5567		0.3748		0.3892	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (21.6)	19 (29.7)	16 (28.6)	17 (32.1)	10 (23.3)	7 (20.6)	0.3504
Number (%) of patients censored	40 (78.4)	45 (70.3)	40 (71.4)	36 (67.9)	33 (76.7)	27 (79.4)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	14.69 (5.552 to NC)	8.61 (2.628 to NC)	4.86 (1.938 to NC)	8.11 (2.201 to 10.021)	5.59 (1.084 to NC)	NC (1.840 to NC)	
Median (95% CI)	NC (14.686 to NC)	15.67 (15.671 to NC)	NC (10.678 to NC)	NC (9.396 to NC)	NC (8.378 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.671 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2652		0.9501		0.3763	
Hazard ratio (95% CI) vs Pd	-	1.52 (0.72 to 3.20)		1.02 (0.52 to 2.02)		0.65 (0.24 to 1.71)	
P-value	-	0.2687		0.9501		0.3799	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (29.0)	9 (23.1)	22 (22.4)	23 (23.2)	6 (25.0)	7 (43.8)	0.6425
Number (%) of patients censored	22 (71.0)	30 (76.9)	76 (77.6)	76 (76.8)	18 (75.0)	9 (56.3)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	6.14 (1.051 to NC)	NC (1.938 to NC)	NC (2.300 to NC)	NC (3.023 to NC)	2.00 (0.986 to NC)	1.38 (0.986 to 4.698)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.004 to NC)	4.70 (1.117 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.698 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6018		0.9063		0.4586	
Hazard ratio (95% CI) vs Pd	-	0.78 (0.31 to 1.97)		0.97 (0.54 to 1.73)		1.51 (0.51 to 4.50)	
P-value	-	0.6027		0.9063		0.4617	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (61.3)	18 (46.2)	49 (50.0)	60 (60.6)	7 (29.2)	8 (50.0)	0.2555
Number (%) of patients censored	12 (38.7)	21 (53.8)	49 (50.0)	39 (39.4)	17 (70.8)	8 (50.0)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	1.94 (1.117 to 2.891)	1.91 (1.084 to 3.811)	2.10 (1.117 to 2.825)	1.12 (1.084 to 1.906)	1.91 (1.084 to NC)	1.02 (0.953 to 6.538)	
Median (95% CI)	4.73 (2.037 to NC)	15.67 (2.858 to 15.671)	6.64 (3.745 to NC)	4.27 (2.628 to 8.608)	8.38 (1.906 to NC)	6.54 (0.986 to NC)	
75% quantile (95% CI)	NC (6.111 to NC)	15.67 (NC to NC)	NC (NC to NC)	13.86 (12.485 to NC)	NC (8.378 to NC)	NC (6.538 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3837		0.1492		0.4477	
Hazard ratio (95% CI) vs Pd	-	0.75 (0.39 to 1.43)		1.32 (0.90 to 1.92)		1.49 (0.53 to 4.18)	
P-value	-	0.3853		0.1510		0.4504	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (12.9)	3 (7.7)	9 (9.2)	7 (7.1)	3 (12.5)	5 (31.3)	0.4882
Number (%) of patients censored	27 (87.1)	36 (92.3)	89 (90.8)	92 (92.9)	21 (87.5)	11 (68.8)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	NC (8.903 to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.018 to NC)	10.48 (1.117 to 14.817)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	14.82 (4.698 to 14.817)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	14.82 (10.480 to 14.817)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4764		0.5349		0.3916	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_imppl_seriss_de_i_t_x.rtf (08APR2021 14:48)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (16.1)	9 (23.1)	29 (29.6)	31 (31.3)	4 (16.7)	4 (25.0)	0.7564
Number (%) of patients censored	26 (83.9)	30 (76.9)	69 (70.4)	68 (68.7)	20 (83.3)	12 (75.0)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	14.69 (5.651 to NC)	15.67 (2.891 to NC)	4.86 (2.333 to NC)	8.11 (4.731 to 11.203)	8.38 (1.084 to NC)	6.54 (0.953 to NC)	
Median (95% CI)	NC (14.686 to NC)	15.67 (15.671 to NC)	NC (NC to NC)	NC (12.287 to NC)	NC (8.378 to NC)	NC (1.840 to NC)	
75% quantile (95% CI)	NC (14.686 to NC)	NC (15.671 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4755		0.9531		0.7989	
Hazard ratio (95% CI) vs Pd	-	1.49 (0.50 to 4.44)		0.98 (0.59 to 1.63)		1.20 (0.29 to 4.89)	
P-value	-	0.4784		0.9531		0.7992	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (13.0)	6 (42.9)	24 (25.3)	29 (24.6)	0.0666
Number (%) of patients censored	20 (87.0)	8 (57.1)	71 (74.7)	89 (75.4)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (1.018 to NC)	2.66 (1.018 to 7.458)	5.62 (1.938 to NC)	7.98 (3.055 to NC)	
Median (95% CI)	NC (NC to NC)	7.46 (1.150 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (4.698 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0615		0.6715	
Hazard ratio (95% CI) vs Pd	-	3.46 (0.87 to 13.86)		0.89 (0.52 to 1.53)	
P-value	-	0.0792		0.6717	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (39.1)	4 (28.6)	44 (46.3)	70 (59.3)	0.3527
Number (%) of patients censored	14 (60.9)	10 (71.4)	51 (53.7)	48 (40.7)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	2.10 (0.986 to 5.224)	2.99 (0.953 to NC)	1.91 (1.117 to 2.891)	1.15 (1.084 to 2.136)	
Median (95% CI)	5.22 (2.103 to NC)	NC (1.840 to NC)	11.17 (3.811 to NC)	4.80 (2.858 to 9.495)	
75% quantile (95% CI)	NC (5.224 to NC)	NC (NC to NC)	NC (NC to NC)	15.67 (13.864 to 15.671)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7252		0.1084	
Hazard ratio (95% CI) vs Pd	-	0.81 (0.25 to 2.64)		1.36 (0.93 to 1.98)	
P-value	-	0.7257		0.1098	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (13.0)	3 (21.4)	11 (11.6)	11 (9.3)	0.3059
Number (%) of patients censored	20 (87.0)	11 (78.6)	84 (88.4)	107 (90.7)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (1.018 to NC)	4.70 (1.018 to NC)	NC (11.466 to NC)	NC (14.554 to NC)	
Median (95% CI)	NC (9.561 to NC)	NC (2.661 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5620		0.3862	
Hazard ratio (95% CI) vs Pd	-	1.60 (0.32 to 7.96)		0.69 (0.30 to 1.60)	
P-value	-	0.5655		0.3889	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (17.4)	3 (21.4)	24 (25.3)	35 (29.7)	0.7000
Number (%) of patients censored	19 (82.6)	11 (78.6)	71 (74.7)	83 (70.3)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	4.86 (1.018 to NC)	NC (0.953 to NC)	10.68 (2.530 to NC)	8.97 (5.552 to 15.671)	
Median (95% CI)	NC (4.862 to NC)	NC (1.840 to NC)	NC (NC to NC)	NC (15.671 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6848		0.8879	
Hazard ratio (95% CI) vs Pd	-	1.36 (0.30 to 6.09)		1.04 (0.62 to 1.75)	
P-value	-	0.6860		0.8883	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (19.4)	9 (37.5)	19 (24.4)	25 (24.3)	0.2183
Number (%) of patients censored	29 (80.6)	15 (62.5)	59 (75.6)	78 (75.7)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (1.183 to NC)	4.70 (1.018 to 7.458)	6.51 (1.938 to NC)	NC (3.023 to NC)	
Median (95% CI)	NC (NC to NC)	NC (4.698 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1988		0.7791	
Hazard ratio (95% CI) vs Pd	-	1.89 (0.70 to 5.08)		0.92 (0.51 to 1.67)	
P-value	-	0.2064		0.7792	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (47.2)	11 (45.8)	34 (43.6)	60 (58.3)	0.4104
Number (%) of patients censored	19 (52.8)	13 (54.2)	44 (56.4)	43 (41.7)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.35 (1.051 to 3.745)	1.48 (0.953 to 4.797)	2.14 (1.216 to 3.647)	1.12 (1.084 to 2.201)	
Median (95% CI)	5.22 (1.906 to NC)	6.54 (1.840 to NC)	12.02 (5.618 to NC)	5.55 (2.858 to 13.864)	
75% quantile (95% CI)	NC (5.224 to NC)	NC (6.538 to NC)	NC (NC to NC)	15.67 (13.864 to 15.671)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9506		0.0851	
Hazard ratio (95% CI) vs Pd	-	0.98 (0.46 to 2.09)		1.44 (0.95 to 2.20)	
P-value	-	0.9508		0.0868	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (11.1)	4 (16.7)	10 (12.8)	10 (9.7)	0.2721
Number (%) of patients censored	32 (88.9)	20 (83.3)	68 (87.2)	93 (90.3)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (2.168 to NC)	NC (1.018 to NC)	NC (11.466 to NC)	NC (14.554 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6001		0.2765	
Hazard ratio (95% CI) vs Pd	-	1.45 (0.36 to 5.79)		0.61 (0.25 to 1.49)	
P-value	-	0.6021		0.2810	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (19.4)	5 (20.8)	19 (24.4)	33 (32.0)	0.8176
Number (%) of patients censored	29 (80.6)	19 (79.2)	59 (75.6)	70 (68.0)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (1.281 to NC)	10.02 (0.953 to NC)	10.68 (3.450 to NC)	8.11 (4.862 to 12.287)	
Median (95% CI)	NC (NC to NC)	NC (10.021 to NC)	NC (NC to NC)	15.67 (15.671 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.671 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9291		0.5427	
Hazard ratio (95% CI) vs Pd	-	1.05 (0.33 to 3.33)		1.19 (0.68 to 2.10)	
P-value	-	0.9287		0.5432	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (20.0)	22 (26.5)	19 (30.2)	17 (23.9)	0.1313
Number (%) of patients censored	72 (80.0)	61 (73.5)	44 (69.8)	54 (76.1)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (2.004 to NC)	7.13 (2.234 to NC)	3.15 (1.248 to NC)	7.98 (3.023 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3928		0.1865	
Hazard ratio (95% CI) vs Pd	-	1.31 (0.70 to 2.44)		0.65 (0.34 to 1.24)	
P-value	-	0.3949		0.1900	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (55.6)	44 (53.0)	25 (39.7)	42 (59.2)	0.1387
Number (%) of patients censored	40 (44.4)	39 (47.0)	38 (60.3)	29 (40.8)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	2.04 (1.281 to 2.825)	1.64 (1.117 to 2.628)	1.94 (1.051 to 4.731)	1.08 (0.986 to 1.906)	
Median (95% CI)	5.22 (2.924 to 11.532)	9.49 (2.858 to 13.864)	NC (4.731 to NC)	4.73 (2.136 to 9.002)	
75% quantile (95% CI)	NC (12.025 to NC)	15.67 (13.864 to 15.671)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8772		0.0821	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.65 to 1.45)		1.55 (0.94 to 2.54)	
P-value	-	0.8773		0.0845	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (10.0)	10 (12.0)	7 (11.1)	5 (7.0)	0.2859
Number (%) of patients censored	81 (90.0)	73 (88.0)	56 (88.9)	66 (93.0)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (NC to NC)	14.82 (14.554 to NC)	NC (9.561 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7887		0.3061	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.46 to 2.79)		0.55 (0.18 to 1.75)	
P-value	-	0.7890		0.3130	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (27.8)	26 (31.3)	13 (20.6)	18 (25.4)	0.8783
Number (%) of patients censored	65 (72.2)	57 (68.7)	50 (79.4)	53 (74.6)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	5.65 (2.891 to NC)	7.43 (2.628 to 12.287)	NC (4.205 to NC)	9.00 (5.125 to NC)	
Median (95% CI)	NC (14.686 to NC)	15.67 (15.671 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.671 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7462		0.9462	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.63 to 1.90)		1.02 (0.50 to 2.09)	
P-value	-	0.7462		0.9463	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	36 (23.8)	39 (25.7)	0.9799
Number (%) of patients censored	1 (50.0)	2 (100.0)	115 (76.2)	113 (74.3)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.08 (1.084 to NC)	NC (NC to NC)	6.51 (2.793 to NC)	7.46 (3.055 to NC)	
Median (95% CI)	NC (1.084 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.084 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.9696	
Hazard ratio (95% CI) vs Pd	-			0.99 (0.63 to 1.56)	
P-value	-	0.9990		0.9696	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	2 (100.0)	74 (49.0)	84 (55.3)	0.0958
Number (%) of patients censored	1 (50.0)	0 (0.0)	77 (51.0)	68 (44.7)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	6.57 (6.571 to NC)	1.08 (1.084 to 1.117)	1.94 (1.281 to 2.530)	1.41 (1.084 to 2.037)	
Median (95% CI)	NC (6.571 to NC)	1.10 (1.084 to 1.117)	6.64 (3.811 to NC)	5.55 (2.990 to 12.682)	
75% quantile (95% CI)	NC (6.571 to NC)	1.12 (1.084 to 1.117)	NC (NC to NC)	15.67 (13.864 to 15.671)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.4189	
Hazard ratio (95% CI) vs Pd	-			1.14 (0.83 to 1.55)	
P-value	-	0.9985		0.4199	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	15 (9.9)	15 (9.9)	0.9894
Number (%) of patients censored	1 (50.0)	2 (100.0)	136 (90.1)	137 (90.1)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	11.47 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	
Median (95% CI)	11.47 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	11.47 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.7484	
Hazard ratio (95% CI) vs Pd	-			0.89 (0.43 to 1.82)	
P-value	-			0.7480	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	38 (25.2)	43 (28.3)	0.9800
Number (%) of patients censored	2 (100.0)	1 (50.0)	113 (74.8)	109 (71.7)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (NC to NC)	1.12 (1.117 to NC)	5.65 (3.877 to NC)	8.97 (5.552 to 15.671)	
Median (95% CI)	NC (NC to NC)	NC (1.117 to NC)	NC (14.686 to NC)	NC (15.671 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.117 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.9676	
Hazard ratio (95% CI) vs Pd	-			1.01 (0.65 to 1.56)	
P-value	-	0.9990		0.9676	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (24.8)	28 (26.9)	9 (22.0)	7 (21.2)	0.8669
Number (%) of patients censored	76 (75.2)	76 (73.1)	32 (78.0)	26 (78.8)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	6.51 (1.938 to NC)	7.13 (2.431 to NC)	6.14 (1.971 to NC)	NC (1.117 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9760		0.7812	
Hazard ratio (95% CI) vs Pd	-	1.01 (0.59 to 1.73)		0.87 (0.32 to 2.34)	
P-value	-	0.9760		0.7813	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (50.5)	57 (54.8)	19 (46.3)	20 (60.6)	0.8320
Number (%) of patients censored	50 (49.5)	47 (45.2)	22 (53.7)	13 (39.4)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.94 (1.150 to 2.333)	1.15 (1.084 to 2.267)	2.53 (1.051 to 2.957)	1.91 (1.084 to 2.858)	
Median (95% CI)	6.64 (3.811 to NC)	5.62 (2.891 to 13.864)	6.11 (2.891 to NC)	4.73 (1.906 to NC)	
75% quantile (95% CI)	NC (NC to NC)	15.67 (13.864 to 15.671)	NC (NC to NC)	NC (4.830 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6890		0.3655	
Hazard ratio (95% CI) vs Pd	-	1.08 (0.74 to 1.58)		1.34 (0.71 to 2.51)	
P-value	-	0.6893		0.3672	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (11.9)	11 (10.6)	3 (7.3)	3 (9.1)	0.9014
Number (%) of patients censored	89 (88.1)	93 (89.4)	38 (92.7)	30 (90.9)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (11.466 to NC)	NC (14.554 to NC)	NC (8.903 to NC)	14.82 (14.817 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6054		0.9214	
Hazard ratio (95% CI) vs Pd	-	0.81 (0.36 to 1.83)		1.08 (0.22 to 5.38)	
P-value	-	0.6061		0.9213	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (27.7)	30 (28.8)	8 (19.5)	9 (27.3)	0.7459
Number (%) of patients censored	73 (72.3)	74 (71.2)	33 (80.5)	24 (72.7)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	5.65 (2.333 to NC)	8.97 (4.928 to 15.671)	NC (3.647 to NC)	8.97 (1.906 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (15.671 to NC)	NC (NC to NC)	NC (11.203 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7578		0.6662	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.55 to 1.55)		1.23 (0.47 to 3.21)	
P-value	-	0.7573		0.6664	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (24.0)	27 (26.5)	12 (23.1)	12 (23.5)	0.8392
Number (%) of patients censored	76 (76.0)	75 (73.5)	40 (76.9)	39 (76.5)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	8.31 (2.004 to NC)	7.46 (2.858 to NC)	6.14 (1.741 to NC)	6.64 (2.661 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9387		0.8349	
Hazard ratio (95% CI) vs Pd	-	1.02 (0.59 to 1.77)		0.92 (0.41 to 2.04)	
P-value	-	0.9387		0.8348	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (50.0)	55 (53.9)	24 (46.2)	30 (58.8)	0.5223
Number (%) of patients censored	50 (50.0)	47 (46.1)	28 (53.8)	21 (41.2)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.94 (1.150 to 2.333)	1.13 (1.084 to 2.497)	2.53 (1.051 to 2.924)	1.64 (1.084 to 2.201)	
Median (95% CI)	7.62 (3.811 to NC)	6.54 (2.891 to 13.864)	5.22 (2.891 to NC)	4.73 (2.037 to 12.485)	
75% quantile (95% CI)	NC (NC to NC)	15.67 (13.864 to 15.671)	NC (NC to NC)	NC (8.575 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7424		0.3295	
Hazard ratio (95% CI) vs Pd	-	1.07 (0.73 to 1.57)		1.31 (0.76 to 2.23)	
P-value	-	0.7426		0.3310	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (11.0)	11 (10.8)	4 (7.7)	4 (7.8)	0.9992
Number (%) of patients censored	89 (89.0)	91 (89.2)	48 (92.3)	47 (92.2)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (11.466 to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (14.817 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7900		0.8236	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.39 to 2.06)		0.85 (0.21 to 3.44)	
P-value	-	0.7897		0.8238	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (28.0)	29 (28.4)	10 (19.2)	14 (27.5)	0.4282
Number (%) of patients censored	72 (72.0)	73 (71.6)	42 (80.8)	37 (72.5)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	5.62 (2.333 to 14.686)	8.97 (4.928 to 15.671)	NC (3.877 to NC)	8.61 (2.201 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (15.671 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6627		0.4891	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.53 to 1.50)		1.33 (0.59 to 3.00)	
P-value	-	0.6620		0.4905	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (20.0)	5 (35.7)	35 (24.5)	34 (24.3)	0.5740
Number (%) of patients censored	8 (80.0)	9 (64.3)	108 (75.5)	106 (75.7)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (1.741 to NC)	1.91 (1.084 to NC)	6.51 (2.300 to NC)	7.66 (3.778 to NC)	
Median (95% CI)	NC (1.741 to NC)	NC (1.380 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5072		0.7027	
Hazard ratio (95% CI) vs Pd	-	1.73 (0.33 to 8.96)		0.91 (0.57 to 1.46)	
P-value	-	0.5127		0.7026	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (40.0)	9 (64.3)	71 (49.7)	77 (55.0)	0.9727
Number (%) of patients censored	6 (60.0)	5 (35.7)	72 (50.3)	63 (45.0)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.91 (0.920 to NC)	1.54 (0.986 to 3.811)	2.04 (1.347 to 2.825)	1.28 (1.084 to 2.037)	
Median (95% CI)	NC (0.920 to NC)	3.81 (1.117 to NC)	6.64 (3.844 to NC)	4.83 (2.891 to 12.682)	
75% quantile (95% CI)	NC (2.333 to NC)	13.86 (3.811 to NC)	NC (NC to NC)	15.67 (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7878		0.3726	
Hazard ratio (95% CI) vs Pd	-	1.18 (0.36 to 3.88)		1.16 (0.84 to 1.60)	
P-value	-	0.7880		0.3728	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	2 (14.3)	15 (10.5)	13 (9.3)	0.9580
Number (%) of patients censored	9 (90.0)	12 (85.7)	128 (89.5)	127 (90.7)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (1.938 to NC)	NC (2.661 to NC)	NC (NC to NC)	NC (14.554 to NC)	
Median (95% CI)	NC (1.938 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9413		0.5831	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.08 to 10.27)		0.81 (0.39 to 1.71)	
P-value	-	0.9413		0.5839	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (30.0)	4 (28.6)	35 (24.5)	40 (28.6)	0.3239
Number (%) of patients censored	7 (70.0)	10 (71.4)	108 (75.5)	100 (71.4)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	2.33 (0.920 to NC)	7.43 (1.117 to NC)	10.68 (4.665 to NC)	8.97 (5.552 to 15.671)	
Median (95% CI)	NC (0.920 to NC)	NC (1.840 to NC)	NC (14.686 to NC)	NC (15.671 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6308		0.7197	
Hazard ratio (95% CI) vs Pd	-	0.69 (0.15 to 3.21)		1.09 (0.69 to 1.71)	
P-value	-	0.6326		0.7202	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (21.9)	20 (23.0)	15 (30.6)	15 (27.3)	0.6173
Number (%) of patients censored	75 (78.1)	67 (77.0)	34 (69.4)	40 (72.7)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (2.300 to NC)	NC (3.778 to NC)	3.32 (0.986 to NC)	5.88 (2.333 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (8.312 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9125		0.4597	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.52 to 1.78)		0.76 (0.37 to 1.56)	
P-value	-	0.9125		0.4610	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (53.1)	47 (54.0)	22 (44.9)	35 (63.6)	0.4691
Number (%) of patients censored	45 (46.9)	40 (46.0)	27 (55.1)	20 (36.4)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	2.04 (1.216 to 2.793)	1.12 (1.084 to 1.906)	1.94 (1.018 to 2.891)	1.64 (1.018 to 2.595)	
Median (95% CI)	6.11 (2.957 to 12.025)	5.55 (2.628 to NC)	5.62 (2.825 to NC)	4.80 (2.595 to 9.495)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.864 to NC)	NC (NC to NC)	15.67 (9.002 to 15.671)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7977		0.2976	
Hazard ratio (95% CI) vs Pd	-	1.05 (0.71 to 1.57)		1.33 (0.78 to 2.27)	
P-value	-	0.7974		0.2993	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (10.4)	7 (8.0)	5 (10.2)	6 (10.9)	0.7696
Number (%) of patients censored	86 (89.6)	80 (92.0)	44 (89.8)	49 (89.1)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (7.491 to NC)	14.82 (10.480 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4547		0.6729	
Hazard ratio (95% CI) vs Pd	-	0.69 (0.26 to 1.82)		0.77 (0.22 to 2.65)	
P-value	-	0.4572		0.6738	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_imppl_crcl_de_i_t_x.rtf (08APR2021 14:47)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (21.9)	27 (31.0)	16 (32.7)	16 (29.1)	0.1244
Number (%) of patients censored	75 (78.1)	60 (69.0)	33 (67.3)	39 (70.9)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	14.69 (4.205 to NC)	7.43 (2.891 to 12.287)	4.67 (1.150 to 10.743)	9.00 (4.928 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (10.678 to NC)	15.67 (15.671 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.671 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2641		0.2157	
Hazard ratio (95% CI) vs Pd	-	1.38 (0.78 to 2.45)		0.64 (0.32 to 1.30)	
P-value	-	0.2662		0.2194	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	37 (24.5)	38 (25.0)	0.9818
Number (%) of patients censored	2 (100.0)	1 (50.0)	114 (75.5)	114 (75.0)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (NC to NC)	1.91 (1.906 to NC)	6.14 (2.300 to NC)	7.46 (3.088 to NC)	
Median (95% CI)	NC (NC to NC)	NC (1.906 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.906 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.7621	
Hazard ratio (95% CI) vs Pd	-			0.93 (0.59 to 1.47)	
P-value	-	0.9990		0.7619	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	74 (49.0)	86 (56.6)	0.9791
Number (%) of patients censored	1 (50.0)	2 (100.0)	77 (51.0)	66 (43.4)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (NC to NC)	2.04 (1.347 to 2.793)	1.28 (1.084 to 1.906)	
Median (95% CI)	NC (1.281 to NC)	NC (NC to NC)	6.57 (3.844 to NC)	4.80 (2.891 to 12.485)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	15.67 (13.864 to 15.671)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.2653	
Hazard ratio (95% CI) vs Pd	-			1.19 (0.87 to 1.63)	
P-value	-	0.9990		0.2666	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	16 (10.6)	14 (9.2)	0.9876
Number (%) of patients censored	2 (100.0)	1 (50.0)	135 (89.4)	138 (90.8)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (NC to NC)	5.09 (5.092 to NC)	NC (NC to NC)	NC (14.554 to NC)	
Median (95% CI)	NC (NC to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.4934	
Hazard ratio (95% CI) vs Pd	-			0.78 (0.38 to 1.60)	
P-value	-	0.9991		0.4945	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	37 (24.5)	44 (28.9)	0.9857
Number (%) of patients censored	1 (50.0)	2 (100.0)	114 (75.5)	108 (71.1)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (NC to NC)	8.38 (4.205 to NC)	8.61 (5.125 to 12.287)	
Median (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (15.671 to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.7383	
Hazard ratio (95% CI) vs Pd	-			1.08 (0.70 to 1.67)	
P-value	-	0.9990		0.7389	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (24.3)	29 (24.6)	9 (23.7)	10 (27.8)	0.6425
Number (%) of patients censored	87 (75.7)	89 (75.4)	29 (76.3)	26 (72.2)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	6.51 (2.300 to NC)	7.66 (3.088 to NC)	NC (1.018 to NC)	4.17 (1.117 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6940		0.7528	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.54 to 1.51)		1.16 (0.47 to 2.84)	
P-value	-	0.6934		0.7530	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	57 (49.6)	70 (59.3)	18 (47.4)	16 (44.4)	0.6052
Number (%) of patients censored	58 (50.4)	48 (40.7)	20 (52.6)	20 (55.6)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.94 (1.216 to 2.825)	1.18 (1.084 to 1.906)	2.07 (1.051 to 2.891)	1.54 (1.084 to 2.661)	
Median (95% CI)	6.57 (3.877 to 12.025)	4.80 (2.858 to 9.495)	NC (2.530 to NC)	NC (2.267 to NC)	
75% quantile (95% CI)	NC (NC to NC)	15.67 (12.682 to 15.671)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3140		0.9606	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.84 to 1.70)		0.98 (0.50 to 1.93)	
P-value	-	0.3146		0.9606	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (10.4)	10 (8.5)	4 (10.5)	5 (13.9)	0.3966
Number (%) of patients censored	103 (89.6)	108 (91.5)	34 (89.5)	31 (86.1)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (11.466 to NC)	NC (14.554 to NC)	NC (3.745 to NC)	14.82 (6.702 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3826		0.6171	
Hazard ratio (95% CI) vs Pd	-	0.69 (0.30 to 1.60)		1.40 (0.37 to 5.22)	
P-value	-	0.3853		0.6188	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (27.0)	34 (28.8)	7 (18.4)	10 (27.8)	0.3232
Number (%) of patients censored	84 (73.0)	84 (71.2)	31 (81.6)	26 (72.2)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	5.59 (3.647 to NC)	8.11 (4.862 to 15.671)	14.69 (2.333 to NC)	9.00 (2.201 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.671 to NC)	NC (14.686 to NC)	NC (9.396 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7578		0.3508	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.57 to 1.51)		1.58 (0.60 to 4.17)	
P-value	-	0.7572		0.3549	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (24.3)	35 (23.8)	2 (22.2)	4 (57.1)	0.1229
Number (%) of patients censored	109 (75.7)	112 (76.2)	7 (77.8)	3 (42.9)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	6.51 (2.004 to NC)	7.98 (4.107 to NC)	NC (0.986 to NC)	1.05 (1.018 to 3.778)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	3.78 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.117 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5911		0.1849	
Hazard ratio (95% CI) vs Pd	-	0.88 (0.55 to 1.40)		3.00 (0.55 to 16.49)	
P-value	-	0.5904		0.2065	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	68 (47.2)	84 (57.1)	7 (77.8)	2 (28.6)	0.0724
Number (%) of patients censored	76 (52.8)	63 (42.9)	2 (22.2)	5 (71.4)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	2.04 (1.281 to 2.825)	1.31 (1.084 to 1.906)	2.07 (0.986 to 2.168)	1.02 (0.986 to NC)	
Median (95% CI)	7.62 (4.008 to NC)	4.80 (2.891 to 9.495)	2.17 (0.986 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	15.67 (13.864 to 15.671)	4.73 (2.136 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1625		0.1307	
Hazard ratio (95% CI) vs Pd	-	1.26 (0.91 to 1.73)		0.31 (0.06 to 1.53)	
P-value	-	0.1634		0.1515	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (11.1)	13 (8.8)	0 (0.0)	2 (28.6)	0.9888
Number (%) of patients censored	128 (88.9)	134 (91.2)	9 (100.0)	5 (71.4)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	1.12 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2970		0.0954	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.33 to 1.41)			
P-value	-	0.2999		0.9977	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (23.6)	42 (28.6)	4 (44.4)	2 (28.6)	0.6965
Number (%) of patients censored	110 (76.4)	105 (71.4)	5 (55.6)	5 (71.4)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	8.38 (4.205 to NC)	8.61 (5.552 to 15.671)	10.68 (0.986 to 14.686)	4.93 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.671 to NC)	14.69 (0.986 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.678 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7396		0.9628	
Hazard ratio (95% CI) vs Pd	-	1.08 (0.69 to 1.70)		0.96 (0.16 to 5.82)	
P-value	-	0.7404		0.9630	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (25.0)	22 (23.7)	15 (23.1)	17 (27.9)	0.7718
Number (%) of patients censored	66 (75.0)	71 (76.3)	50 (76.9)	44 (72.1)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	6.14 (2.004 to NC)	7.98 (3.023 to NC)	8.31 (1.084 to NC)	5.88 (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7380		0.9165	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.50 to 1.63)		1.04 (0.52 to 2.08)	
P-value	-	0.7377		0.9166	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (48.9)	50 (53.8)	32 (49.2)	36 (59.0)	0.7675
Number (%) of patients censored	45 (51.1)	43 (46.2)	33 (50.8)	25 (41.0)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.94 (1.150 to 2.825)	1.48 (1.117 to 2.136)	2.04 (1.150 to 2.924)	1.08 (0.986 to 2.891)	
Median (95% CI)	8.38 (3.811 to NC)	4.27 (2.661 to NC)	6.57 (2.924 to NC)	6.54 (2.990 to 13.864)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.025 to NC)	13.86 (12.682 to 15.671)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3887		0.8009	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.80 to 1.80)		1.06 (0.66 to 1.72)	
P-value	-	0.3900		0.8011	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (13.6)	10 (10.8)	4 (6.2)	5 (8.2)	0.5905
Number (%) of patients censored	76 (86.4)	83 (89.2)	61 (93.8)	56 (91.8)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (9.561 to NC)	14.82 (14.554 to NC)	NC (11.466 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4571		0.7965	
Hazard ratio (95% CI) vs Pd	-	0.73 (0.31 to 1.69)		1.19 (0.32 to 4.43)	
P-value	-	0.4589		0.7968	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Dyspnea
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (22.7)	25 (26.9)	18 (27.7)	19 (31.1)	0.5755
Number (%) of patients censored	68 (77.3)	68 (73.1)	47 (72.3)	42 (68.9)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	10.74 (4.205 to NC)	9.00 (3.384 to NC)	4.76 (1.906 to NC)	7.43 (4.731 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (15.671 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6304		0.7227	
Hazard ratio (95% CI) vs Pd	-	1.16 (0.64 to 2.08)		0.89 (0.46 to 1.70)	
P-value	-	0.6307		0.7220	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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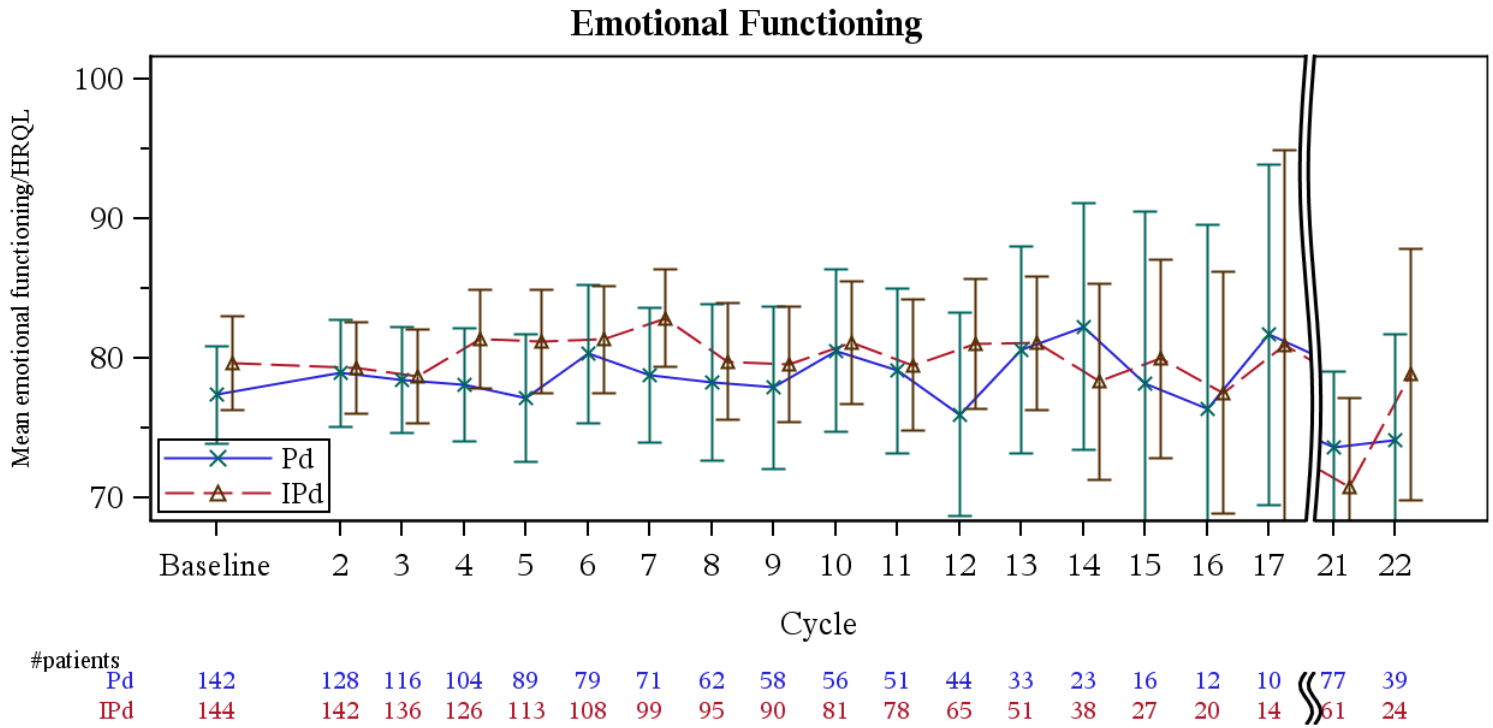
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Emotional functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-C30 - Mean and 95% CI for emotional functioning score over time (LOCF) - ITT population



A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Emotional functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-C30 - Time to first improvement by 15 pt in emotional functioning (LOCF) - ITT population

First improvement 15 points Emotional functioning (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	44 (28.8)	54 (35.1)
Number (%) of patients censored	109 (71.2)	100 (64.9)
Kaplan-Meier estimates of emotional functioning in months		
25% quantile (95% CI)	2.83 (1.117 to NC)	2.83 (1.906 to 6.998)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5778
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.12 (0.75 to 1.67)
P-value	-	0.5793
Probability (95% CI)[c]		
2 Months	0.23 (0.168 to 0.304)	0.21 (0.145 to 0.273)
4 Months	0.27 (0.200 to 0.344)	0.29 (0.224 to 0.369)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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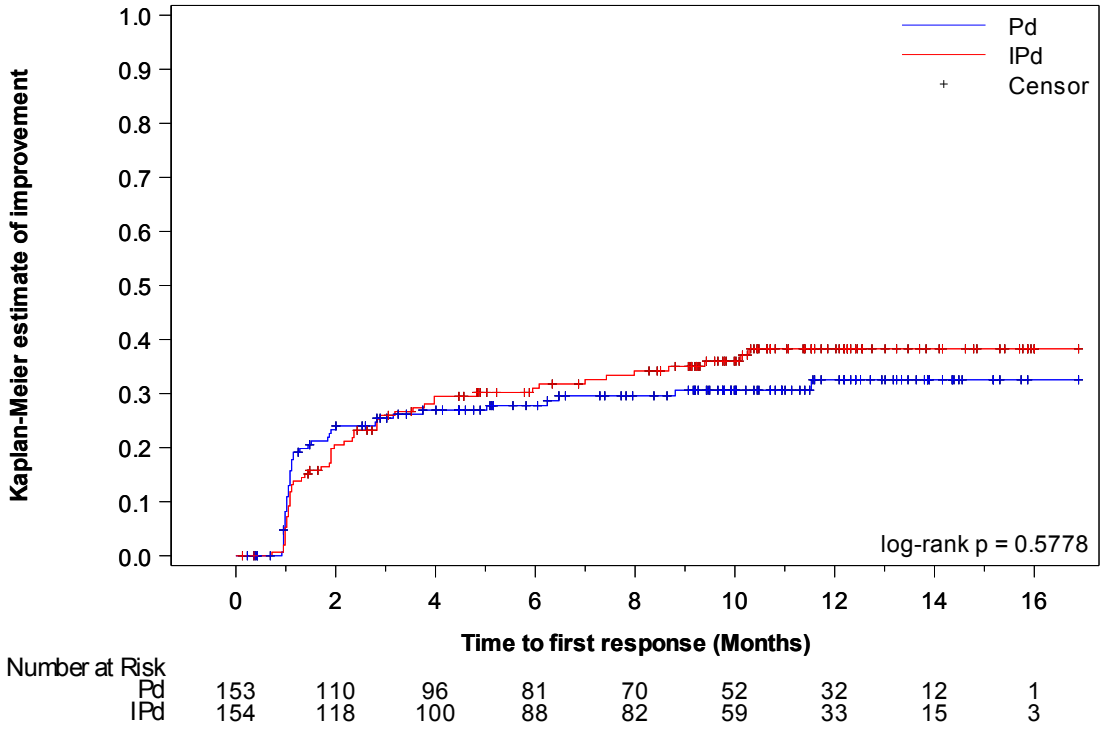
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Emotional functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-C30 - Time to first improvement by 15 pt in emotional functioning - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_imp15l_de_i_f_x.rtf (08APR2021 15:31)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Emotional functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-C30 - Time to first deterioration by 15 pt in emotional functioning (LOCF) - ITT population

First deterioration 15 points Emotional functioning (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	69 (45.1)	80 (51.9)
Number (%) of patients censored	84 (54.9)	74 (48.1)
Kaplan-Meier estimates of emotional functioning in months		
25% quantile (95% CI)	2.50 (1.906 to 2.957)	2.20 (1.906 to 2.924)
Median (95% CI)	9.46 (5.585 to NC)	7.10 (4.731 to NC)
75% quantile (95% CI)	NC (15.211 to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4789
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.12 (0.81 to 1.55)
P-value	-	0.4800
Probability (95% CI)[c]		
2 Months	0.79 (0.719 to 0.851)	0.78 (0.706 to 0.839)
4 Months	0.63 (0.542 to 0.701)	0.61 (0.530 to 0.687)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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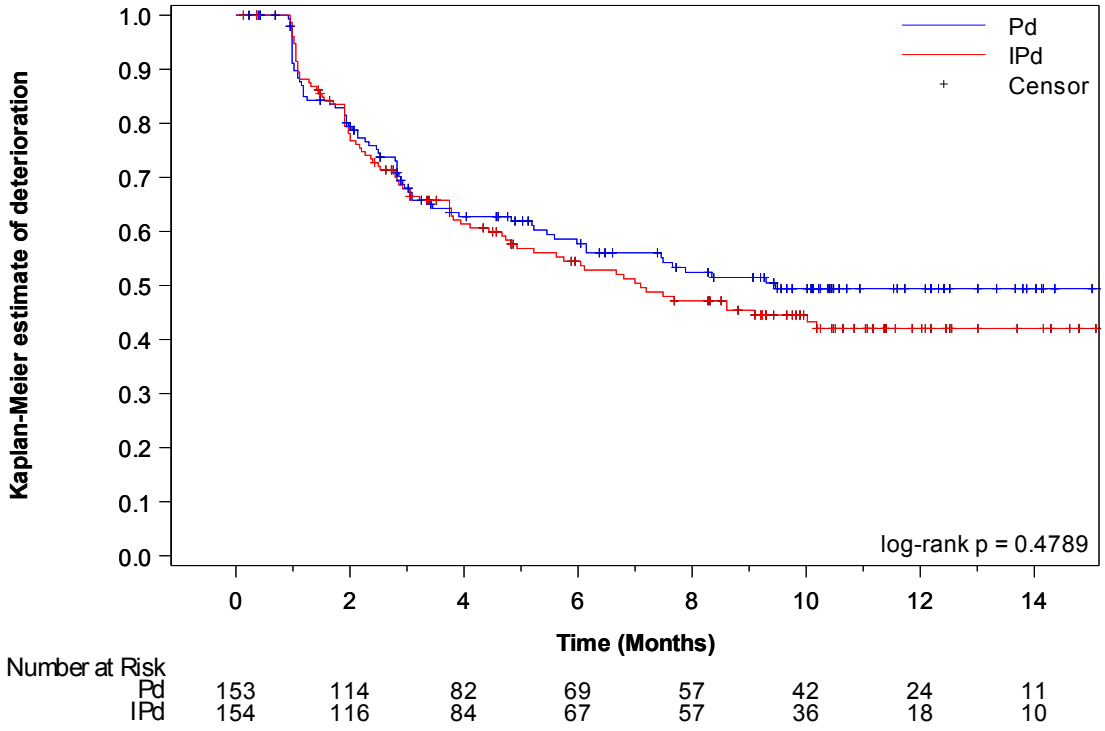
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Emotional functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-C30 - Time to first deterioration by 15 pt in emotional functioning - Kaplan-Meier curve (LOCF) - ITT population



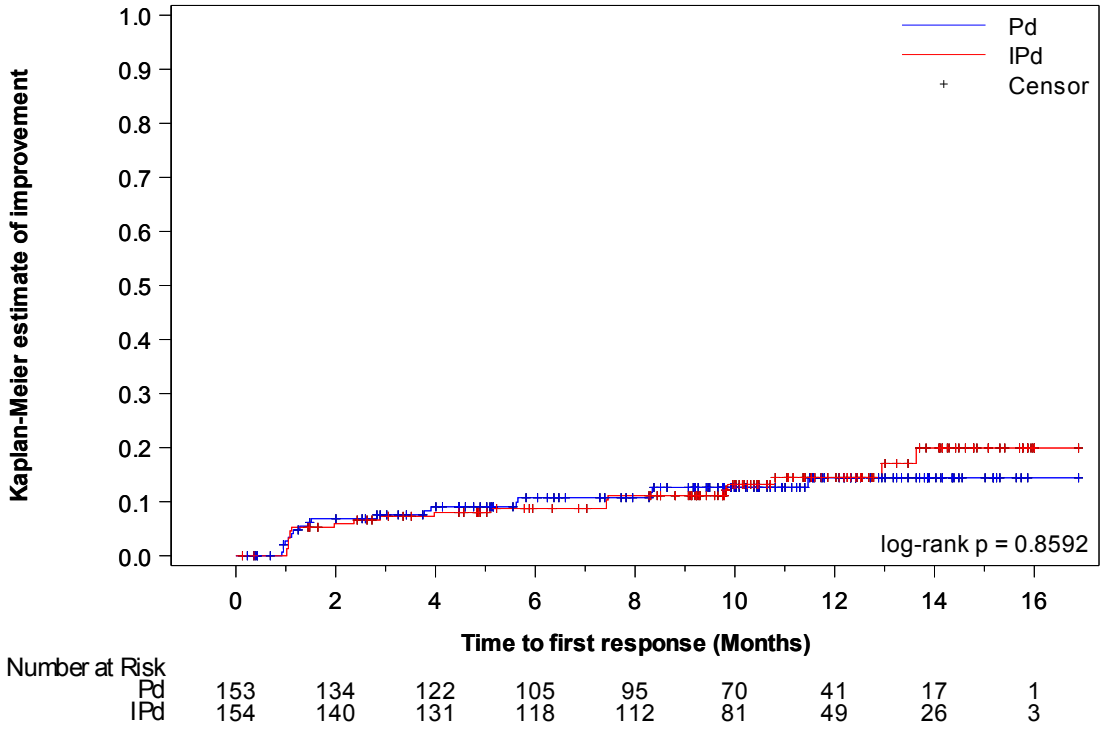
A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_det15l_de_i_f_x.rtf (08APR2021 15:31)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Emotional functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in emotional functioning (LOCF) - ITT population

First permanent improvement 15 points Emotional functioning (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	18 (11.8)	21 (13.6)
Number (%) of patients censored	135 (88.2)	133 (86.4)
Kaplan-Meier estimates of emotional functioning in months		
25% quantile (95% CI)	NC (NC to NC)	NC (12.945 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8592
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.06 (0.56 to 1.99)
P-value	-	0.8594
Probability (95% CI)[c]		
2 Months	0.07 (0.035 to 0.117)	0.06 (0.029 to 0.105)
4 Months	0.09 (0.051 to 0.144)	0.08 (0.044 to 0.130)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_imp15pl_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Emotional functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-C30 - Time until permanent improvement by 15 pt in emotional functioning - Kaplan-Meier curve (LOCF) - ITT population



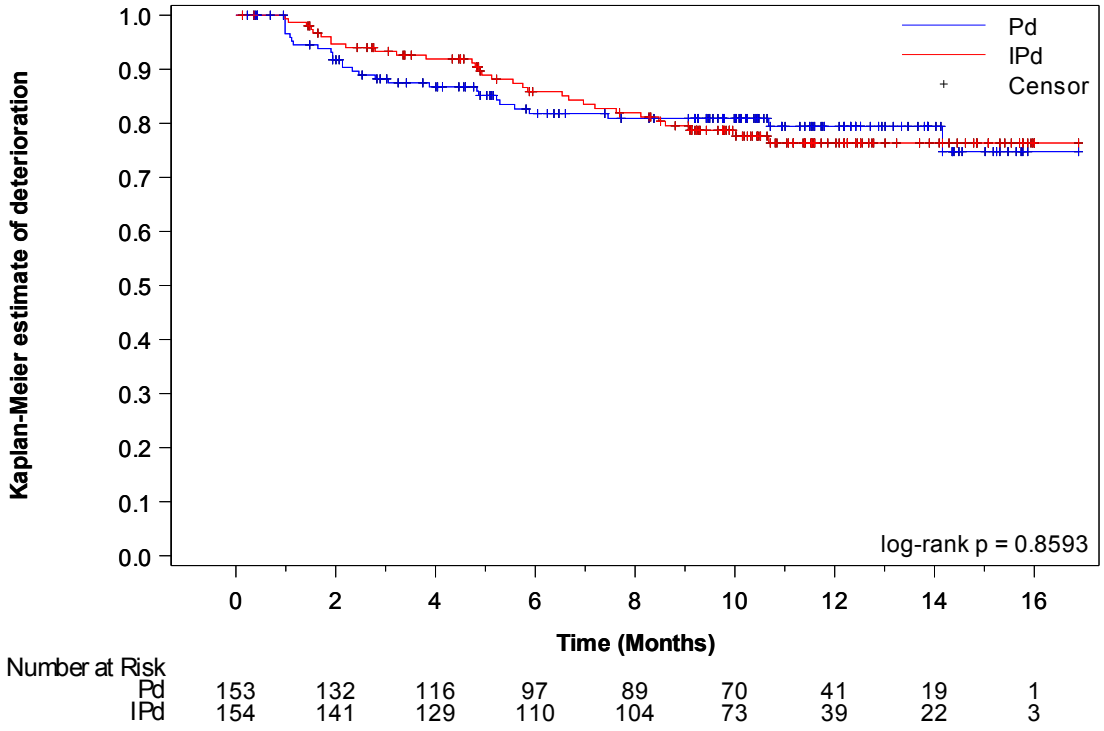
A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_imp15pl_de_i_f_x.rtf (08APR2021 15:31)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Emotional functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in emotional functioning (LOCF) - ITT population

First permanent deterioration 15 points Emotional functioning (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	28 (18.3)	31 (20.1)
Number (%) of patients censored	125 (81.7)	123 (79.9)
Kaplan-Meier estimates of emotional functioning in months		
25% quantile (95% CI)	14.16 (5.881 to NC)	NC (7.622 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8593
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.95 (0.57 to 1.59)
P-value	-	0.8591
Probability (95% CI)[c]		
2 Months	0.92 (0.859 to 0.952)	0.95 (0.896 to 0.973)
4 Months	0.87 (0.800 to 0.913)	0.92 (0.862 to 0.953)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_det15pl_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Emotional functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-C30 - Time until permanent deterioration by 15 pt in emotional functioning - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_det15pl_de_i_f_x.rtf (08APR2021 15:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (32.9)	19 (35.2)	14 (25.9)	22 (32.4)	7 (24.1)	13 (40.6)	0.6383
Number (%) of patients censored	47 (67.1)	35 (64.8)	40 (74.1)	46 (67.6)	22 (75.9)	19 (59.4)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	1.30 (1.018 to NC)	1.97 (1.150 to NC)	6.24 (1.117 to NC)	7.00 (1.478 to 10.283)	11.53 (1.084 to NC)	2.35 (1.051 to 8.674)	
Median (95% CI)	NC (NC to NC)	NC (5.947 to NC)	NC (NC to NC)	NC (10.283 to NC)	NC (11.532 to NC)	NC (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.532 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8802		0.5943		0.3410	
Hazard ratio (95% CI) vs Pd	-	0.95 (0.52 to 1.75)		1.20 (0.61 to 2.35)		1.56 (0.62 to 3.92)	
P-value	-	0.8805		0.5948		0.3449	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_impl_age_de_i_t_x.rtf (08APR2021 14:36)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (45.7)	23 (42.6)	21 (38.9)	39 (57.4)	16 (55.2)	18 (56.3)	0.2095
Number (%) of patients censored	38 (54.3)	31 (57.4)	33 (61.1)	29 (42.6)	13 (44.8)	14 (43.8)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	2.79 (1.906 to 3.910)	3.06 (1.544 to 4.435)	3.06 (1.248 to 7.458)	2.10 (1.281 to 2.924)	1.18 (0.986 to 2.464)	1.94 (1.051 to 3.745)	
Median (95% CI)	9.46 (5.191 to NC)	NC (4.435 to NC)	15.21 (6.144 to NC)	6.11 (3.055 to 10.185)	3.42 (1.183 to NC)	4.58 (2.168 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.211 to NC)	NC (10.185 to NC)	NC (5.585 to NC)	NC (7.688 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6411		0.0775		0.6335	
Hazard ratio (95% CI) vs Pd	-	0.88 (0.52 to 1.50)		1.61 (0.94 to 2.74)		0.85 (0.43 to 1.67)	
P-value	-	0.6413		0.0803		0.6339	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detl_age_de_i_t_x.rtf (08APR2021 14:36)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (17.1)	7 (13.0)	4 (7.4)	9 (13.2)	2 (6.9)	5 (15.6)	0.3685
Number (%) of patients censored	58 (82.9)	47 (87.0)	50 (92.6)	59 (86.8)	27 (93.1)	27 (84.4)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	NC (5.651 to NC)	NC (7.458 to NC)	NC (NC to NC)	NC (12.945 to NC)	NC (3.778 to NC)	NC (1.117 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4398		0.3798		0.4143	
Hazard ratio (95% CI) vs Pd	-	0.69 (0.27 to 1.76)		1.69 (0.52 to 5.48)		1.96 (0.38 to 10.18)	
P-value	-	0.4423		0.3853		0.4229	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_imppl_age_de_i_t_x.rtf (08APR2021 14:37)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (18.6)	12 (22.2)	7 (13.0)	11 (16.2)	8 (27.6)	8 (25.0)	0.7647
Number (%) of patients censored	57 (81.4)	42 (77.8)	47 (87.0)	57 (83.8)	21 (72.4)	24 (75.0)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	NC (3.877 to NC)	8.61 (4.797 to NC)	14.16 (5.224 to NC)	NC (8.115 to NC)	5.59 (0.986 to NC)	8.48 (4.731 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.160 to NC)	NC (NC to NC)	NC (5.881 to NC)	NC (10.678 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7684		0.7900		0.5595	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.51 to 2.47)		1.14 (0.44 to 2.94)		0.75 (0.28 to 1.99)	
P-value	-	0.7685		0.7901		0.5608	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detpl_age_de_i_t_x.rtf (08APR2021 14:36)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (27.7)	35 (34.3)	16 (30.8)	19 (36.5)	0.7390
Number (%) of patients censored	73 (72.3)	67 (65.7)	36 (69.2)	33 (63.5)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.83 (1.117 to NC)	2.83 (1.478 to 9.396)	3.15 (0.986 to NC)	2.83 (1.117 to 7.425)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (8.805 to NC)	NC (6.078 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4957		0.9014	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.72 to 1.95)		1.04 (0.54 to 2.03)	
P-value	-	0.4963		0.9015	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_impl_plne_de_i_t_x.rtf (08APR2021 14:36)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	45 (44.6)	53 (52.0)	24 (46.2)	27 (51.9)	0.6379
Number (%) of patients censored	56 (55.4)	49 (48.0)	28 (53.8)	25 (48.1)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.53 (1.643 to 3.910)	2.20 (1.906 to 3.220)	2.50 (1.018 to 3.417)	2.17 (1.281 to 3.745)	
Median (95% CI)	9.46 (5.585 to NC)	6.80 (4.731 to NC)	7.89 (3.088 to NC)	7.49 (3.055 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.211 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3556		0.9310	
Hazard ratio (95% CI) vs Pd	-	1.21 (0.81 to 1.79)		1.02 (0.59 to 1.78)	
P-value	-	0.3572		0.9311	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detl_plne_de_i_t_x.rtf (08APR2021 14:36)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	10 (9.9)	10 (9.8)	8 (15.4)	11 (21.2)	0.6082
Number (%) of patients censored	91 (90.1)	92 (90.2)	44 (84.6)	41 (78.8)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (12.945 to NC)	NC (5.651 to NC)	NC (2.891 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8233		0.6309	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.38 to 2.18)		1.25 (0.50 to 3.11)	
P-value	-	0.8231		0.6316	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_imppl_plne_de_i_t_x.rtf (08APR2021 14:37)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (14.9)	19 (18.6)	13 (25.0)	12 (23.1)	0.4375
Number (%) of patients censored	86 (85.1)	83 (81.4)	39 (75.0)	40 (76.9)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (7.458 to NC)	NC (7.195 to NC)	10.68 (2.333 to NC)	10.68 (5.125 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.160 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6149		0.5260	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.60 to 2.34)		0.78 (0.35 to 1.70)	
P-value	-	0.6154		0.5271	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detpl_plne_de_i_t_x.rtf (08APR2021 14:37)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (18.6)	25 (28.1)	31 (37.3)	29 (44.6)	0.4534
Number (%) of patients censored	57 (81.4)	64 (71.9)	52 (62.7)	36 (55.4)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (1.511 to NC)	6.08 (1.906 to NC)	1.28 (1.051 to 3.745)	2.17 (1.084 to 3.975)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (8.805 to NC)	NC (3.975 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2515		0.7878	
Hazard ratio (95% CI) vs Pd	-	1.48 (0.76 to 2.89)		1.07 (0.65 to 1.78)	
P-value	-	0.2546		0.7875	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (44.3)	47 (52.8)	38 (45.8)	33 (50.8)	0.5537
Number (%) of patients censored	39 (55.7)	42 (47.2)	45 (54.2)	32 (49.2)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.79 (1.906 to 5.454)	2.20 (1.906 to 3.778)	2.46 (1.150 to 3.088)	1.91 (1.117 to 3.745)	
Median (95% CI)	15.21 (5.585 to NC)	7.00 (3.943 to NC)	8.34 (3.745 to NC)	8.61 (3.745 to NC)	
75% quantile (95% CI)	NC (15.211 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3203		0.9073	
Hazard ratio (95% CI) vs Pd	-	1.26 (0.80 to 1.98)		1.03 (0.64 to 1.64)	
P-value	-	0.3214		0.9072	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (7.1)	10 (11.2)	13 (15.7)	11 (16.9)	0.4973
Number (%) of patients censored	65 (92.9)	79 (88.8)	70 (84.3)	54 (83.1)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (12.945 to NC)	NC (8.345 to NC)	NC (7.458 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4386		0.9393	
Hazard ratio (95% CI) vs Pd	-	1.52 (0.52 to 4.46)		0.97 (0.43 to 2.17)	
P-value	-	0.4421		0.9394	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (15.7)	14 (15.7)	17 (20.5)	17 (26.2)	0.7323
Number (%) of patients censored	59 (84.3)	75 (84.3)	66 (79.5)	48 (73.8)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (5.585 to NC)	NC (7.195 to NC)	10.68 (4.830 to NC)	8.48 (5.125 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8954		0.7140	
Hazard ratio (95% CI) vs Pd	-	0.95 (0.43 to 2.09)		1.13 (0.58 to 2.22)	
P-value	-	0.8951		0.7135	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (27.0)	41 (34.7)	9 (47.4)	10 (41.7)	0.4168
Number (%) of patients censored	92 (73.0)	77 (65.3)	10 (52.6)	14 (58.3)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	5.03 (1.511 to NC)	3.19 (1.906 to 8.674)	1.08 (0.986 to 1.150)	2.17 (0.986 to 3.975)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.084 to NC)	NC (2.333 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4712		0.5661	
Hazard ratio (95% CI) vs Pd	-	1.18 (0.75 to 1.86)		0.77 (0.31 to 1.89)	
P-value	-	0.4717		0.5672	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	60 (47.6)	64 (54.2)	7 (36.8)	12 (50.0)	0.4325
Number (%) of patients censored	66 (52.4)	54 (45.8)	12 (63.2)	12 (50.0)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.14 (1.248 to 2.825)	2.20 (1.544 to 2.858)	4.83 (1.084 to NC)	2.00 (0.986 to 7.195)	
Median (95% CI)	7.89 (5.224 to NC)	6.11 (3.811 to NC)	NC (4.830 to NC)	10.18 (2.004 to NC)	
75% quantile (95% CI)	NC (15.211 to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.185 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6994		0.3865	
Hazard ratio (95% CI) vs Pd	-	1.07 (0.75 to 1.52)		1.51 (0.59 to 3.86)	
P-value	-	0.6996		0.3897	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (8.7)	18 (15.3)	6 (31.6)	2 (8.3)	0.0219
Number (%) of patients censored	115 (91.3)	100 (84.7)	13 (68.4)	22 (91.7)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (12.945 to NC)	3.91 (0.986 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.910 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1909		0.0383	
Hazard ratio (95% CI) vs Pd	-	1.64 (0.78 to 3.48)		0.21 (0.04 to 1.06)	
P-value	-	0.1954		0.0592	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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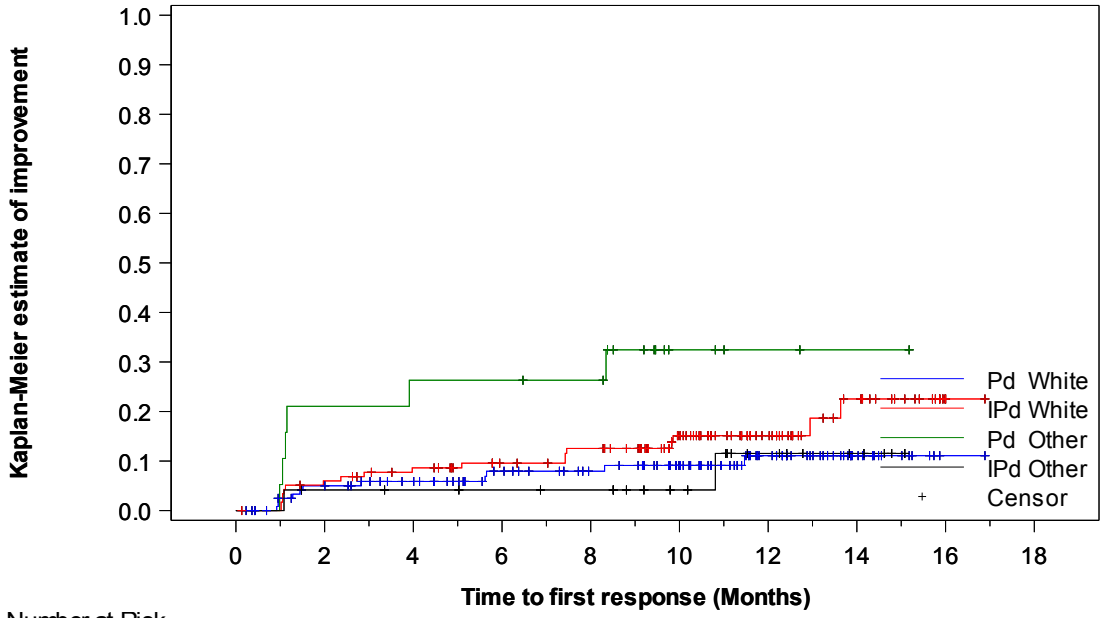
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to race (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd White	126	107	88	77	38	7	0
IPd White	118	105	93	84	37	12	0
Pd Other	19	15	14	9	2	1	0
IPd Other	24	22	20	16	8	1	0

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.7 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (19.8)	24 (20.3)	3 (15.8)	5 (20.8)	0.6415
Number (%) of patients censored	101 (80.2)	94 (79.7)	16 (84.2)	19 (79.2)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (5.224 to NC)	NC (8.115 to NC)	14.16 (1.084 to 14.160)	NC (4.797 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	14.16 (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	14.16 (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7542		0.7781	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.52 to 1.60)		1.23 (0.29 to 5.25)	
P-value	-	0.7542		0.7785	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	2 (50.0)	39 (29.1)	48 (36.9)	0.6518
Number (%) of patients censored	2 (66.7)	2 (50.0)	95 (70.9)	82 (63.1)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	8.20 (6.998 to NC)	3.15 (1.117 to NC)	2.83 (1.906 to 5.947)	
Median (95% CI)	NC (1.281 to NC)	NC (6.998 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (6.998 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4504		0.3969	
Hazard ratio (95% CI) vs Pd	-	0.35 (0.02 to 5.89)		1.20 (0.79 to 1.83)	
P-value	-	0.4689		0.3976	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	2 (50.0)	63 (47.0)	69 (53.1)	0.6742
Number (%) of patients censored	2 (66.7)	2 (50.0)	71 (53.0)	61 (46.9)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.27 (2.267 to NC)	3.47 (2.497 to NC)	2.50 (1.741 to 2.957)	2.00 (1.708 to 2.924)	
Median (95% CI)	NC (2.267 to NC)	NC (2.497 to NC)	8.34 (5.191 to NC)	7.20 (4.665 to NC)	
75% quantile (95% CI)	NC (2.267 to NC)	NC (2.497 to NC)	NC (15.211 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4504		0.6217	
Hazard ratio (95% CI) vs Pd	-	0.35 (0.02 to 5.89)		1.09 (0.77 to 1.53)	
P-value	-	0.4689		0.6221	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	0 (0.0)	15 (11.2)	20 (15.4)	0.9892
Number (%) of patients censored	2 (66.7)	4 (100.0)	119 (88.8)	110 (84.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.945 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.4495	
Hazard ratio (95% CI) vs Pd	-			1.29 (0.66 to 2.53)	
P-value	-	0.9990		0.4507	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_imppl_ethn_de_i_t_x.rtf (08APR2021 14:37)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	26 (19.4)	28 (21.5)	1.0000
Number (%) of patients censored	3 (100.0)	4 (100.0)	108 (80.6)	102 (78.5)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	14.16 (5.290 to NC)	NC (7.195 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.9643	
Hazard ratio (95% CI) vs Pd	-			1.01 (0.59 to 1.73)	
P-value	-			0.9643	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detpl_ethn_de_i_t_x.rtf (08APR2021 14:36)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Number (%) of events	20 (26.3)	16 (29.1)	4 (20.0)	9 (32.1)	2 (40.0)	5 (71.4)	7 (46.7)	8 (38.1)	11 (29.7)	16 (37.2)	0.9005
Number (%) of patients censored	56 (73.7)	39 (70.9)	16 (80.0)	19 (67.9)	3 (60.0)	2 (28.6)	8 (53.3)	13 (61.9)	26 (70.3)	27 (62.8)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	6.47 (1.840 to NC)	1.91 (1.018 to NC)	NC (0.986 to NC)	5.03 (1.084 to NC)	1.12 (0.953 to NC)	1.91 (1.708 to 6.998)	1.08 (0.986 to 1.150)	2.17 (0.986 to NC)	1.51 (0.986 to NC)	3.19 (1.380 to 7.984)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.078 to NC)	NC (0.953 to NC)	7.00 (1.708 to NC)	NC (1.051 to NC)	NC (2.168 to NC)	NC (NC to NC)	NC (5.947 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (2.366 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_impl_greg_de_i_t_x.rtf (08APR2021 14:36)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.8016		0.4790		0.5750		0.5556		0.8228	
Hazard ratio (95% CI) vs Pd	-	1.09 (0.56 to 2.10)		1.53 (0.47 to 4.96)		1.60 (0.31 to 8.33)		0.74 (0.27 to 2.04)		1.09 (0.51 to 2.36)	
P-value	-	0.8016		0.4823		0.5784		0.5571		0.8229	
Improvement probability (95% CI)[b]											
2 Months	0.183 (0.104 to 0.281)	0.260 (0.152 to 0.382)	0.158 (0.039 to 0.349)	0.143 (0.045 to 0.295)	0.400 (0.052 to 0.753)	0.286 (0.041 to 0.612)	0.467 (0.212 to 0.687)	0.238 (0.087 to 0.431)	0.251 (0.125 to 0.399)	0.144 (0.058 to 0.266)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_impl_greg_de_i_t_x.rtf (08APR2021 14:36)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	28 (36.8)	27 (49.1)	14 (70.0)	16 (57.1)	1 (20.0)	3 (42.9)	6 (40.0)	11 (52.4)	20 (54.1)	23 (53.5)	0.3335
Number (%) of patients censored	48 (63.2)	28 (50.9)	6 (30.0)	12 (42.9)	4 (80.0)	4 (57.1)	9 (60.0)	10 (47.6)	17 (45.9)	20 (46.5)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	2.33 (1.183 to 5.979)	2.37 (1.413 to 3.745)	0.99 (0.953 to 2.825)	1.94 (1.018 to 4.435)	NC (2.267 to NC)	2.79 (2.530 to NC)	4.83 (1.084 to NC)	2.00 (0.986 to 7.195)	2.53 (1.741 to 3.088)	2.83 (1.117 to 4.107)	
Median (95% CI)	NC (6.144 to NC)	5.75 (3.745 to NC)	2.96 (0.986 to 8.345)	4.93 (2.168 to NC)	NC (2.267 to NC)	NC (2.530 to NC)	NC (3.088 to NC)	8.61 (2.004 to NC)	5.45 (2.825 to NC)	7.49 (3.778 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	8.34 (2.957 to NC)	NC (6.801 to NC)	NC (2.267 to NC)	NC (3.778 to NC)	NC (NC to NC)	NC (10.185 to NC)	15.21 (9.462 to NC)	NC (10.021 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detl_greg_de_i_t_x.rtf (08APR2021 14:36)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.2732		0.2294		0.5240		0.4453		0.6790	
Hazard ratio (95% CI) vs Pd	-	1.34 (0.79 to 2.28)		0.65 (0.31 to 1.33)		2.06 (0.21 to 19.83)		1.48 (0.54 to 4.04)		0.88 (0.48 to 1.61)	
P-value	-	0.2749		0.2331		0.5328		0.4481		0.6792	
Deterioration probability (95% CI)[b]											
2 Months	0.775 (0.659 to 0.856)	0.815 (0.683 to 0.896)	0.632 (0.379 to 0.804)	0.714 (0.509 to 0.846)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.933 (0.613 to 0.990)	0.756 (0.509 to 0.891)	0.831 (0.661 to 0.920)	0.759 (0.598 to 0.863)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detl_greg_de_i_t_x.rtf (08APR2021 14:36)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Number (%) of events	6 (7.9)	5 (9.1)	0 (0.0)	6 (21.4)	1 (20.0)	0 (0.0)	4 (26.7)	1 (4.8)	7 (18.9)	9 (20.9)	0.6325
Number (%) of patients censored	70 (92.1)	50 (90.9)	20 (100.0)	22 (78.6)	4 (80.0)	7 (100.0)	11 (73.3)	20 (95.2)	30 (81.1)	34 (79.1)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (11.466 to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.084 to NC)	NC (1.117 to NC)	NC (NC to NC)	8.34 (1.051 to NC)	NC (1.084 to NC)	NC (1.446 to NC)	12.94 (7.425 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.117 to NC)	NC (NC to NC)	NC (3.910 to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.634 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.117 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_imppl_greg_de_i_t_x.rtf (08APR2021 14:37)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.8863		0.0349		0.2367		0.0745		0.8208	
Hazard ratio (95% CI) vs Pd	-	1.09 (0.33 to 3.57)						0.17 (0.02 to 1.54)		0.89 (0.33 to 2.40)	
P-value	-	0.8864		0.9962		0.9984		0.1158		0.8209	
Improvement probability (95% CI)[b]											
2 Months	0.028 (0.005 to 0.088)	0.056 (0.015 to 0.139)		0.107 (0.027 to 0.251)	0.200 (0.008 to 0.582)		0.133 (0.022 to 0.346)	0.048 (0.003 to 0.197)	0.140 (0.051 to 0.272)	0.048 (0.009 to 0.142)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_imppl_greg_de_i_t_x.rtf (08APR2021 14:37)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Number (%) of events	13 (17.1)	13 (23.6)	5 (25.0)	4 (14.3)	0 (0.0)	0 (0.0)	3 (20.0)	4 (19.0)	7 (18.9)	10 (23.3)	0.7085
Number (%) of patients censored	63 (82.9)	42 (76.4)	15 (75.0)	24 (85.7)	5 (100.0)	7 (100.0)	12 (80.0)	17 (81.0)	30 (81.1)	33 (76.7)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (5.224 to NC)	8.48 (3.220 to NC)	3.88 (0.986 to NC)	NC (2.793 to NC)	NC (NC to NC)	NC (NC to NC)	14.16 (1.084 to 14.160)	NC (4.797 to NC)	NC (2.136 to NC)	10.02 (6.538 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.877 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	14.16 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	14.16 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detpl_greg_de_i_t_x.rtf (08APR2021 14:37)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.3979		0.2914				0.8628		0.9677	
Hazard ratio (95% CI) vs Pd	-	1.39 (0.64 to 3.00)		0.50 (0.13 to 1.86)				0.87 (0.19 to 4.00)		0.98 (0.37 to 2.58)	
P-value	-	0.4000		0.3010				0.8629		0.9676	
Deterioration probability (95% CI)[b]											
2 Months	0.930 (0.839 to 0.970)	0.907 (0.792 to 0.960)	0.789 (0.532 to 0.915)	0.964 (0.772 to 0.995)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.933 (0.613 to 0.990)	1.000 (1.000 to 1.000)	0.944 (0.793 to 0.986)	0.951 (0.819 to 0.988)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detpl_greg_de_i_t_x.rtf (08APR2021 14:37)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (26.8)	26 (33.8)	18 (32.1)	28 (36.4)	0.7959
Number (%) of patients censored	71 (73.2)	51 (66.2)	38 (67.9)	49 (63.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	5.03 (1.281 to NC)	2.37 (1.150 to 10.119)	1.15 (1.051 to NC)	2.89 (1.906 to 7.425)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.283 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5650		0.8552	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.68 to 2.02)		1.06 (0.58 to 1.91)	
P-value	-	0.5654		0.8560	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_impl_rreg_de_i_t_x.rtf (08APR2021 14:36)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (39.2)	37 (48.1)	31 (55.4)	43 (55.8)	0.5601
Number (%) of patients censored	59 (60.8)	40 (51.9)	25 (44.6)	34 (44.2)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.33 (1.741 to 3.745)	2.50 (1.544 to 3.745)	2.53 (1.084 to 3.088)	1.91 (1.314 to 2.924)	
Median (95% CI)	NC (6.144 to NC)	7.69 (3.811 to NC)	6.14 (2.957 to NC)	7.00 (4.435 to 10.185)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	15.21 (15.211 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4689		0.9435	
Hazard ratio (95% CI) vs Pd	-	1.18 (0.75 to 1.86)		0.98 (0.62 to 1.56)	
P-value	-	0.4694		0.9434	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (11.3)	7 (9.1)	7 (12.5)	14 (18.2)	0.3265
Number (%) of patients censored	86 (88.7)	70 (90.9)	49 (87.5)	63 (81.8)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (11.466 to NC)	NC (NC to NC)	NC (8.345 to NC)	13.63 (7.425 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4951		0.4614	
Hazard ratio (95% CI) vs Pd	-	0.72 (0.28 to 1.86)		1.40 (0.57 to 3.48)	
P-value	-	0.4970		0.4636	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (18.6)	16 (20.8)	10 (17.9)	15 (19.5)	0.8701
Number (%) of patients censored	79 (81.4)	61 (79.2)	46 (82.1)	62 (80.5)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (5.224 to NC)	NC (5.125 to NC)	14.16 (3.877 to NC)	NC (7.195 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.160 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8811		0.9302	
Hazard ratio (95% CI) vs Pd	-	1.05 (0.54 to 2.06)		0.96 (0.43 to 2.15)	
P-value	-	0.8809		0.9300	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detpl_rreg_de_i_t_x.rtf (08APR2021 14:37)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (26.3)	45 (32.6)	8 (50.0)	9 (56.3)	0.9469
Number (%) of patients censored	101 (73.7)	93 (67.4)	8 (50.0)	7 (43.8)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	6.24 (1.150 to NC)	3.78 (1.971 to 9.396)	1.08 (0.953 to 2.793)	1.08 (1.018 to 1.906)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	2.83 (0.986 to NC)	2.83 (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.825 to NC)	NC (1.906 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5318		0.7959	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.74 to 1.78)		1.13 (0.44 to 2.95)	
P-value	-	0.5321		0.7962	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	64 (46.7)	77 (55.8)	5 (31.3)	3 (18.8)	0.3778
Number (%) of patients censored	73 (53.3)	61 (44.2)	11 (68.8)	13 (81.3)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.46 (1.906 to 2.957)	2.17 (1.708 to 2.825)	2.79 (0.986 to NC)	NC (0.986 to NC)	
Median (95% CI)	9.30 (5.454 to NC)	6.67 (4.107 to 10.021)	NC (1.084 to NC)	NC (5.224 to NC)	
75% quantile (95% CI)	NC (15.211 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3488		0.4803	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.84 to 1.63)		0.60 (0.14 to 2.52)	
P-value	-	0.3493		0.4850	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (9.5)	17 (12.3)	5 (31.3)	4 (25.0)	0.5118
Number (%) of patients censored	124 (90.5)	121 (87.7)	11 (68.8)	12 (75.0)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (12.945 to NC)	8.31 (0.953 to NC)	7.43 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.825 to NC)	NC (7.425 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (8.345 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6034		0.5876	
Hazard ratio (95% CI) vs Pd	-	1.21 (0.59 to 2.49)		0.69 (0.18 to 2.68)	
P-value	-	0.6040		0.5896	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (17.5)	30 (21.7)	4 (25.0)	1 (6.3)	0.1882
Number (%) of patients censored	113 (82.5)	108 (78.3)	12 (75.0)	15 (93.8)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	14.16 (7.458 to NC)	NC (7.195 to NC)	4.83 (0.986 to NC)	NC (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.793 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6794		0.1998	
Hazard ratio (95% CI) vs Pd	-	1.12 (0.65 to 1.92)		0.26 (0.03 to 2.36)	
P-value	-	0.6795		0.2332	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (33.3)	22 (34.4)	13 (23.2)	18 (34.0)	13 (30.2)	14 (41.2)	0.8255
Number (%) of patients censored	34 (66.7)	42 (65.6)	43 (76.8)	35 (66.0)	30 (69.8)	20 (58.8)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	1.87 (1.018 to NC)	2.89 (1.117 to 10.119)	8.80 (1.084 to NC)	3.55 (1.150 to 10.283)	1.51 (0.986 to NC)	2.17 (1.051 to 3.975)	
Median (95% CI)	NC (11.532 to NC)	NC (10.119 to NC)	NC (NC to NC)	NC (10.283 to NC)	NC (6.242 to NC)	NC (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9320		0.3737		0.6420	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.55 to 1.94)		1.38 (0.68 to 2.82)		1.20 (0.56 to 2.55)	
P-value	-	0.9321		0.3758		0.6418	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (49.0)	28 (43.8)	26 (46.4)	30 (56.6)	17 (39.5)	20 (58.8)	0.5425
Number (%) of patients censored	26 (51.0)	36 (56.3)	30 (53.6)	23 (43.4)	26 (60.5)	14 (41.2)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	2.53 (1.183 to 3.910)	2.40 (1.511 to 5.618)	2.50 (1.183 to 3.417)	2.20 (1.281 to 2.793)	2.14 (0.986 to 6.144)	1.91 (1.051 to 3.745)	
Median (95% CI)	15.21 (3.745 to NC)	NC (5.618 to NC)	9.30 (3.088 to NC)	6.05 (2.793 to NC)	8.34 (3.088 to NC)	4.93 (2.924 to 8.608)	
75% quantile (95% CI)	NC (15.211 to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.021 to NC)	NC (9.462 to NC)	8.61 (6.111 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7090		0.3456		0.3055	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.53 to 1.55)		1.29 (0.76 to 2.18)		1.40 (0.73 to 2.68)	
P-value	-	0.7091		0.3462		0.3078	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detl_seiss_de_i_t_x.rtf (08APR2021 14:36)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (13.7)	7 (10.9)	4 (7.1)	8 (15.1)	6 (14.0)	6 (17.6)	0.5509
Number (%) of patients censored	44 (86.3)	57 (89.1)	52 (92.9)	45 (84.9)	37 (86.0)	28 (82.4)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	NC (8.345 to NC)	NC (12.945 to NC)	NC (NC to NC)	NC (7.458 to NC)	NC (1.511 to NC)	NC (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7260		0.2544		0.9137	
Hazard ratio (95% CI) vs Pd	-	0.83 (0.29 to 2.37)		1.98 (0.60 to 6.59)		1.06 (0.34 to 3.31)	
P-value	-	0.7264		0.2637		0.9136	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (19.6)	8 (12.5)	11 (19.6)	13 (24.5)	6 (14.0)	9 (26.5)	0.4845
Number (%) of patients censored	41 (80.4)	56 (87.5)	45 (80.4)	40 (75.5)	37 (86.0)	25 (73.5)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	14.16 (5.224 to NC)	NC (10.678 to NC)	NC (3.055 to NC)	9.10 (5.552 to NC)	NC (1.117 to NC)	7.62 (3.220 to NC)	
Median (95% CI)	NC (14.160 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.115 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3713		0.7367		0.4738	
Hazard ratio (95% CI) vs Pd	-	0.66 (0.26 to 1.66)		1.15 (0.51 to 2.56)		1.46 (0.52 to 4.10)	
P-value	-	0.3748		0.7375		0.4763	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (32.3)	13 (33.3)	24 (24.5)	35 (35.4)	10 (41.7)	6 (37.5)	0.3297
Number (%) of patients censored	21 (67.7)	26 (66.7)	74 (75.5)	64 (64.6)	14 (58.3)	10 (62.5)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	1.12 (0.986 to NC)	5.95 (1.018 to NC)	8.80 (1.873 to NC)	2.83 (1.478 to 7.425)	1.08 (0.953 to 1.511)	1.38 (0.723 to NC)	
Median (95% CI)	NC (2.793 to NC)	NC (10.119 to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.084 to NC)	NC (1.314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9005		0.1615		0.4731	
Hazard ratio (95% CI) vs Pd	-	0.95 (0.42 to 2.16)		1.45 (0.86 to 2.43)		0.69 (0.25 to 1.91)	
P-value	-	0.9001		0.1639		0.4755	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (45.2)	14 (35.9)	52 (53.1)	57 (57.6)	3 (12.5)	9 (56.3)	0.0402
Number (%) of patients censored	17 (54.8)	25 (64.1)	46 (46.9)	42 (42.4)	21 (87.5)	7 (43.8)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	2.53 (1.084 to 7.885)	4.73 (1.051 to NC)	2.14 (1.183 to 2.858)	2.10 (1.708 to 2.793)	NC (1.084 to NC)	1.12 (0.986 to 3.745)	
Median (95% CI)	15.21 (3.910 to 15.211)	NC (6.998 to NC)	6.14 (3.088 to NC)	5.75 (3.745 to 9.101)	NC (NC to NC)	3.75 (1.051 to 8.608)	
75% quantile (95% CI)	15.21 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	8.61 (3.745 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5097		0.6855		0.0066	
Hazard ratio (95% CI) vs Pd	-	0.78 (0.37 to 1.64)		1.08 (0.74 to 1.57)		5.15 (1.38 to 19.14)	
P-value	-	0.5108		0.6858		0.0145	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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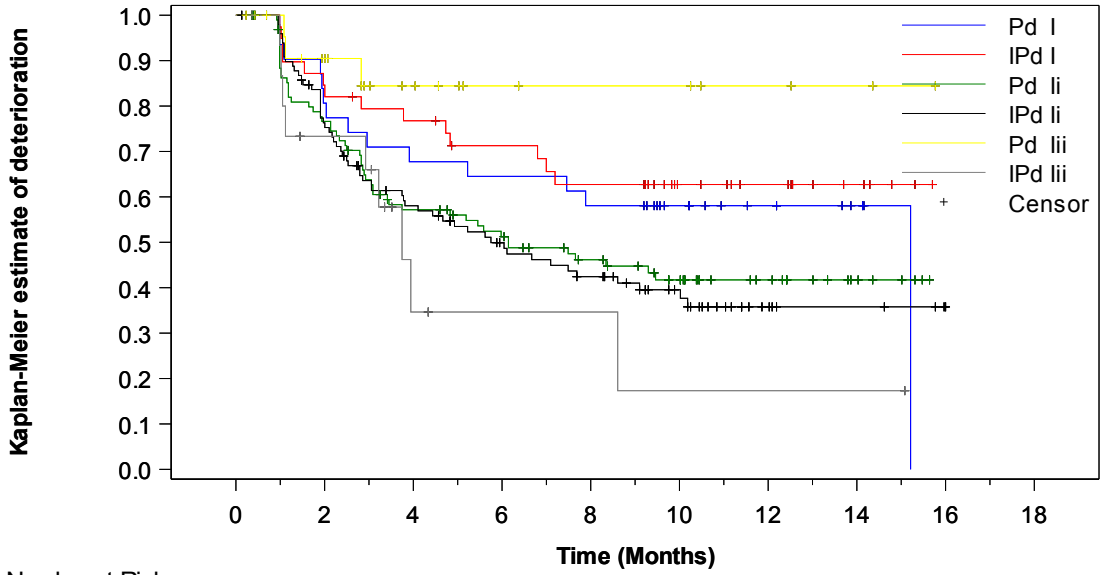
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to R-ISS stage (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd I	31	22	20	18	7	1	0
IPd I	39	30	25	22	10	2	0
Pd Ii	98	59	43	31	14	4	0
IPd Ii	99	58	40	28	7	3	0
Pd Iii	24	12	6	5	3	1	0
IPd Iii	16	9	2	1	1	1	0

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (22.6)	5 (12.8)	5 (5.1)	15 (15.2)	6 (25.0)	1 (6.3)	0.0180
Number (%) of patients censored	24 (77.4)	34 (87.2)	93 (94.9)	84 (84.8)	18 (75.0)	15 (93.8)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	NC (1.117 to NC)	NC (9.856 to NC)	NC (NC to NC)	NC (9.823 to NC)	3.78 (0.953 to NC)	NC (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.778 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2731		0.0299		0.0851	
Hazard ratio (95% CI) vs Pd	-	0.53 (0.17 to 1.68)		2.92 (1.06 to 8.02)		0.19 (0.02 to 1.57)	
P-value	-	0.2811		0.0383		0.1231	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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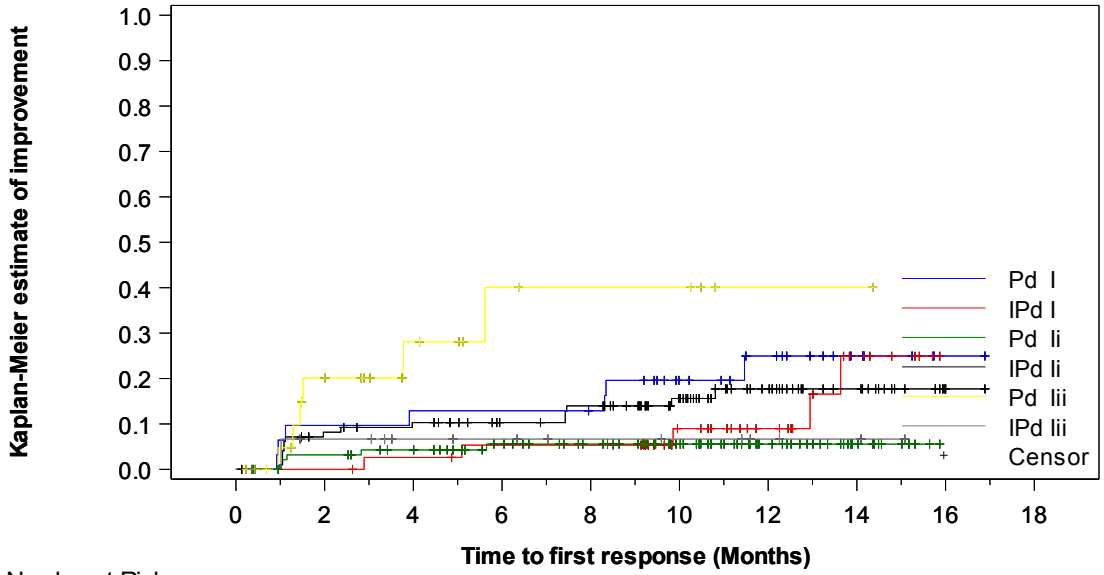
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.7 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to R-ISS stage (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd I	31	28	27	24	13	3	0
IPd I	39	37	35	34	16	4	0
Pd Ii	98	88	73	61	27	6	0
IPd Ii	99	85	74	64	30	9	0
Pd Iii	24	12	5	4	1	0	0
IPd Iii	16	13	9	7	3	1	0

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.8 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (12.9)	4 (10.3)	22 (22.4)	22 (22.2)	2 (8.3)	5 (31.3)	0.4431
Number (%) of patients censored	27 (87.1)	35 (89.7)	76 (77.6)	77 (77.8)	22 (91.7)	11 (68.8)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	NC (5.224 to NC)	NC (7.195 to NC)	14.16 (3.877 to NC)	10.68 (5.749 to NC)	NC (1.084 to NC)	6.54 (3.220 to 8.608)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.160 to NC)	NC (NC to NC)	NC (NC to NC)	8.61 (5.848 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.622 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7903		0.7803		0.2745	
Hazard ratio (95% CI) vs Pd	-	0.83 (0.21 to 3.31)		0.92 (0.51 to 1.66)		2.44 (0.47 to 12.70)	
P-value	-	0.7906		0.7801		0.2897	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (21.7)	4 (28.6)	26 (27.4)	47 (39.8)	0.9366
Number (%) of patients censored	18 (78.3)	10 (71.4)	69 (72.6)	71 (60.2)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	11.53 (0.953 to NC)	1.31 (0.986 to NC)	3.15 (1.117 to NC)	2.83 (1.708 to 4.830)	
Median (95% CI)	NC (11.532 to NC)	NC (1.150 to NC)	NC (NC to NC)	NC (10.119 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5335		0.1699	
Hazard ratio (95% CI) vs Pd	-	1.52 (0.40 to 5.79)		1.40 (0.86 to 2.25)	
P-value	-	0.5364		0.1719	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (34.8)	6 (42.9)	42 (44.2)	62 (52.5)	0.8454
Number (%) of patients censored	15 (65.2)	8 (57.1)	53 (55.8)	56 (47.5)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.83 (0.986 to NC)	3.22 (1.051 to 6.669)	2.79 (1.741 to 3.745)	2.17 (1.708 to 2.858)	
Median (95% CI)	NC (2.825 to NC)	5.62 (1.971 to NC)	NC (6.144 to NC)	7.20 (4.107 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (5.618 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9403		0.3101	
Hazard ratio (95% CI) vs Pd	-	1.04 (0.36 to 3.01)		1.22 (0.83 to 1.81)	
P-value	-	0.9401		0.3109	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (13.0)	2 (14.3)	11 (11.6)	17 (14.4)	0.9658
Number (%) of patients censored	20 (87.0)	12 (85.7)	84 (88.4)	101 (85.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (1.281 to NC)	7.46 (1.084 to NC)	NC (11.466 to NC)	NC (12.945 to NC)	
Median (95% CI)	NC (5.618 to NC)	NC (7.458 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (7.458 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9092		0.7028	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.19 to 6.64)		1.16 (0.54 to 2.48)	
P-value	-	0.9093		0.7030	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (8.7)	2 (14.3)	17 (17.9)	25 (21.2)	0.6548
Number (%) of patients censored	21 (91.3)	12 (85.7)	78 (82.1)	93 (78.8)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (1.117 to NC)	NC (3.220 to NC)	14.16 (5.881 to NC)	NC (7.622 to NC)	
Median (95% CI)	NC (NC to NC)	NC (6.669 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6842		0.8090	
Hazard ratio (95% CI) vs Pd	-	1.50 (0.21 to 10.64)		1.08 (0.58 to 2.00)	
P-value	-	0.6862		0.8090	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (25.0)	9 (37.5)	21 (26.9)	40 (38.8)	0.6945
Number (%) of patients censored	27 (75.0)	15 (62.5)	57 (73.1)	63 (61.2)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	11.53 (1.150 to NC)	1.31 (0.986 to NC)	2.83 (1.084 to NC)	2.83 (1.873 to 6.078)	
Median (95% CI)	NC (11.532 to NC)	NC (1.478 to NC)	NC (NC to NC)	NC (10.119 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2697		0.2685	
Hazard ratio (95% CI) vs Pd	-	1.68 (0.66 to 4.26)		1.35 (0.79 to 2.28)	
P-value	-	0.2749		0.2702	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (36.1)	12 (50.0)	35 (44.9)	53 (51.5)	0.7211
Number (%) of patients censored	23 (63.9)	12 (50.0)	43 (55.1)	50 (48.5)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.83 (1.183 to 7.491)	3.22 (1.018 to 5.618)	2.53 (1.150 to 3.417)	2.10 (1.708 to 2.924)	
Median (95% CI)	NC (3.450 to NC)	6.67 (3.220 to NC)	9.46 (5.191 to NC)	7.00 (4.107 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (6.669 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4368		0.5371	
Hazard ratio (95% CI) vs Pd	-	1.36 (0.62 to 2.99)		1.14 (0.75 to 1.75)	
P-value	-	0.4386		0.5374	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (11.1)	3 (12.5)	10 (12.8)	15 (14.6)	0.8605
Number (%) of patients censored	32 (88.9)	21 (87.5)	68 (87.2)	88 (85.4)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (1.446 to NC)	NC (1.084 to NC)	NC (11.466 to NC)	NC (12.945 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8789		0.9367	
Hazard ratio (95% CI) vs Pd	-	1.12 (0.25 to 5.02)		1.03 (0.46 to 2.30)	
P-value	-	0.8789		0.9369	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (8.3)	5 (20.8)	15 (19.2)	20 (19.4)	0.2129
Number (%) of patients censored	33 (91.7)	19 (79.2)	63 (80.8)	83 (80.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (4.862 to NC)	10.02 (3.220 to NC)	14.16 (5.290 to NC)	NC (7.622 to NC)	
Median (95% CI)	NC (NC to NC)	NC (8.476 to NC)	NC (14.160 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2350		0.7745	
Hazard ratio (95% CI) vs Pd	-	2.32 (0.55 to 9.74)		0.91 (0.46 to 1.77)	
P-value	-	0.2487		0.7746	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (35.6)	23 (27.7)	12 (19.0)	31 (43.7)	0.0083
Number (%) of patients censored	58 (64.4)	60 (72.3)	51 (81.0)	40 (56.3)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	1.45 (1.051 to 5.027)	3.55 (1.906 to NC)	NC (1.906 to NC)	2.83 (1.117 to 6.078)	
Median (95% CI)	NC (11.532 to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.998 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2004		0.0169	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.41 to 1.21)		2.21 (1.13 to 4.30)	
P-value	-	0.2027		0.0200	
Hazard ratio inverted (95% CI) vs IPd		-		0.45 (0.23 to 0.88)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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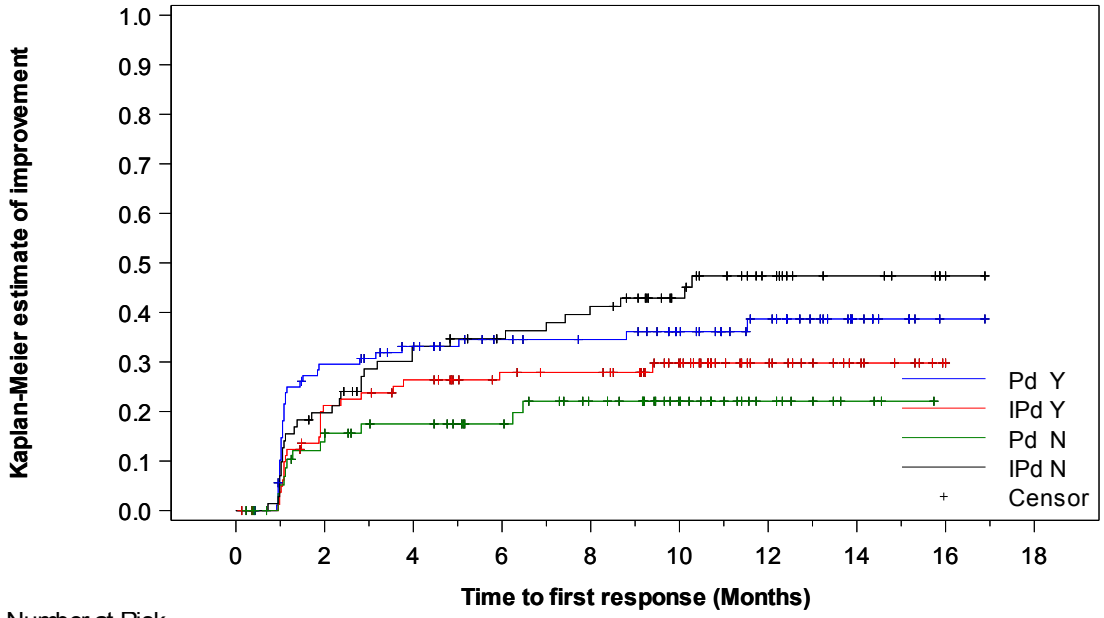
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to previous autologous stem-cell (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd Y	90	58	44	40	23	5	0
IPd Y	83	60	48	43	17	5	0
Pd N	63	44	37	27	9	1	0
IPd N	71	47	40	33	16	5	0

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (43.3)	38 (45.8)	30 (47.6)	42 (59.2)	0.5984
Number (%) of patients censored	51 (56.7)	45 (54.2)	33 (52.4)	29 (40.8)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.83 (2.037 to 3.745)	2.92 (2.004 to 4.435)	1.18 (0.986 to 3.417)	1.91 (1.084 to 2.267)	
Median (95% CI)	NC (5.454 to NC)	10.02 (5.618 to NC)	7.89 (3.417 to NC)	5.22 (2.398 to 9.101)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.211 to NC)	NC (10.185 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9076		0.4100	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.66 to 1.61)		1.22 (0.76 to 1.96)	
P-value	-	0.9076		0.4108	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (15.6)	8 (9.6)	4 (6.3)	13 (18.3)	0.0469
Number (%) of patients censored	76 (84.4)	75 (90.4)	59 (93.7)	58 (81.7)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (8.312 to NC)	NC (13.634 to NC)	NC (NC to NC)	12.94 (9.823 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2395		0.1070	
Hazard ratio (95% CI) vs Pd	-	0.60 (0.25 to 1.42)		2.45 (0.80 to 7.52)	
P-value	-	0.2447		0.1187	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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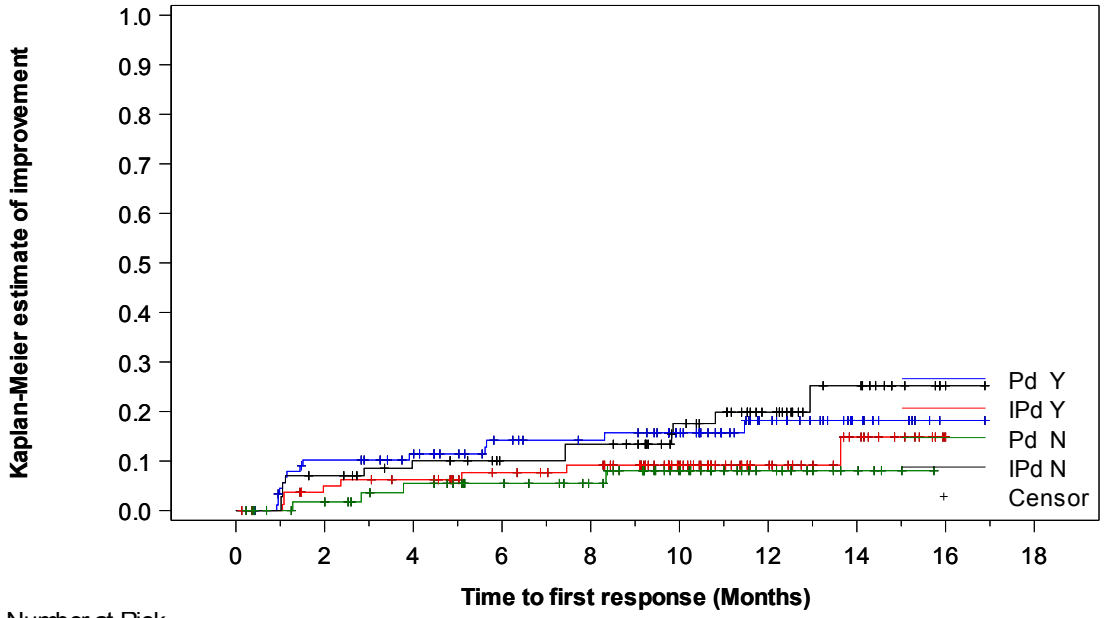
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.7 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to previous autologous stem-cell (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd Y	90	76	61	56	28	7	0
IPd Y	83	74	64	56	23	8	0
Pd N	63	52	44	33	13	2	0
IPd N	71	61	54	49	26	6	0

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.8 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (17.8)	17 (20.5)	12 (19.0)	14 (19.7)	0.6291
Number (%) of patients censored	74 (82.2)	66 (79.5)	51 (81.0)	57 (80.3)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	14.16 (5.290 to NC)	NC (6.538 to NC)	NC (2.464 to NC)	NC (6.965 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7649		0.7397	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.56 to 2.20)		0.88 (0.41 to 1.90)	
P-value	-	0.7649		0.7399	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	0 (0.0)	42 (27.8)	54 (35.5)	0.9762
Number (%) of patients censored	0 (0.0)	2 (100.0)	109 (72.2)	98 (64.5)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	1.02 (1.018 to 1.084)	NC (NC to NC)	3.15 (1.150 to NC)	2.83 (1.906 to 6.078)	
Median (95% CI)	1.05 (1.018 to 1.084)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	1.08 (1.018 to 1.084)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.3711	
Hazard ratio (95% CI) vs Pd	-			1.20 (0.80 to 1.80)	
P-value	-	0.9991		0.3718	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	69 (45.7)	79 (52.0)	0.9816
Number (%) of patients censored	2 (100.0)	1 (50.0)	82 (54.3)	73 (48.0)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (NC to NC)	4.11 (4.107 to NC)	2.46 (1.906 to 2.957)	2.20 (1.906 to 2.924)	
Median (95% CI)	NC (NC to NC)	NC (4.107 to NC)	9.30 (5.585 to NC)	7.10 (4.830 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (4.107 to NC)	NC (15.211 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.5098	
Hazard ratio (95% CI) vs Pd	-			1.11 (0.81 to 1.54)	
P-value	-	0.9990		0.5107	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	0 (0.0)	16 (10.6)	21 (13.8)	0.9852
Number (%) of patients censored	0 (0.0)	2 (100.0)	135 (89.4)	131 (86.2)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	5.65 (5.651 to 11.466)	NC (NC to NC)	NC (NC to NC)	NC (12.945 to NC)	
Median (95% CI)	8.56 (5.651 to 11.466)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	11.47 (5.651 to 11.466)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.5657	
Hazard ratio (95% CI) vs Pd	-			1.21 (0.63 to 2.32)	
P-value	-	0.9990		0.5663	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	28 (18.5)	31 (20.4)	1.0000
Number (%) of patients censored	2 (100.0)	2 (100.0)	123 (81.5)	121 (79.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	14.16 (5.585 to NC)	NC (7.195 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.9959	
Hazard ratio (95% CI) vs Pd	-			1.00 (0.60 to 1.67)	
P-value	-			0.9959	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (30.7)	35 (33.7)	11 (26.8)	12 (36.4)	0.5578
Number (%) of patients censored	70 (69.3)	69 (66.3)	30 (73.2)	21 (63.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	3.15 (1.117 to 11.532)	3.98 (1.906 to 7.984)	1.87 (1.051 to NC)	2.83 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.187 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9890		0.6304	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.62 to 1.63)		1.22 (0.54 to 2.77)	
P-value	-	0.9890		0.6309	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (48.5)	54 (51.9)	15 (36.6)	19 (57.6)	0.3283
Number (%) of patients censored	52 (51.5)	50 (48.1)	26 (63.4)	14 (42.4)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.14 (1.183 to 2.891)	2.27 (1.906 to 3.220)	2.96 (1.938 to 8.345)	2.20 (1.084 to 3.745)	
Median (95% CI)	7.89 (3.910 to NC)	7.00 (4.107 to NC)	NC (4.830 to NC)	6.11 (2.366 to NC)	
75% quantile (95% CI)	NC (15.211 to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.101 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9347		0.0950	
Hazard ratio (95% CI) vs Pd	-	1.02 (0.69 to 1.50)		1.77 (0.90 to 3.48)	
P-value	-	0.9347		0.0995	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (11.9)	16 (15.4)	4 (9.8)	3 (9.1)	0.7607
Number (%) of patients censored	89 (88.1)	88 (84.6)	37 (90.2)	30 (90.9)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (11.466 to NC)	NC (10.809 to NC)	NC (3.910 to NC)	NC (7.425 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6529		0.8436	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.56 to 2.51)		0.86 (0.19 to 3.85)	
P-value	-	0.6533		0.8437	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (18.8)	25 (24.0)	7 (17.1)	4 (12.1)	0.5197
Number (%) of patients censored	82 (81.2)	79 (76.0)	34 (82.9)	29 (87.9)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	14.16 (5.585 to NC)	10.02 (5.749 to NC)	NC (2.464 to NC)	NC (8.115 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5674		0.4303	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.66 to 2.16)		0.61 (0.18 to 2.10)	
P-value	-	0.5679		0.4349	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (31.0)	34 (33.3)	13 (25.0)	20 (39.2)	0.3345
Number (%) of patients censored	69 (69.0)	68 (66.7)	39 (75.0)	31 (60.8)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.79 (1.117 to 11.532)	3.78 (1.906 to 9.396)	2.83 (1.051 to NC)	1.91 (1.117 to 6.078)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.078 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9447		0.2718	
Hazard ratio (95% CI) vs Pd	-	0.98 (0.60 to 1.60)		1.48 (0.73 to 2.97)	
P-value	-	0.9446		0.2749	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (48.0)	52 (51.0)	20 (38.5)	27 (52.9)	0.2861
Number (%) of patients censored	52 (52.0)	50 (49.0)	32 (61.5)	24 (47.1)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.14 (1.183 to 2.891)	2.38 (1.906 to 3.778)	2.92 (1.741 to 5.454)	2.17 (1.117 to 3.745)	
Median (95% CI)	7.89 (5.191 to NC)	7.10 (4.435 to NC)	NC (4.830 to NC)	7.69 (2.793 to NC)	
75% quantile (95% CI)	NC (15.211 to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.185 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9596		0.1815	
Hazard ratio (95% CI) vs Pd	-	1.01 (0.68 to 1.50)		1.48 (0.83 to 2.64)	
P-value	-	0.9596		0.1843	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (12.0)	16 (15.7)	6 (11.5)	5 (9.8)	0.5279
Number (%) of patients censored	88 (88.0)	86 (84.3)	46 (88.5)	46 (90.2)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (11.466 to NC)	13.63 (10.809 to NC)	NC (3.910 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6410		0.6903	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.56 to 2.53)		0.79 (0.24 to 2.58)	
P-value	-	0.6414		0.6913	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (19.0)	24 (23.5)	9 (17.3)	7 (13.7)	0.3821
Number (%) of patients censored	81 (81.0)	78 (76.5)	43 (82.7)	44 (86.3)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	14.16 (5.585 to NC)	10.02 (5.749 to NC)	NC (2.464 to NC)	NC (8.608 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6494		0.4682	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.63 to 2.10)		0.70 (0.26 to 1.87)	
P-value	-	0.6497		0.4710	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detpl_dghc_de_i_t_x.rtf (08APR2021 14:36)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	5 (35.7)	43 (30.1)	49 (35.0)	0.3339
Number (%) of patients censored	9 (90.0)	9 (64.3)	100 (69.9)	91 (65.0)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (0.953 to NC)	1.91 (1.084 to NC)	2.79 (1.117 to 11.532)	3.19 (1.906 to 6.998)	
Median (95% CI)	NC (0.953 to NC)	NC (1.380 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2497		0.6901	
Hazard ratio (95% CI) vs Pd	-	3.29 (0.38 to 28.17)		1.09 (0.72 to 1.64)	
P-value	-	0.2775		0.6907	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (40.0)	7 (50.0)	65 (45.5)	73 (52.1)	0.6628
Number (%) of patients censored	6 (60.0)	7 (50.0)	78 (54.5)	67 (47.9)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.33 (1.741 to NC)	2.83 (0.986 to 8.608)	2.53 (1.906 to 3.088)	2.20 (1.906 to 2.924)	
Median (95% CI)	3.06 (1.741 to NC)	8.61 (1.084 to NC)	9.46 (5.979 to NC)	7.00 (4.731 to NC)	
75% quantile (95% CI)	NC (3.055 to NC)	NC (8.608 to NC)	NC (15.211 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7943		0.3998	
Hazard ratio (95% CI) vs Pd	-	0.85 (0.24 to 2.97)		1.15 (0.83 to 1.61)	
P-value	-	0.7945		0.4006	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	2 (14.3)	17 (11.9)	19 (13.6)	0.9467
Number (%) of patients censored	9 (90.0)	12 (85.7)	126 (88.1)	121 (86.4)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (0.953 to NC)	NC (1.084 to NC)	NC (NC to NC)	NC (12.945 to NC)	
Median (95% CI)	NC (0.953 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9350		0.8330	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.10 to 12.25)		1.07 (0.56 to 2.06)	
P-value	-	0.9351		0.8333	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (20.0)	3 (21.4)	26 (18.2)	28 (20.0)	0.6052
Number (%) of patients censored	8 (80.0)	11 (78.6)	117 (81.8)	112 (80.0)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	3.06 (2.333 to NC)	8.61 (3.220 to NC)	NC (5.881 to NC)	NC (7.195 to NC)	
Median (95% CI)	NC (2.333 to NC)	NC (8.608 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4312		0.9181	
Hazard ratio (95% CI) vs Pd	-	0.48 (0.08 to 3.05)		1.03 (0.60 to 1.75)	
P-value	-	0.4402		0.9181	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (32.3)	26 (29.9)	12 (24.5)	25 (45.5)	0.0704
Number (%) of patients censored	65 (67.7)	61 (70.1)	37 (75.5)	30 (54.5)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	1.84 (1.084 to 11.532)	5.95 (1.873 to NC)	6.24 (1.446 to NC)	2.33 (1.314 to 3.778)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.778 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4711		0.0864	
Hazard ratio (95% CI) vs Pd	-	0.83 (0.49 to 1.39)		1.81 (0.91 to 3.61)	
P-value	-	0.4728		0.0911	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (45.8)	45 (51.7)	23 (46.9)	31 (56.4)	0.8968
Number (%) of patients censored	52 (54.2)	42 (48.3)	26 (53.1)	24 (43.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.50 (1.643 to 3.088)	2.00 (1.708 to 2.858)	2.79 (1.018 to 5.224)	2.50 (1.117 to 4.435)	
Median (95% CI)	15.21 (4.830 to NC)	6.05 (3.745 to NC)	7.66 (3.450 to NC)	7.49 (3.943 to 10.021)	
75% quantile (95% CI)	NC (15.211 to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.101 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5522		0.7525	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.75 to 1.72)		1.09 (0.64 to 1.87)	
P-value	-	0.5517		0.7526	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (14.6)	11 (12.6)	3 (6.1)	9 (16.4)	0.1385
Number (%) of patients censored	82 (85.4)	76 (87.4)	46 (93.9)	46 (83.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (11.466 to NC)	NC (13.634 to NC)	NC (NC to NC)	NC (10.809 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5356		0.1411	
Hazard ratio (95% CI) vs Pd	-	0.78 (0.35 to 1.72)		2.57 (0.70 to 9.51)	
P-value	-	0.5366		0.1561	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (15.6)	17 (19.5)	13 (26.5)	12 (21.8)	0.2482
Number (%) of patients censored	81 (84.4)	70 (80.5)	36 (73.5)	43 (78.2)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (5.881 to NC)	NC (5.125 to NC)	5.59 (1.906 to NC)	10.68 (6.538 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.678 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6226		0.2449	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.59 to 2.38)		0.63 (0.29 to 1.38)	
P-value	-	0.6232		0.2491	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	43 (28.5)	53 (34.9)	0.8151
Number (%) of patients censored	1 (50.0)	1 (50.0)	108 (71.5)	99 (65.1)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	1.91 (1.906 to NC)	2.83 (1.117 to NC)	2.89 (1.906 to 6.998)	
Median (95% CI)	NC (1.281 to NC)	NC (1.906 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (1.906 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.5181	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		1.14 (0.76 to 1.71)	
P-value	-	0.8092		0.5184	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (100.0)	69 (45.7)	78 (51.3)	0.9743
Number (%) of patients censored	2 (100.0)	0 (0.0)	82 (54.3)	74 (48.7)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (NC to NC)	2.83 (2.825 to 7.688)	2.46 (1.906 to 2.957)	2.20 (1.906 to 3.055)	
Median (95% CI)	NC (NC to NC)	5.26 (2.825 to 7.688)	9.30 (5.585 to NC)	7.10 (4.731 to NC)	
75% quantile (95% CI)	NC (NC to NC)	7.69 (2.825 to 7.688)	NC (15.211 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.5527	
Hazard ratio (95% CI) vs Pd	-			1.10 (0.80 to 1.52)	
P-value	-	0.9990		0.5534	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detl_prmab_de_i_t_x.rtf (08APR2021 14:36)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	17 (11.3)	20 (13.2)	0.6728
Number (%) of patients censored	1 (50.0)	1 (50.0)	134 (88.7)	132 (86.8)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	5.09 (5.092 to NC)	NC (NC to NC)	NC (12.945 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.8037	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		1.09 (0.57 to 2.07)	
P-value	-	0.8092		0.8042	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	28 (18.5)	31 (20.4)	1.0000
Number (%) of patients censored	2 (100.0)	2 (100.0)	123 (81.5)	121 (79.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	14.16 (5.585 to NC)	NC (7.195 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.9733	
Hazard ratio (95% CI) vs Pd	-			1.01 (0.61 to 1.68)	
P-value	-			0.9733	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (28.7)	47 (39.8)	11 (28.9)	7 (19.4)	0.1124
Number (%) of patients censored	82 (71.3)	71 (60.2)	27 (71.1)	29 (80.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	3.75 (1.150 to NC)	2.17 (1.314 to 3.778)	1.84 (1.018 to NC)	NC (2.366 to NC)	
Median (95% CI)	NC (NC to NC)	NC (8.674 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2052		0.2603	
Hazard ratio (95% CI) vs Pd	-	1.33 (0.85 to 2.08)		0.58 (0.23 to 1.51)	
P-value	-	0.2067		0.2660	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (42.6)	62 (52.5)	20 (52.6)	18 (50.0)	0.6240
Number (%) of patients censored	66 (57.4)	56 (47.5)	18 (47.4)	18 (50.0)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.33 (1.643 to 3.450)	2.17 (1.906 to 3.055)	2.83 (1.018 to 3.088)	2.20 (1.084 to 3.778)	
Median (95% CI)	15.21 (5.585 to NC)	7.00 (4.665 to NC)	7.46 (2.957 to NC)	9.10 (3.220 to NC)	
75% quantile (95% CI)	NC (15.211 to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.021 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3666		0.9722	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.82 to 1.73)		0.99 (0.52 to 1.87)	
P-value	-	0.3672		0.9722	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (11.3)	19 (16.1)	5 (13.2)	2 (5.6)	0.2231
Number (%) of patients censored	102 (88.7)	99 (83.9)	33 (86.8)	34 (94.4)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (10.809 to NC)	NC (5.618 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4934		0.2760	
Hazard ratio (95% CI) vs Pd	-	1.28 (0.63 to 2.59)		0.41 (0.08 to 2.13)	
P-value	-	0.4945		0.2915	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (19.1)	25 (21.2)	6 (15.8)	6 (16.7)	0.9139
Number (%) of patients censored	93 (80.9)	93 (78.8)	32 (84.2)	30 (83.3)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (5.224 to NC)	NC (6.538 to NC)	14.16 (3.055 to NC)	NC (8.115 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.160 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9568		0.8771	
Hazard ratio (95% CI) vs Pd	-	0.98 (0.55 to 1.75)		1.09 (0.35 to 3.41)	
P-value	-	0.9567		0.8770	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (28.5)	51 (34.7)	3 (33.3)	3 (42.9)	0.6911
Number (%) of patients censored	103 (71.5)	96 (65.3)	6 (66.7)	4 (57.1)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.83 (1.150 to NC)	2.89 (1.906 to 6.998)	8.80 (0.986 to NC)	0.99 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.971 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5962		0.6564	
Hazard ratio (95% CI) vs Pd	-	1.12 (0.74 to 1.69)		1.44 (0.29 to 7.19)	
P-value	-	0.5979		0.6581	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	62 (43.1)	78 (53.1)	7 (77.8)	2 (28.6)	0.0910
Number (%) of patients censored	82 (56.9)	69 (46.9)	2 (22.2)	5 (71.4)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.46 (1.906 to 2.957)	2.17 (1.906 to 2.858)	3.09 (0.986 to 6.144)	4.93 (1.117 to NC)	
Median (95% CI)	NC (5.585 to NC)	7.00 (4.435 to 10.185)	6.14 (0.986 to 15.211)	NC (1.117 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	15.21 (3.910 to 15.211)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2359		0.1631	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.88 to 1.71)		0.34 (0.07 to 1.68)	
P-value	-	0.2367		0.1838	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (12.5)	19 (12.9)	0 (0.0)	2 (28.6)	0.9872
Number (%) of patients censored	126 (87.5)	128 (87.1)	9 (100.0)	5 (71.4)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (12.945 to NC)	NC (NC to NC)	7.46 (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.458 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8341		0.0805	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.49 to 1.78)			
P-value	-	0.8338		0.9977	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (18.1)	30 (20.4)	2 (22.2)	1 (14.3)	0.7204
Number (%) of patients censored	118 (81.9)	117 (79.6)	7 (77.8)	6 (85.7)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	14.16 (5.585 to NC)	NC (7.195 to NC)	10.68 (0.986 to NC)	NC (4.928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (4.928 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9417		0.7791	
Hazard ratio (95% CI) vs Pd	-	1.02 (0.60 to 1.72)		0.71 (0.06 to 7.93)	
P-value	-	0.9418		0.7802	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (27.3)	31 (33.3)	20 (30.8)	23 (37.7)	0.6643
Number (%) of patients censored	64 (72.7)	62 (66.7)	45 (69.2)	38 (62.3)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	3.75 (1.117 to NC)	2.89 (1.314 to 7.984)	1.87 (1.084 to NC)	2.83 (1.873 to 10.119)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (8.805 to NC)	NC (10.119 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4665		0.9713	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.72 to 2.08)		1.01 (0.56 to 1.84)	
P-value	-	0.4673		0.9713	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (48.9)	47 (50.5)	26 (40.0)	33 (54.1)	0.5030
Number (%) of patients censored	45 (51.1)	46 (49.5)	39 (60.0)	28 (45.9)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.14 (1.183 to 2.858)	2.27 (1.544 to 3.220)	2.92 (1.741 to 4.830)	2.17 (1.281 to 3.745)	
Median (95% CI)	7.89 (3.745 to NC)	7.20 (3.943 to NC)	15.21 (4.830 to NC)	6.05 (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.211 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8795		0.3315	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.68 to 1.56)		1.29 (0.77 to 2.16)	
P-value	-	0.8796		0.3328	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detl_llen_de_i_t_x.rtf (08APR2021 14:36)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (13.6)	13 (14.0)	6 (9.2)	8 (13.1)	0.7292
Number (%) of patients censored	76 (86.4)	80 (86.0)	59 (90.8)	53 (86.9)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (8.345 to NC)	NC (10.809 to NC)	NC (11.466 to NC)	NC (7.458 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9672		0.6972	
Hazard ratio (95% CI) vs Pd	-	0.98 (0.45 to 2.16)		1.23 (0.43 to 3.56)	
P-value	-	0.9671		0.6977	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Emotional functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (21.6)	17 (18.3)	9 (13.8)	14 (23.0)	0.2867
Number (%) of patients censored	69 (78.4)	76 (81.7)	56 (86.2)	47 (77.0)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	14.16 (4.862 to NC)	NC (8.115 to NC)	NC (5.290 to NC)	10.68 (5.125 to NC)	
Median (95% CI)	NC (14.160 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5128		0.4038	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.42 to 1.55)		1.43 (0.62 to 3.30)	
P-value	-	0.5129		0.4063	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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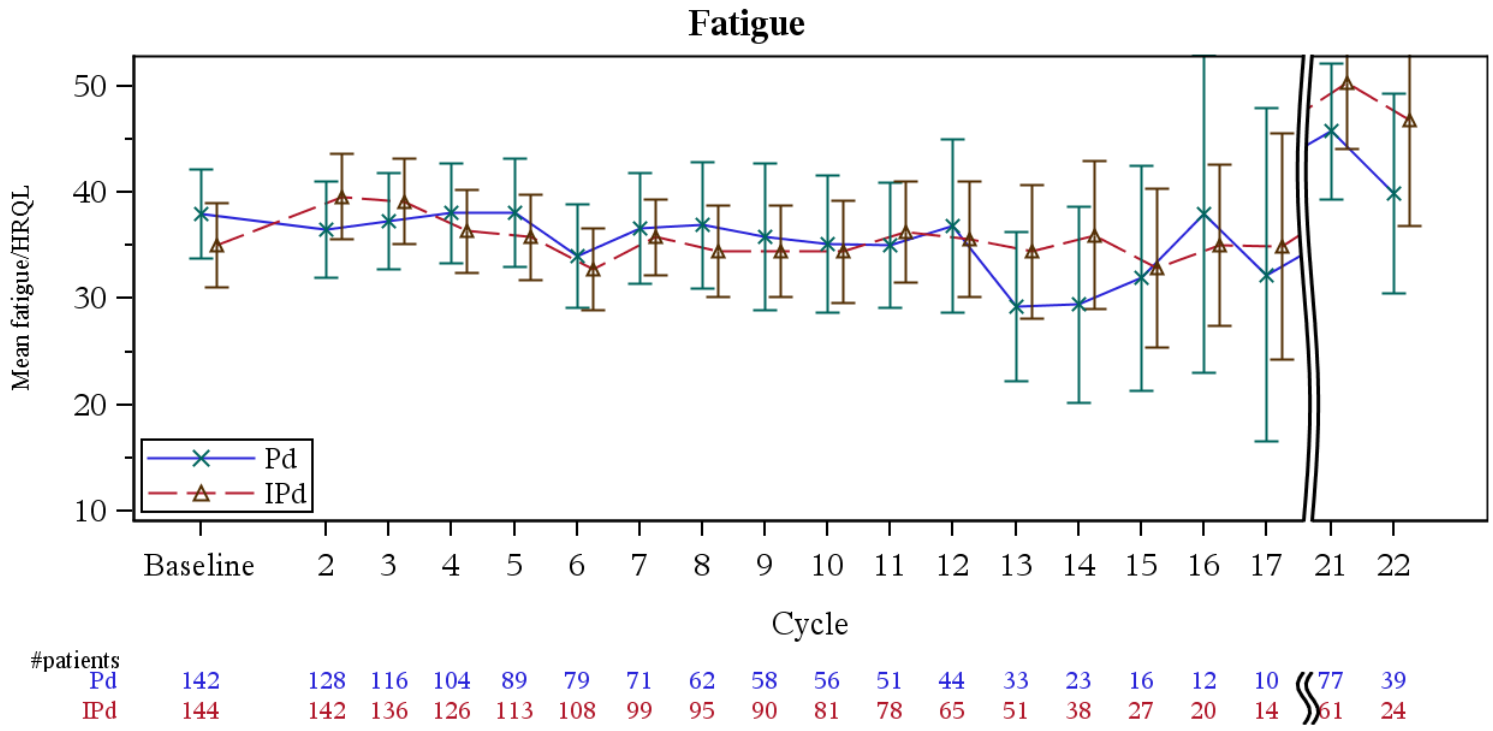
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Fatigue
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-C30 - Mean and 95% CI for fatigue score over time (LOCF) - ITT population



A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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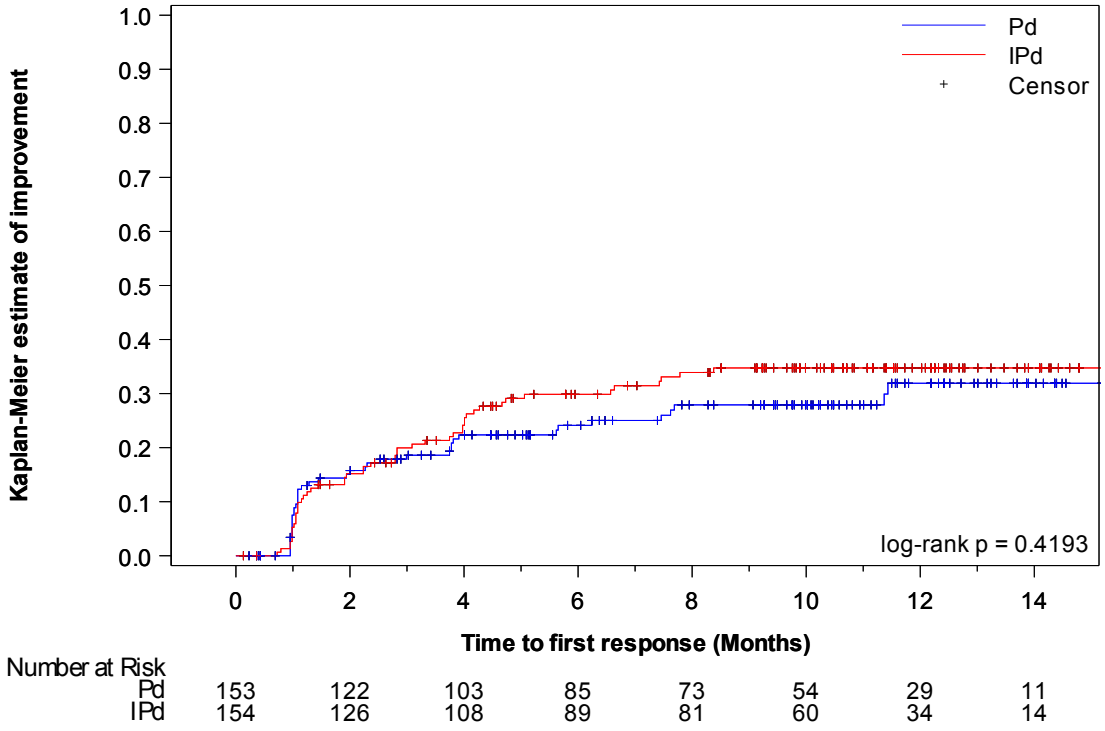
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Fatigue
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-C30 - Time to first improvement by 15 pt in fatigue (LOCF) - ITT population

First improvement 15 points Fatigue (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	40 (26.1)	50 (32.5)
Number (%) of patients censored	113 (73.9)	104 (67.5)
Kaplan-Meier estimates of fatigue in months		
25% quantile (95% CI)	6.24 (2.530 to NC)	4.01 (2.793 to 7.425)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4193
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.19 (0.78 to 1.80)
P-value	-	0.4198
Probability (95% CI)[c]		
2 Months	0.15 (0.098 to 0.214)	0.15 (0.100 to 0.214)
4 Months	0.22 (0.159 to 0.295)	0.24 (0.176 to 0.313)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_imp15l_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Fatigue
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-C30 - Time to first improvement by 15 pt in fatigue - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_imp15l_de_i_f_x.rtf (08APR2021 15:31)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Fatigue
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-C30 - Time to first deterioration by 15 pt in fatigue (LOCF) - ITT population

First deterioration 15 points Fatigue (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	75 (49.0)	90 (58.4)
Number (%) of patients censored	78 (51.0)	64 (41.6)
Kaplan-Meier estimates of fatigue in months		
25% quantile (95% CI)	2.27 (1.873 to 3.088)	1.84 (1.084 to 2.037)
Median (95% CI)	7.06 (4.731 to NC)	5.91 (3.745 to 8.246)
75% quantile (95% CI)	NC (NC to NC)	NC (13.832 to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2615
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.19 (0.88 to 1.63)
P-value	-	0.2621
Probability (95% CI)[c]		
2 Months	0.79 (0.711 to 0.845)	0.69 (0.608 to 0.756)
4 Months	0.61 (0.524 to 0.685)	0.56 (0.479 to 0.639)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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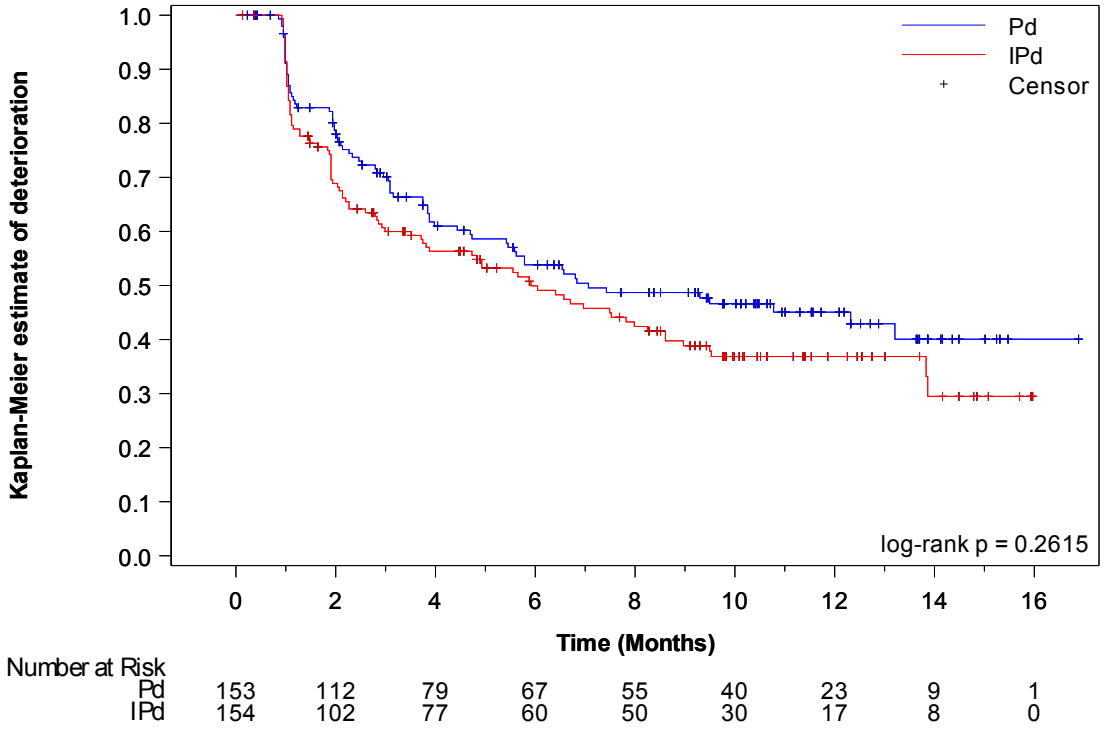
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Fatigue
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-C30 - Time to first deterioration by 15 pt in fatigue - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Fatigue
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in fatigue (LOCF) - ITT population

First permanent improvement 15 points Fatigue (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	9 (5.9)	13 (8.4)
Number (%) of patients censored	144 (94.1)	141 (91.6)
Kaplan-Meier estimates of fatigue in months		
25% quantile (95% CI)	NC (NC to NC)	16.79 (NC to NC)
Median (95% CI)	NC (NC to NC)	16.79 (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	16.79 (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5079
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.33 (0.57 to 3.12)
P-value	-	0.5093
Probability (95% CI)[c]		
2 Months	0.03 (0.013 to 0.073)	0.03 (0.012 to 0.071)
4 Months	0.03 (0.013 to 0.073)	0.04 (0.016 to 0.080)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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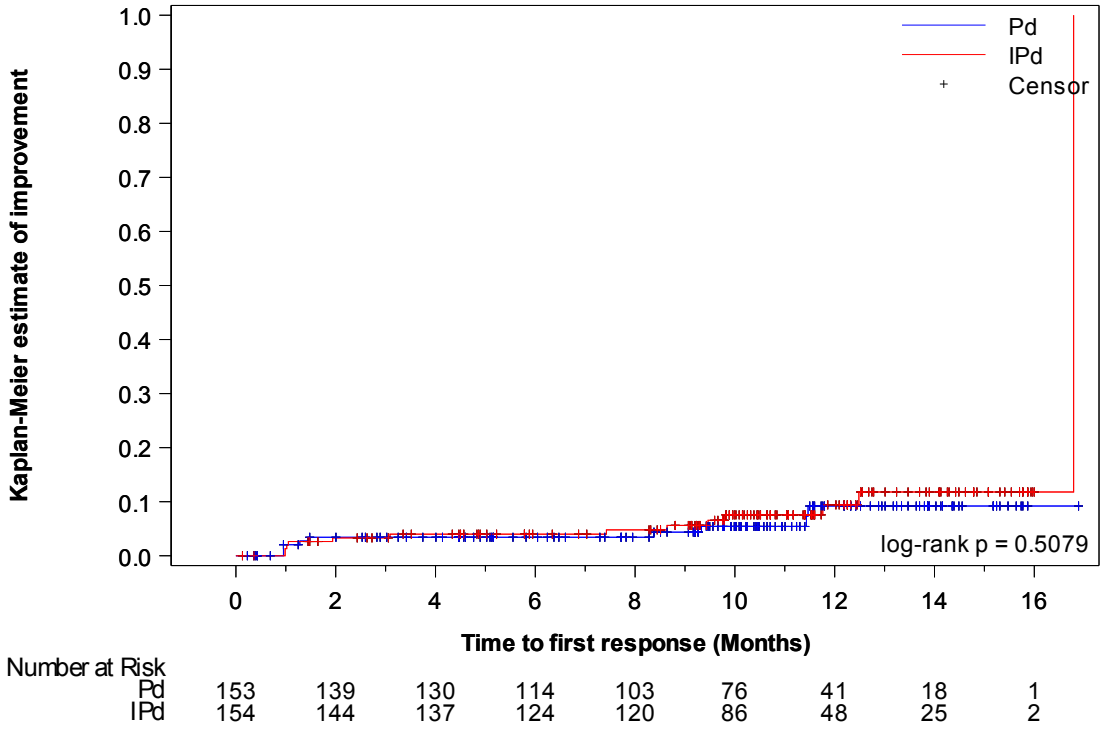
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Fatigue
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-C30 - Time until permanent improvement by 15 pt in fatigue - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Fatigue
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in fatigue (LOCF) - ITT population

First permanent deterioration 15 points Fatigue (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	40 (26.1)	35 (22.7)
Number (%) of patients censored	113 (73.9)	119 (77.3)
Kaplan-Meier estimates of fatigue in months		
25% quantile (95% CI)	8.77 (3.844 to NC)	10.84 (8.411 to NC)
Median (95% CI)	NC (NC to NC)	NC (15.310 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1481
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.72 (0.45 to 1.13)
P-value	-	0.1499
Probability (95% CI)[c]		
2 Months	0.92 (0.868 to 0.958)	0.95 (0.897 to 0.973)
4 Months	0.81 (0.732 to 0.864)	0.91 (0.845 to 0.943)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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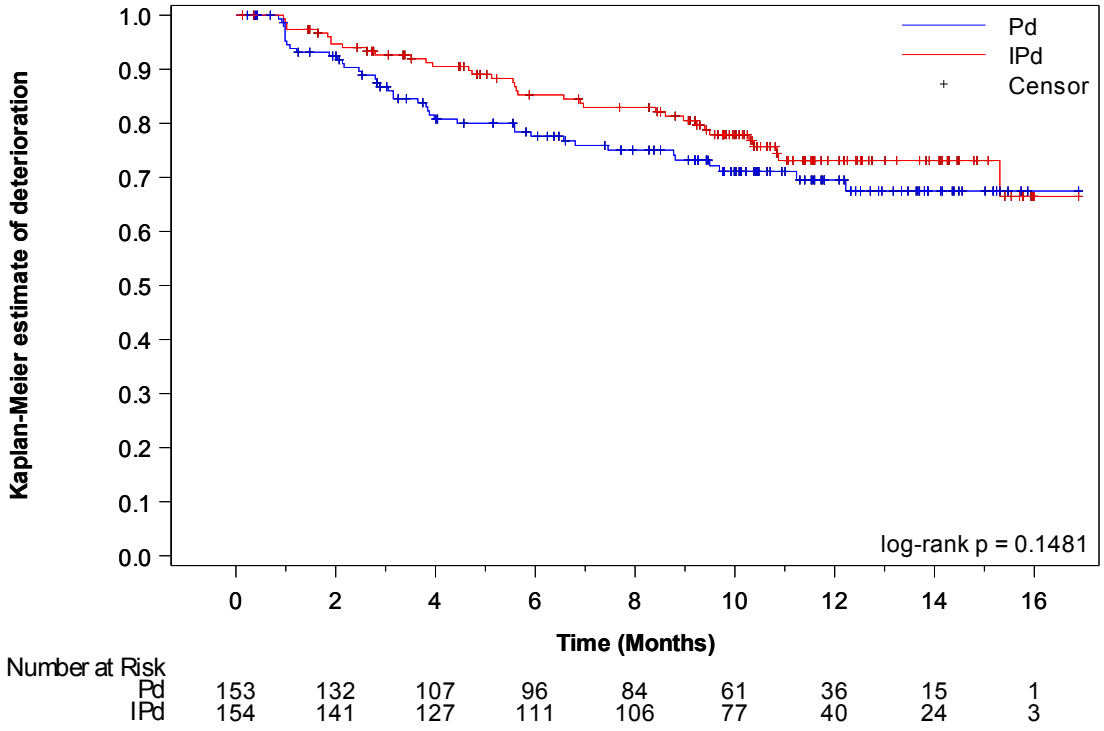
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Fatigue
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-C30 - Time until permanent deterioration by 15 pt in fatigue - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_det15pl_de_i_f_x.rtf (08APR2021 15:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (50.0)	36 (66.7)	27 (50.0)	31 (45.6)	14 (48.3)	15 (46.9)	0.2741
Number (%) of patients censored	35 (50.0)	18 (33.3)	27 (50.0)	37 (54.4)	15 (51.7)	17 (53.1)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	1.07 (1.018 to 1.906)	1.08 (0.986 to 1.708)	1.51 (0.986 to 3.745)	2.23 (1.183 to 3.187)	1.12 (0.986 to 2.924)	1.61 (1.018 to 4.994)	
Median (95% CI)	4.27 (2.004 to NC)	2.23 (1.708 to 4.008)	7.49 (3.023 to NC)	NC (3.318 to NC)	6.64 (1.281 to NC)	7.00 (2.168 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (4.008 to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.411 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1681		0.5139		0.6043	
Hazard ratio (95% CI) vs Pd	-	1.39 (0.87 to 2.21)		0.84 (0.50 to 1.41)		0.82 (0.40 to 1.71)	
P-value	-	0.1700		0.5144		0.6049	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (68.6)	33 (61.1)	32 (59.3)	56 (82.4)	24 (82.8)	25 (78.1)	0.0004
Number (%) of patients censored	22 (31.4)	21 (38.9)	22 (40.7)	12 (17.6)	5 (17.2)	7 (21.9)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	1.15 (1.018 to 1.938)	1.41 (1.018 to 2.201)	1.74 (0.986 to 2.103)	1.02 (0.986 to 1.084)	1.02 (0.953 to 1.051)	1.08 (0.986 to 1.873)	
Median (95% CI)	2.83 (1.971 to 4.731)	4.11 (2.201 to 13.864)	3.45 (2.103 to 5.585)	1.91 (1.084 to 2.267)	1.18 (1.018 to 2.464)	2.46 (1.117 to 6.965)	
75% quantile (95% CI)	9.33 (4.731 to NC)	13.86 (8.838 to NC)	NC (5.224 to NC)	4.73 (2.891 to 6.472)	3.75 (1.938 to 4.698)	7.98 (4.731 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1776		0.0042		0.0155	
Hazard ratio (95% CI) vs Pd	-	0.74 (0.47 to 1.15)		1.87 (1.21 to 2.90)		0.48 (0.27 to 0.88)	
P-value	-	0.1793		0.0048		0.0176	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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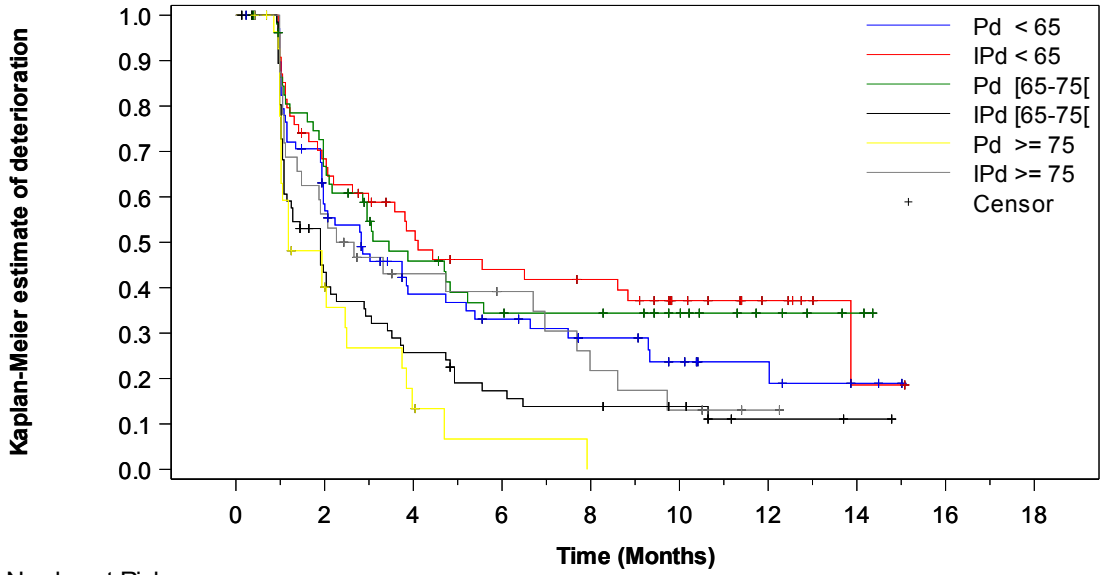
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to age (IRT) (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd < 65	70	29	17	12	5	1	0
IPd < 65	54	30	20	16	6	1	0
Pd [65-75[	54	26	15	13	5	0	0
IPd [65-75[	68	21	10	7	2	0	0
Pd >= 75	29	6	1	0	0	0	0
IPd >= 75	32	13	9	4	1	0	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_detl_age_de_i_f_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (22.9)	11 (20.4)	6 (11.1)	11 (16.2)	2 (6.9)	6 (18.8)	0.4895
Number (%) of patients censored	54 (77.1)	43 (79.6)	48 (88.9)	57 (83.8)	27 (93.1)	26 (81.3)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	11.30 (6.407 to NC)	NC (1.938 to NC)	NC (11.170 to NC)	14.95 (8.838 to NC)	NC (1.281 to NC)	NC (6.637 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.949 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7133		0.5644		0.2915	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.40 to 1.87)		1.34 (0.49 to 3.62)		2.31 (0.47 to 11.47)	
P-value	-	0.7136		0.5658		0.3055	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_imppl_age_de_i_t_x.rtf (08APR2021 14:42)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.7 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (34.3)	19 (35.2)	16 (29.6)	25 (36.8)	18 (62.1)	15 (46.9)	0.3375
Number (%) of patients censored	46 (65.7)	35 (64.8)	38 (70.4)	43 (63.2)	11 (37.9)	17 (53.1)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	4.44 (1.347 to 8.805)	4.70 (2.628 to 14.390)	3.15 (1.216 to NC)	5.68 (1.051 to 9.495)	1.18 (0.986 to 3.844)	3.32 (0.986 to 10.283)	
Median (95% CI)	NC (8.805 to NC)	15.67 (14.390 to NC)	NC (10.382 to NC)	NC (10.021 to NC)	5.59 (2.464 to 9.331)	11.66 (4.731 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.671 to NC)	NC (NC to NC)	NC (NC to NC)	10.97 (8.378 to NC)	13.67 (11.663 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7423		0.5836		0.1048	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.49 to 1.65)		1.19 (0.64 to 2.23)		0.57 (0.29 to 1.13)	
P-value	-	0.7424		0.5841		0.1092	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	47 (46.5)	45 (44.1)	29 (55.8)	37 (71.2)	0.3188
Number (%) of patients censored	54 (53.5)	57 (55.9)	23 (44.2)	15 (28.8)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.28 (1.051 to 2.530)	1.94 (1.117 to 2.825)	1.08 (0.986 to 1.938)	1.08 (1.018 to 1.873)	
Median (95% CI)	9.10 (3.910 to NC)	NC (4.271 to NC)	3.78 (1.938 to 8.476)	2.83 (1.873 to 3.745)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.768 to NC)	NC (3.745 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5744		0.3837	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.59 to 1.34)		1.24 (0.76 to 2.02)	
P-value	-	0.5743		0.3846	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	67 (66.3)	76 (74.5)	37 (71.2)	38 (73.1)	0.2722
Number (%) of patients censored	34 (33.7)	26 (25.5)	15 (28.8)	14 (26.9)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.15 (1.018 to 1.906)	1.07 (0.986 to 1.248)	1.08 (1.018 to 1.938)	1.12 (1.018 to 1.314)	
Median (95% CI)	2.86 (1.971 to 3.844)	2.14 (1.840 to 3.417)	2.50 (1.938 to 3.877)	3.32 (1.314 to 5.552)	
75% quantile (95% CI)	NC (4.731 to NC)	7.69 (4.435 to NC)	7.92 (3.877 to NC)	13.86 (5.552 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3477		0.4605	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.84 to 1.63)		0.84 (0.53 to 1.33)	
P-value	-	0.3486		0.4610	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	15 (14.9)	19 (18.6)	9 (17.3)	9 (17.3)	0.6294
Number (%) of patients censored	86 (85.1)	83 (81.4)	43 (82.7)	43 (82.7)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	NC (10.251 to NC)	13.14 (9.823 to NC)	NC (3.745 to NC)	NC (3.581 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.949 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6596		0.8472	
Hazard ratio (95% CI) vs Pd	-	1.16 (0.59 to 2.29)		0.91 (0.36 to 2.30)	
P-value	-	0.6599		0.8470	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_imppl_plne_de_i_t_x.rtf (08APR2021 14:42)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	37 (36.6)	39 (38.2)	21 (40.4)	20 (38.5)	0.6441
Number (%) of patients censored	64 (63.4)	63 (61.8)	31 (59.6)	32 (61.5)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	2.79 (1.183 to 5.585)	3.94 (1.413 to 8.115)	3.81 (1.084 to 8.378)	5.55 (3.384 to 11.663)	
Median (95% CI)	NC (9.331 to NC)	NC (10.283 to NC)	10.97 (8.345 to NC)	13.67 (11.663 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.667 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9058		0.4081	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.62 to 1.53)		0.77 (0.42 to 1.43)	
P-value	-	0.9057		0.4094	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (51.4)	52 (58.4)	40 (48.2)	30 (46.2)	0.1975
Number (%) of patients censored	34 (48.6)	37 (41.6)	43 (51.8)	35 (53.8)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.12 (1.018 to 2.004)	1.10 (1.018 to 1.906)	1.12 (1.018 to 2.267)	1.94 (1.117 to 3.285)	
Median (95% CI)	7.49 (2.661 to NC)	3.25 (2.136 to 7.359)	6.64 (2.891 to NC)	NC (3.778 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4059		0.3429	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.78 to 1.83)		0.80 (0.50 to 1.28)	
P-value	-	0.4066		0.3439	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (60.0)	65 (73.0)	62 (74.7)	49 (75.4)	0.1304
Number (%) of patients censored	28 (40.0)	24 (27.0)	21 (25.3)	16 (24.6)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.74 (1.051 to 2.004)	1.08 (1.018 to 1.446)	1.02 (0.986 to 1.183)	1.05 (0.986 to 1.248)	
Median (95% CI)	3.75 (2.037 to 5.388)	2.20 (1.906 to 3.778)	2.07 (1.906 to 3.023)	2.27 (1.281 to 4.041)	
75% quantile (95% CI)	NC (9.298 to NC)	8.84 (4.928 to NC)	5.22 (3.450 to 9.331)	6.97 (4.435 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1321		0.4891	
Hazard ratio (95% CI) vs Pd	-	1.35 (0.91 to 1.99)		0.88 (0.60 to 1.28)	
P-value	-	0.1335		0.4894	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (17.1)	17 (19.1)	12 (14.5)	11 (16.9)	0.9617
Number (%) of patients censored	58 (82.9)	72 (80.9)	71 (85.5)	54 (83.1)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	NC (9.331 to NC)	13.14 (8.838 to NC)	NC (8.378 to NC)	NC (5.749 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.949 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8441		0.8337	
Hazard ratio (95% CI) vs Pd	-	1.08 (0.51 to 2.25)		1.09 (0.48 to 2.48)	
P-value	-	0.8449		0.8333	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (34.3)	27 (30.3)	34 (41.0)	32 (49.2)	0.3047
Number (%) of patients censored	46 (65.7)	62 (69.7)	49 (59.0)	33 (50.8)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	3.81 (1.873 to 8.542)	6.57 (3.811 to 15.671)	2.83 (1.018 to 6.538)	1.63 (0.986 to 4.830)	
Median (95% CI)	NC (8.542 to NC)	NC (15.671 to NC)	NC (8.378 to NC)	12.75 (4.830 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.390 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3378		0.6251	
Hazard ratio (95% CI) vs Pd	-	0.76 (0.44 to 1.33)		1.13 (0.70 to 1.83)	
P-value	-	0.3392		0.6253	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_detpl_sex_de_i_t_x.rtf (08APR2021 14:42)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	63 (50.0)	63 (53.4)	12 (63.2)	15 (62.5)	0.6657
Number (%) of patients censored	63 (50.0)	55 (46.6)	7 (36.8)	9 (37.5)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.28 (1.018 to 2.070)	1.51 (1.051 to 1.971)	1.05 (0.986 to 1.117)	1.58 (1.018 to 2.234)	
Median (95% CI)	6.87 (3.778 to NC)	5.82 (2.891 to NC)	1.15 (1.051 to NC)	2.79 (1.906 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.150 to NC)	NC (2.825 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9787		0.5070	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.70 to 1.41)		0.77 (0.36 to 1.66)	
P-value	-	0.9787		0.5082	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	84 (66.7)	91 (77.1)	15 (78.9)	19 (79.2)	0.9755
Number (%) of patients censored	42 (33.3)	27 (22.9)	4 (21.1)	5 (20.8)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.12 (1.018 to 1.906)	1.05 (1.018 to 1.150)	1.97 (0.953 to 2.957)	1.22 (0.986 to 1.906)	
Median (95% CI)	2.83 (1.971 to 3.844)	2.07 (1.643 to 3.581)	3.02 (1.971 to 5.388)	2.66 (1.314 to 4.928)	
75% quantile (95% CI)	9.33 (4.731 to NC)	7.98 (4.830 to NC)	5.59 (3.023 to NC)	5.55 (2.891 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3812		0.6386	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.85 to 1.54)		1.18 (0.60 to 2.32)	
P-value	-	0.3815		0.6389	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_detl_race_de_i_t_x.rtf (08APR2021 14:41)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (17.5)	23 (19.5)	2 (10.5)	2 (8.3)	0.7118
Number (%) of patients censored	104 (82.5)	95 (80.5)	17 (89.5)	22 (91.7)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	NC (9.331 to NC)	14.95 (9.823 to NC)	NC (1.018 to NC)	NC (6.965 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9677		0.7924	
Hazard ratio (95% CI) vs Pd	-	1.01 (0.56 to 1.82)		0.77 (0.11 to 5.46)	
P-value	-	0.9677		0.7930	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_imppl_race_de_i_t_x.rtf (08APR2021 14:42)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (35.7)	46 (39.0)	8 (42.1)	12 (50.0)	0.7385
Number (%) of patients censored	81 (64.3)	72 (61.0)	11 (57.9)	12 (50.0)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	3.65 (1.873 to 6.538)	3.81 (1.643 to 8.608)	4.83 (0.953 to NC)	4.80 (0.986 to 9.495)	
Median (95% CI)	NC (10.382 to NC)	15.67 (11.663 to NC)	NC (4.830 to NC)	10.87 (4.928 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.671 to NC)	NC (NC to NC)	NC (13.667 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9292		0.8333	
Hazard ratio (95% CI) vs Pd	-	0.98 (0.65 to 1.48)		1.10 (0.45 to 2.72)	
P-value	-	0.9292		0.8334	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	3 (75.0)	70 (52.2)	71 (54.6)	0.6779
Number (%) of patients censored	2 (66.7)	1 (25.0)	64 (47.8)	59 (45.4)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	1.17 (1.018 to 9.626)	1.12 (1.018 to 1.906)	1.71 (1.084 to 1.971)	
Median (95% CI)	NC (1.281 to NC)	5.47 (1.018 to NC)	6.64 (2.891 to NC)	4.99 (2.825 to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9835		0.8643	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.09 to 10.98)		0.97 (0.70 to 1.35)	
P-value	-	0.9834		0.8643	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	3 (75.0)	91 (67.9)	100 (76.9)	0.9095
Number (%) of patients censored	2 (66.7)	1 (25.0)	43 (32.1)	30 (23.1)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.35 (1.347 to NC)	2.78 (2.136 to 4.435)	1.18 (1.018 to 1.938)	1.05 (1.018 to 1.117)	
Median (95% CI)	NC (1.347 to NC)	3.93 (2.136 to NC)	2.86 (2.037 to 3.844)	2.04 (1.643 to 3.515)	
75% quantile (95% CI)	NC (1.347 to NC)	NC (2.136 to NC)	9.33 (4.830 to NC)	7.98 (4.928 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7741		0.3023	
Hazard ratio (95% CI) vs Pd	-	0.70 (0.06 to 7.92)		1.16 (0.87 to 1.54)	
P-value	-	0.7751		0.3026	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	1 (25.0)	20 (14.9)	24 (18.5)	0.3081
Number (%) of patients censored	2 (66.7)	3 (75.0)	114 (85.1)	106 (81.5)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (8.838 to NC)	NC (11.302 to NC)	14.95 (10.448 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (8.838 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (8.838 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4504		0.6610	
Hazard ratio (95% CI) vs Pd	-	0.35 (0.02 to 5.89)		1.14 (0.63 to 2.07)	
P-value	-	0.4689		0.6622	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	0 (0.0)	50 (37.3)	57 (43.8)	0.9834
Number (%) of patients censored	2 (66.7)	4 (100.0)	84 (62.7)	73 (56.2)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.35 (1.347 to NC)	NC (NC to NC)	3.81 (2.168 to 5.914)	3.75 (1.840 to 5.848)	
Median (95% CI)	NC (1.347 to NC)	NC (NC to NC)	NC (9.331 to NC)	13.67 (10.021 to NC)	
75% quantile (95% CI)	NC (1.347 to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.671 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.6345	
Hazard ratio (95% CI) vs Pd	-			1.10 (0.75 to 1.60)	
P-value	-	0.9990		0.6351	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	32 (42.1)	22 (40.0)	11 (55.0)	17 (60.7)	3 (60.0)	5 (71.4)	10 (66.7)	12 (57.1)	20 (54.1)	26 (60.5)	0.9185
Number (%) of patients censored	44 (57.9)	33 (60.0)	9 (45.0)	11 (39.3)	2 (40.0)	2 (28.6)	5 (33.3)	9 (42.9)	17 (45.9)	17 (39.5)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	2.00 (1.084 to 3.910)	1.94 (1.117 to 4.008)	1.08 (0.986 to 5.027)	1.07 (0.986 to 2.070)	0.99 (0.953 to NC)	1.02 (0.920 to 1.708)	1.05 (0.986 to 1.117)	2.17 (1.051 to 2.793)	1.18 (0.986 to 1.938)	1.12 (0.986 to 2.825)	
Median (95% CI)	9.30 (4.074 to NC)	NC (3.318 to NC)	6.64 (1.084 to NC)	3.06 (1.511 to NC)	1.12 (0.953 to NC)	1.71 (0.920 to NC)	1.15 (1.018 to NC)	3.75 (2.168 to NC)	3.78 (1.511 to NC)	3.35 (2.760 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.637 to NC)	NC (6.998 to NC)	NC (0.953 to NC)	NC (1.248 to NC)	NC (1.150 to NC)	NC (3.745 to NC)	NC (6.768 to NC)	NC (5.322 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_impl_greg_de_i_t_x.rtf (08APR2021 14:41)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.7430		0.8994		0.9992		0.2527		0.9331	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.53 to 1.57)		1.05 (0.49 to 2.25)		1.00 (0.24 to 4.21)		0.61 (0.26 to 1.43)		1.03 (0.57 to 1.84)	
P-value	-	0.7431		0.8998		0.9992		0.2572		0.9332	
Improvement probability (95% CI)[b]											
2 Months	0.239 (0.147 to 0.342)	0.299 (0.183 to 0.423)	0.316 (0.129 to 0.522)	0.393 (0.217 to 0.565)	0.600 (0.126 to 0.882)	0.571 (0.172 to 0.837)	0.533 (0.263 to 0.744)	0.241 (0.088 to 0.436)	0.392 (0.235 to 0.547)	0.310 (0.179 to 0.451)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_impl_greg_de_i_t_x.rtf (08APR2021 14:41)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Number (%) of events	45 (59.2)	36 (65.5)	16 (80.0)	19 (67.9)	3 (60.0)	6 (85.7)	12 (80.0)	16 (76.2)	28 (75.7)	37 (86.0)	0.8874
Number (%) of patients censored	31 (40.8)	19 (34.5)	4 (20.0)	9 (32.1)	2 (40.0)	1 (14.3)	3 (20.0)	5 (23.8)	9 (24.3)	6 (14.0)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	1.08 (1.018 to 1.938)	1.22 (1.018 to 1.840)	1.22 (0.986 to 1.971)	1.00 (0.953 to 1.084)	1.35 (0.986 to NC)	1.08 (0.953 to 1.906)	1.97 (1.018 to 3.023)	1.12 (0.986 to 1.906)	1.02 (0.986 to 1.741)	1.12 (0.986 to 1.380)	
Median (95% CI)	2.86 (1.971 to 5.224)	3.42 (1.840 to 6.965)	2.50 (1.216 to 3.975)	2.61 (1.018 to 10.645)	2.96 (0.986 to NC)	1.91 (0.953 to 4.731)	3.75 (1.150 to 5.388)	2.66 (1.117 to 5.552)	1.97 (1.150 to 3.088)	1.97 (1.281 to 3.713)	
75% quantile (95% CI)	NC (7.491 to NC)	NC (6.702 to NC)	4.73 (2.497 to NC)	10.64 (3.844 to NC)	NC (0.986 to NC)	4.73 (1.150 to NC)	5.59 (3.745 to NC)	8.61 (2.661 to NC)	4.73 (2.858 to NC)	5.55 (2.924 to 9.725)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.9272		0.6871		0.4029		0.7002		0.8582	
Hazard ratio (95% CI) vs Pd	-	1.02 (0.66 to 1.58)		0.87 (0.45 to 1.70)		1.80 (0.45 to 7.26)		1.16 (0.55 to 2.46)		0.96 (0.58 to 1.57)	
P-value	-	0.9271		0.6873		0.4094		0.7005		0.8577	
Deterioration probability (95% CI)[b]											
2 Months	0.619 (0.496 to 0.721)	0.629 (0.486 to 0.742)	0.526 (0.287 to 0.719)	0.500 (0.306 to 0.666)	0.600 (0.126 to 0.882)	0.429 (0.098 to 0.734)	0.667 (0.375 to 0.846)	0.564 (0.328 to 0.745)	0.491 (0.319 to 0.642)	0.495 (0.337 to 0.635)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_detl_greg_de_i_t_x.rtf (08APR2021 14:41)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	13 (17.1)	11 (20.0)	2 (10.0)	6 (21.4)	0 (0.0)	1 (14.3)	2 (13.3)	2 (9.5)	7 (18.9)	8 (18.6)	0.8380
Number (%) of patients censored	63 (82.9)	44 (80.0)	18 (90.0)	22 (78.6)	5 (100.0)	6 (85.7)	13 (86.7)	19 (90.5)	30 (81.1)	35 (81.4)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (8.378 to NC)	13.14 (5.749 to NC)	NC (6.242 to NC)	NC (0.986 to NC)	NC (NC to NC)	NC (8.838 to NC)	NC (1.018 to NC)	NC (6.965 to NC)	11.30 (4.271 to NC)	14.95 (5.815 to NC)	
Median (95% CI)	NC (NC to NC)	NC (13.142 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.838 to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.302 to NC)	NC (14.949 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.838 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.7384		0.3174		0.3173		0.7056		0.6761	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.51 to 2.56)		2.22 (0.45 to 10.99)				0.69 (0.10 to 4.88)		0.80 (0.29 to 2.23)	
P-value	-	0.7385		0.3300		0.9984		0.7072		0.6767	
Improvement probability (95% CI)[b]											

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	22 (28.9)	16 (29.1)	11 (55.0)	13 (46.4)	2 (40.0)	3 (42.9)	6 (40.0)	10 (47.6)	17 (45.9)	17 (39.5)	0.8257
Number (%) of patients censored	54 (71.1)	39 (70.9)	9 (45.0)	15 (53.6)	3 (60.0)	4 (57.1)	9 (60.0)	11 (52.4)	20 (54.1)	26 (60.5)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	5.59 (2.464 to NC)	3.94 (1.051 to NC)	1.22 (0.986 to 9.331)	2.61 (0.953 to 10.283)	1.35 (0.986 to NC)	2.63 (1.150 to NC)	5.19 (1.971 to NC)	5.55 (0.986 to 10.875)	1.61 (0.986 to 3.811)	8.11 (2.628 to 10.021)	
Median (95% CI)	NC (NC to NC)	NC (11.663 to NC)	10.38 (1.216 to NC)	12.75 (4.928 to NC)	NC (0.986 to NC)	NC (1.150 to NC)	NC (4.830 to NC)	13.67 (5.552 to NC)	8.54 (3.055 to NC)	15.67 (8.608 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.382 to NC)	NC (12.747 to NC)	NC (0.986 to NC)	NC (4.731 to NC)	NC (NC to NC)	NC (10.875 to NC)	NC (NC to NC)	NC (15.671 to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.9290		0.7185		0.9180		0.7957		0.1353	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.51 to 1.85)		0.86 (0.38 to 1.93)		0.91 (0.15 to 5.47)		1.14 (0.41 to 3.18)		0.60 (0.30 to 1.18)	
P-value	-	0.9292		0.7187		0.9181		0.7958		0.1393	
Deterioration probability (95% CI)[b]											

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (45.4)	35 (45.5)	32 (57.1)	47 (61.0)	0.7265
Number (%) of patients censored	53 (54.6)	42 (54.5)	24 (42.9)	30 (39.0)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.51 (1.018 to 2.661)	1.71 (1.084 to 3.253)	1.08 (0.986 to 1.446)	1.28 (1.051 to 2.168)	
Median (95% CI)	9.10 (3.778 to NC)	NC (3.351 to NC)	4.27 (1.446 to NC)	2.92 (2.234 to 5.815)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (8.476 to NC)	NC (9.626 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7214		0.9119	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.59 to 1.44)		1.03 (0.65 to 1.61)	
P-value	-	0.7224		0.9121	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	58 (59.8)	55 (71.4)	46 (82.1)	59 (76.6)	0.2957
Number (%) of patients censored	39 (40.2)	22 (28.6)	10 (17.9)	18 (23.4)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.12 (1.018 to 1.938)	1.12 (1.018 to 1.413)	1.12 (1.018 to 1.906)	1.05 (0.986 to 1.281)	
Median (95% CI)	3.06 (2.037 to 4.698)	2.14 (1.478 to 4.731)	2.04 (1.906 to 3.023)	2.63 (1.873 to 3.778)	
75% quantile (95% CI)	NC (7.491 to NC)	8.84 (4.928 to NC)	4.83 (3.023 to 9.298)	8.61 (4.041 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4126		0.4467	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.81 to 1.69)		0.86 (0.58 to 1.27)	
P-value	-	0.4131		0.4471	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (14.4)	12 (15.6)	10 (17.9)	16 (20.8)	0.8511
Number (%) of patients censored	83 (85.6)	65 (84.4)	46 (82.1)	61 (79.2)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	NC (11.170 to NC)	13.14 (9.823 to NC)	NC (6.242 to NC)	14.95 (5.815 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.949 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9911		0.7955	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.46 to 2.17)		1.11 (0.50 to 2.45)	
P-value	-	0.9911		0.7956	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (29.9)	26 (33.8)	29 (51.8)	33 (42.9)	0.3486
Number (%) of patients censored	68 (70.1)	51 (66.2)	27 (48.2)	44 (57.1)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	5.59 (2.037 to 9.331)	3.94 (1.413 to 11.663)	1.97 (1.018 to 4.435)	5.55 (2.628 to 8.838)	
Median (95% CI)	NC (NC to NC)	15.67 (11.663 to NC)	8.54 (4.435 to NC)	13.67 (9.495 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.671 to NC)	NC (NC to NC)	NC (14.390 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9328		0.1934	
Hazard ratio (95% CI) vs Pd	-	1.02 (0.60 to 1.74)		0.72 (0.44 to 1.18)	
P-value	-	0.9328		0.1954	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	67 (48.9)	74 (53.6)	9 (56.3)	8 (50.0)	0.6683
Number (%) of patients censored	70 (51.1)	64 (46.4)	7 (43.8)	8 (50.0)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.12 (1.051 to 2.267)	1.51 (1.084 to 2.136)	1.08 (0.953 to 1.873)	1.08 (0.986 to 1.938)	
Median (95% CI)	7.49 (3.778 to NC)	5.06 (2.891 to NC)	1.97 (0.986 to NC)	7.36 (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.971 to NC)	NC (1.938 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8212		0.7353	
Hazard ratio (95% CI) vs Pd	-	1.04 (0.75 to 1.45)		0.85 (0.33 to 2.20)	
P-value	-	0.8214		0.7357	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	95 (69.3)	106 (76.8)	9 (56.3)	8 (50.0)	0.6282
Number (%) of patients censored	42 (30.7)	32 (23.2)	7 (43.8)	8 (50.0)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.15 (1.018 to 1.873)	1.08 (1.018 to 1.150)	1.02 (0.986 to 2.793)	2.14 (0.953 to 3.713)	
Median (95% CI)	2.83 (1.971 to 3.745)	2.07 (1.873 to 3.318)	4.83 (0.986 to NC)	3.71 (1.018 to NC)	
75% quantile (95% CI)	9.30 (4.698 to NC)	7.69 (4.928 to NC)	NC (4.830 to NC)	NC (3.713 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5644		0.8111	
Hazard ratio (95% CI) vs Pd	-	1.08 (0.82 to 1.43)		0.89 (0.34 to 2.31)	
P-value	-	0.5650		0.8114	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (13.9)	23 (16.7)	5 (31.3)	5 (31.3)	0.6844
Number (%) of patients censored	118 (86.1)	115 (83.3)	11 (68.8)	11 (68.8)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	NC (11.302 to NC)	14.95 (11.762 to NC)	3.75 (0.953 to NC)	8.84 (0.986 to 13.142)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.281 to NC)	13.14 (8.838 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.331 to NC)	NC (9.823 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7290		0.6658	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.61 to 2.04)		0.75 (0.21 to 2.71)	
P-value	-	0.7300		0.6667	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (37.2)	56 (40.6)	7 (43.8)	3 (18.8)	0.1436
Number (%) of patients censored	86 (62.8)	82 (59.4)	9 (56.3)	13 (81.3)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	3.65 (1.873 to 5.651)	4.73 (1.840 to 8.115)	2.79 (0.986 to 8.345)	NC (2.628 to NC)	
Median (95% CI)	NC (9.331 to NC)	14.39 (10.875 to NC)	8.34 (0.986 to NC)	NC (3.515 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.671 to NC)	NC (8.345 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9235		0.1879	
Hazard ratio (95% CI) vs Pd	-	0.98 (0.67 to 1.44)		0.41 (0.11 to 1.60)	
P-value	-	0.9235		0.2021	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (54.9)	31 (48.4)	26 (46.4)	29 (54.7)	20 (46.5)	21 (61.8)	0.5633
Number (%) of patients censored	23 (45.1)	33 (51.6)	30 (53.6)	24 (45.3)	23 (53.5)	13 (38.2)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	1.12 (1.018 to 2.530)	1.87 (1.051 to 3.187)	1.94 (1.018 to 3.745)	1.94 (1.117 to 2.333)	1.12 (0.986 to 2.661)	1.05 (0.986 to 1.906)	
Median (95% CI)	8.48 (2.070 to NC)	9.63 (3.285 to NC)	8.41 (2.300 to NC)	5.82 (2.234 to NC)	3.78 (1.446 to NC)	2.83 (1.117 to 4.271)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.891 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5877		0.6508		0.3373	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.52 to 1.45)		1.13 (0.67 to 1.92)		1.35 (0.73 to 2.49)	
P-value	-	0.5880		0.6513		0.3391	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (78.4)	48 (75.0)	40 (71.4)	41 (77.4)	22 (51.2)	22 (64.7)	0.9429
Number (%) of patients censored	11 (21.6)	16 (25.0)	16 (28.6)	12 (22.6)	21 (48.8)	12 (35.3)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	1.61 (1.084 to 1.971)	1.05 (0.986 to 1.150)	1.05 (1.018 to 1.150)	1.08 (0.986 to 1.281)	1.02 (0.986 to 2.103)	1.84 (0.986 to 2.924)	
Median (95% CI)	2.79 (1.971 to 3.844)	2.04 (1.248 to 3.778)	2.17 (1.150 to 3.877)	2.07 (1.281 to 3.417)	3.75 (2.004 to 9.331)	4.93 (1.971 to 8.608)	
75% quantile (95% CI)	5.59 (3.745 to NC)	8.84 (3.844 to NC)	7.92 (3.450 to NC)	6.97 (3.318 to 13.864)	NC (3.975 to NC)	9.72 (6.702 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7692		0.8642		0.7991	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.70 to 1.62)		1.04 (0.67 to 1.61)		0.93 (0.51 to 1.68)	
P-value	-	0.7697		0.8641		0.7990	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (11.8)	8 (12.5)	9 (16.1)	13 (24.5)	8 (18.6)	7 (20.6)	0.8042
Number (%) of patients censored	45 (88.2)	56 (87.5)	47 (83.9)	40 (75.5)	35 (81.4)	27 (79.4)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	NC (11.466 to NC)	NC (11.762 to NC)	NC (4.271 to NC)	13.14 (4.041 to NC)	11.30 (1.281 to NC)	9.82 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	14.95 (13.142 to NC)	NC (11.302 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.949 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8050		0.4283		0.8962	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.40 to 3.30)		1.41 (0.60 to 3.30)		0.93 (0.34 to 2.59)	
P-value	-	0.8051		0.4305		0.8964	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (39.2)	25 (39.1)	23 (41.1)	19 (35.8)	14 (32.6)	14 (41.2)	0.6706
Number (%) of patients censored	31 (60.8)	39 (60.9)	33 (58.9)	34 (64.2)	29 (67.4)	20 (58.8)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	2.96 (1.610 to 8.772)	4.80 (1.051 to 9.495)	2.46 (1.018 to 5.191)	4.73 (1.150 to 10.875)	4.44 (0.986 to 8.542)	4.70 (0.986 to 9.495)	
Median (95% CI)	NC (8.345 to NC)	15.67 (10.283 to NC)	NC (3.811 to NC)	NC (10.021 to NC)	NC (5.585 to NC)	12.75 (8.115 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.671 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.747 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9256		0.3208		0.9550	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.57 to 1.85)		0.74 (0.40 to 1.35)		0.98 (0.46 to 2.06)	
P-value	-	0.9257		0.3223		0.9550	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (64.5)	17 (43.6)	46 (46.9)	56 (56.6)	10 (41.7)	9 (56.3)	0.1634
Number (%) of patients censored	11 (35.5)	22 (56.4)	52 (53.1)	43 (43.4)	14 (58.3)	7 (43.8)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	1.08 (0.986 to 2.530)	2.83 (0.986 to 4.008)	1.15 (1.018 to 2.267)	1.31 (1.084 to 1.938)	1.28 (0.953 to 2.924)	1.05 (0.723 to 2.760)	
Median (95% CI)	5.03 (1.117 to NC)	NC (3.285 to NC)	7.49 (3.745 to NC)	4.27 (2.234 to NC)	3.78 (1.281 to NC)	2.83 (1.051 to NC)	
75% quantile (95% CI)	NC (8.476 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.778 to NC)	NC (2.760 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1253		0.3826		0.5284	
Hazard ratio (95% CI) vs Pd	-	0.61 (0.32 to 1.16)		1.19 (0.81 to 1.76)		1.33 (0.54 to 3.29)	
P-value	-	0.1292		0.3832		0.5299	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_impl_seriss_de_i_t_x.rtf (08APR2021 14:42)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (80.6)	29 (74.4)	71 (72.4)	75 (75.8)	8 (33.3)	10 (62.5)	0.7599
Number (%) of patients censored	6 (19.4)	10 (25.6)	27 (27.6)	24 (24.2)	16 (66.7)	6 (37.5)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	1.94 (1.216 to 2.037)	1.05 (0.986 to 1.643)	1.02 (1.018 to 1.150)	1.08 (0.986 to 1.150)	2.00 (0.953 to 7.491)	1.91 (0.986 to 2.924)	
Median (95% CI)	2.86 (1.971 to 4.731)	2.14 (1.150 to 4.830)	2.46 (1.347 to 3.450)	2.07 (1.380 to 3.581)	7.49 (2.004 to NC)	3.52 (1.840 to 8.608)	
75% quantile (95% CI)	6.64 (2.957 to NC)	NC (4.107 to NC)	9.30 (3.877 to NC)	7.69 (4.731 to 13.864)	NC (7.491 to NC)	8.61 (2.924 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9232		0.8431		0.4916	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.60 to 1.76)		1.03 (0.75 to 1.43)		1.39 (0.54 to 3.58)	
P-value	-	0.9233		0.8432		0.4934	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (9.7)	6 (15.4)	15 (15.3)	20 (20.2)	6 (25.0)	2 (12.5)	0.3292
Number (%) of patients censored	28 (90.3)	33 (84.6)	83 (84.7)	79 (79.8)	18 (75.0)	14 (87.5)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	NC (11.466 to NC)	NC (6.965 to NC)	NC (10.251 to NC)	13.14 (8.444 to NC)	8.38 (0.953 to NC)	NC (0.953 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.949 to NC)	NC (8.378 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4321		0.5440		0.3011	
Hazard ratio (95% CI) vs Pd	-	1.73 (0.43 to 6.93)		1.23 (0.63 to 2.41)		0.44 (0.09 to 2.18)	
P-value	-	0.4379		0.5447		0.3145	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (38.7)	12 (30.8)	40 (40.8)	40 (40.4)	6 (25.0)	7 (43.8)	0.7260
Number (%) of patients censored	19 (61.3)	27 (69.2)	58 (59.2)	59 (59.6)	18 (75.0)	9 (56.3)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	5.59 (1.610 to NC)	6.57 (1.051 to 15.671)	2.79 (1.051 to 4.830)	3.94 (1.413 to 8.411)	4.44 (0.986 to 8.378)	3.52 (0.986 to 9.495)	
Median (95% CI)	NC (8.345 to NC)	15.67 (14.390 to 15.671)	NC (8.542 to NC)	13.67 (10.283 to NC)	8.38 (4.435 to NC)	9.49 (2.661 to NC)	
75% quantile (95% CI)	NC (NC to NC)	15.67 (14.390 to 15.671)	NC (NC to NC)	NC (NC to NC)	NC (8.378 to NC)	NC (8.608 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5982		0.6424		0.7909	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (34.8)	7 (50.0)	45 (47.4)	65 (55.1)	0.3204
Number (%) of patients censored	15 (65.2)	7 (50.0)	50 (52.6)	53 (44.9)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.45 (0.953 to NC)	1.08 (0.920 to 1.938)	1.87 (1.018 to 2.300)	1.87 (1.084 to 2.168)	
Median (95% CI)	NC (1.446 to NC)	1.94 (1.051 to NC)	8.48 (3.778 to NC)	5.06 (2.924 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.511 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2378		0.5695	
Hazard ratio (95% CI) vs Pd	-	1.84 (0.66 to 5.11)		1.12 (0.76 to 1.63)	
P-value	-	0.2447		0.5697	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (52.2)	7 (50.0)	66 (69.5)	91 (77.1)	0.3379
Number (%) of patients censored	11 (47.8)	7 (50.0)	29 (30.5)	27 (22.9)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.15 (0.986 to 2.168)	2.66 (0.953 to 3.318)	1.08 (0.986 to 1.610)	1.05 (0.986 to 1.084)	
Median (95% CI)	2.83 (1.150 to NC)	3.32 (1.840 to NC)	2.04 (1.938 to 3.745)	2.04 (1.446 to 3.055)	
75% quantile (95% CI)	7.49 (3.450 to NC)	NC (3.318 to NC)	12.02 (4.698 to NC)	6.70 (4.731 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4305		0.3691	
Hazard ratio (95% CI) vs Pd	-	0.69 (0.27 to 1.76)		1.16 (0.84 to 1.59)	
P-value	-	0.4331		0.3695	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (26.1)	1 (7.1)	11 (11.6)	25 (21.2)	0.1048
Number (%) of patients censored	17 (73.9)	13 (92.9)	84 (88.4)	93 (78.8)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	3.75 (0.953 to NC)	NC (1.938 to NC)	NC (11.302 to NC)	13.14 (8.444 to NC)	
Median (95% CI)	NC (3.745 to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.949 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1687		0.1281	
Hazard ratio (95% CI) vs Pd	-	0.25 (0.03 to 2.10)		1.72 (0.85 to 3.51)	
P-value	-	0.2028		0.1330	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (26.1)	4 (28.6)	39 (41.1)	46 (39.0)	0.8193
Number (%) of patients censored	17 (73.9)	10 (71.4)	56 (58.9)	72 (61.0)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	2.89 (0.986 to NC)	3.32 (0.953 to NC)	2.83 (1.084 to 5.585)	4.83 (1.906 to 8.838)	
Median (95% CI)	NC (2.891 to NC)	NC (1.840 to NC)	NC (8.345 to NC)	15.67 (11.663 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.671 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9706		0.4605	
Hazard ratio (95% CI) vs Pd	-	1.02 (0.29 to 3.63)		0.85 (0.55 to 1.31)	
P-value	-	0.9705		0.4610	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (36.1)	11 (45.8)	39 (50.0)	60 (58.3)	0.6850
Number (%) of patients censored	23 (63.9)	13 (54.2)	39 (50.0)	43 (41.7)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.97 (1.117 to 3.745)	1.51 (0.920 to 3.778)	1.08 (0.986 to 2.004)	1.31 (1.051 to 1.971)	
Median (95% CI)	NC (2.891 to NC)	6.64 (1.938 to NC)	7.49 (2.661 to NC)	4.27 (2.793 to 9.626)	
75% quantile (95% CI)	NC (NC to NC)	NC (6.637 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4629		0.6105	
Hazard ratio (95% CI) vs Pd	-	1.35 (0.60 to 3.01)		1.11 (0.74 to 1.66)	
P-value	-	0.4645		0.6106	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (63.9)	15 (62.5)	52 (66.7)	80 (77.7)	0.4206
Number (%) of patients censored	13 (36.1)	9 (37.5)	26 (33.3)	23 (22.3)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.08 (1.018 to 1.183)	1.12 (0.953 to 1.971)	1.15 (0.986 to 1.938)	1.05 (0.986 to 1.150)	
Median (95% CI)	2.17 (1.150 to 3.844)	2.66 (1.248 to 3.844)	2.83 (1.971 to 3.975)	2.14 (1.906 to 3.713)	
75% quantile (95% CI)	4.73 (3.450 to NC)	NC (2.661 to NC)	NC (4.698 to NC)	7.98 (4.731 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7368		0.2933	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.47 to 1.72)		1.21 (0.85 to 1.71)	
P-value	-	0.7370		0.2940	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (19.4)	3 (12.5)	10 (12.8)	22 (21.4)	0.2838
Number (%) of patients censored	29 (80.6)	21 (87.5)	68 (87.2)	81 (78.6)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	NC (1.446 to NC)	NC (1.938 to NC)	NC (11.170 to NC)	13.14 (8.444 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.949 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4685		0.2467	
Hazard ratio (95% CI) vs Pd	-	0.61 (0.16 to 2.36)		1.55 (0.73 to 3.28)	
P-value	-	0.4732		0.2505	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (33.3)	9 (37.5)	31 (39.7)	39 (37.9)	0.6375
Number (%) of patients censored	24 (66.7)	15 (62.5)	47 (60.3)	64 (62.1)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	2.89 (1.150 to NC)	2.66 (0.953 to 10.021)	3.65 (1.084 to 6.538)	5.85 (2.628 to 9.495)	
Median (95% CI)	NC (3.154 to NC)	NC (2.661 to NC)	NC (8.542 to NC)	15.67 (11.663 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.671 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8323		0.4748	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.46 to 2.61)		0.84 (0.52 to 1.35)	
P-value	-	0.8324		0.4754	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (48.9)	47 (56.6)	32 (50.8)	35 (49.3)	0.1546
Number (%) of patients censored	46 (51.1)	36 (43.4)	31 (49.2)	36 (50.7)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.45 (1.051 to 2.070)	1.08 (1.051 to 1.906)	1.12 (0.986 to 2.004)	1.97 (1.216 to 2.825)	
Median (95% CI)	7.49 (2.891 to NC)	3.29 (1.971 to NC)	6.77 (2.924 to NC)	7.00 (3.187 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.298 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3176		0.3062	
Hazard ratio (95% CI) vs Pd	-	1.23 (0.82 to 1.86)		0.78 (0.48 to 1.26)	
P-value	-	0.3185		0.3074	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	63 (70.0)	57 (68.7)	41 (65.1)	57 (80.3)	0.1807
Number (%) of patients censored	27 (30.0)	26 (31.3)	22 (34.9)	14 (19.7)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.15 (1.051 to 1.938)	1.28 (1.051 to 1.906)	1.02 (0.986 to 1.906)	1.02 (0.986 to 1.084)	
Median (95% CI)	2.83 (1.971 to 3.745)	3.42 (1.971 to 4.435)	2.86 (1.906 to 4.698)	1.91 (1.084 to 2.891)	
75% quantile (95% CI)	9.33 (3.877 to NC)	13.86 (4.928 to NC)	9.30 (4.698 to NC)	6.70 (3.055 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5598		0.2536	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.63 to 1.29)		1.26 (0.85 to 1.89)	
P-value	-	0.5603		0.2547	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (14.4)	11 (13.3)	11 (17.5)	17 (23.9)	0.7900
Number (%) of patients censored	77 (85.6)	72 (86.7)	52 (82.5)	54 (76.1)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	NC (11.170 to NC)	NC (11.762 to NC)	11.30 (3.745 to NC)	13.14 (6.637 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.949 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8830		0.8660	
Hazard ratio (95% CI) vs Pd	-	0.94 (0.42 to 2.10)		1.07 (0.50 to 2.29)	
P-value	-	0.8833		0.8668	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (37.8)	27 (32.5)	24 (38.1)	32 (45.1)	0.3638
Number (%) of patients censored	56 (62.2)	56 (67.5)	39 (61.9)	39 (54.9)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	2.89 (1.216 to 5.914)	5.55 (3.384 to 14.390)	3.84 (1.018 to 8.345)	3.52 (1.051 to 8.608)	
Median (95% CI)	NC (8.805 to NC)	15.67 (14.390 to NC)	NC (8.345 to NC)	12.75 (8.838 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.671 to NC)	NC (NC to NC)	NC (13.667 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2526		0.8522	
Hazard ratio (95% CI) vs Pd	-	0.74 (0.45 to 1.24)		1.05 (0.62 to 1.79)	
P-value	-	0.2543		0.8527	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	1 (50.0)	74 (49.0)	81 (53.3)	0.1378
Number (%) of patients censored	0 (0.0)	1 (50.0)	77 (51.0)	71 (46.7)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.02 (1.018 to 1.084)	1.08 (1.084 to NC)	1.15 (1.051 to 1.971)	1.51 (1.084 to 1.971)	
Median (95% CI)	1.05 (1.018 to 1.084)	NC (1.084 to NC)	6.87 (3.778 to NC)	5.06 (2.891 to NC)	
75% quantile (95% CI)	1.08 (1.018 to 1.084)	NC (1.084 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.8218	
Hazard ratio (95% CI) vs Pd	-	0.31 (0.03 to 3.50)		1.04 (0.76 to 1.42)	
P-value	-	0.3429		0.8220	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	2 (100.0)	103 (68.2)	112 (73.7)	0.3990
Number (%) of patients censored	1 (50.0)	0 (0.0)	48 (31.8)	40 (26.3)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	2.07 (2.070 to NC)	1.12 (1.117 to 4.107)	1.12 (1.018 to 1.610)	1.08 (1.018 to 1.216)	
Median (95% CI)	NC (2.070 to NC)	2.61 (1.117 to 4.107)	2.83 (1.971 to 3.745)	2.27 (1.906 to 3.581)	
75% quantile (95% CI)	NC (2.070 to NC)	4.11 (1.117 to 4.107)	9.30 (4.830 to NC)	8.61 (5.552 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4328		0.7333	
Hazard ratio (95% CI) vs Pd	-	2.56 (0.23 to 29.12)		1.05 (0.80 to 1.37)	
P-value	-	0.4482		0.7334	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	0 (0.0)	22 (14.6)	28 (18.4)	0.9848
Number (%) of patients censored	0 (0.0)	2 (100.0)	129 (85.4)	124 (81.6)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	7.03 (7.031 to 11.466)	NC (NC to NC)	NC (11.170 to NC)	14.95 (9.823 to NC)	
Median (95% CI)	9.25 (7.031 to 11.466)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	11.47 (7.031 to 11.466)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.5824	
Hazard ratio (95% CI) vs Pd	-			1.17 (0.67 to 2.04)	
P-value	-	0.9990		0.5828	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	58 (38.4)	58 (38.2)	0.9842
Number (%) of patients censored	2 (100.0)	1 (50.0)	93 (61.6)	94 (61.8)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	NC (NC to NC)	1.12 (1.117 to NC)	3.06 (1.873 to 5.585)	4.80 (2.661 to 8.411)	
Median (95% CI)	NC (NC to NC)	NC (1.117 to NC)	NC (9.331 to NC)	15.67 (11.663 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.117 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.4902	
Hazard ratio (95% CI) vs Pd	-			0.88 (0.61 to 1.27)	
P-value	-	0.9990		0.4894	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (49.5)	59 (56.7)	20 (48.8)	12 (36.4)	0.2398
Number (%) of patients censored	51 (50.5)	45 (43.3)	21 (51.2)	21 (63.6)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.25 (1.051 to 2.070)	1.25 (1.051 to 1.938)	1.05 (0.953 to 2.004)	1.97 (1.051 to NC)	
Median (95% CI)	6.87 (3.023 to NC)	3.78 (2.793 to 9.626)	5.03 (1.446 to NC)	NC (4.271 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5222		0.1583	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.78 to 1.65)		0.60 (0.29 to 1.23)	
P-value	-	0.5235		0.1628	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_impl_semm_de_i_t_x.rtf (08APR2021 14:41)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	74 (73.3)	78 (75.0)	24 (58.5)	26 (78.8)	0.3882
Number (%) of patients censored	27 (26.7)	26 (25.0)	17 (41.5)	7 (21.2)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.05 (0.986 to 1.183)	1.08 (1.018 to 1.281)	1.61 (1.018 to 1.971)	1.08 (0.986 to 1.248)	
Median (95% CI)	2.17 (1.938 to 3.450)	2.20 (1.873 to 3.581)	3.09 (1.938 to 9.331)	2.66 (1.117 to 4.830)	
75% quantile (95% CI)	5.59 (3.844 to NC)	8.61 (4.731 to 13.864)	NC (5.224 to NC)	6.47 (4.041 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7284		0.1605	
Hazard ratio (95% CI) vs Pd	-	0.95 (0.69 to 1.30)		1.49 (0.85 to 2.59)	
P-value	-	0.7281		0.1632	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_detl_semm_de_i_t_x.rtf (08APR2021 14:41)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (13.9)	19 (18.3)	7 (17.1)	5 (15.2)	0.7346
Number (%) of patients censored	87 (86.1)	85 (81.7)	34 (82.9)	28 (84.8)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	NC (11.170 to NC)	13.14 (8.838 to NC)	NC (1.446 to NC)	14.95 (8.641 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.949 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.949 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5615		0.5802	
Hazard ratio (95% CI) vs Pd	-	1.23 (0.61 to 2.45)		0.72 (0.23 to 2.29)	
P-value	-	0.5622		0.5818	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (39.6)	40 (38.5)	15 (36.6)	15 (45.5)	0.8036
Number (%) of patients censored	61 (60.4)	64 (61.5)	26 (63.4)	18 (54.5)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	3.06 (1.051 to 5.585)	4.80 (3.318 to 8.838)	2.46 (1.150 to 9.331)	2.66 (0.986 to 9.495)	
Median (95% CI)	NC (8.378 to NC)	15.67 (10.875 to NC)	NC (8.542 to NC)	14.39 (4.830 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.671 to NC)	NC (NC to NC)	NC (14.390 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4880		0.7214	
Hazard ratio (95% CI) vs Pd	-	0.86 (0.55 to 1.33)		1.14 (0.56 to 2.34)	
P-value	-	0.4884		0.7208	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (49.0)	57 (55.9)	26 (50.0)	24 (47.1)	0.3222
Number (%) of patients censored	51 (51.0)	45 (44.1)	26 (50.0)	27 (52.9)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.28 (1.051 to 2.267)	1.22 (1.051 to 1.938)	1.05 (0.953 to 2.530)	1.91 (1.051 to 3.318)	
Median (95% CI)	6.87 (3.745 to NC)	3.78 (2.793 to NC)	5.03 (2.004 to NC)	7.00 (3.253 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5162		0.4578	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.77 to 1.66)		0.81 (0.47 to 1.41)	
P-value	-	0.5173		0.4586	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	73 (73.0)	76 (74.5)	30 (57.7)	37 (72.5)	0.1701
Number (%) of patients censored	27 (27.0)	26 (25.5)	22 (42.3)	14 (27.5)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.05 (0.986 to 1.183)	1.08 (1.018 to 1.380)	1.91 (1.051 to 2.037)	1.08 (0.986 to 1.248)	
Median (95% CI)	2.10 (1.938 to 3.745)	2.27 (1.906 to 3.713)	3.09 (2.037 to 9.331)	2.20 (1.150 to 4.830)	
75% quantile (95% CI)	5.59 (3.877 to NC)	8.61 (4.731 to 13.864)	NC (5.224 to NC)	8.61 (4.731 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6693		0.1870	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.68 to 1.29)		1.38 (0.85 to 2.24)	
P-value	-	0.6689		0.1887	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (14.0)	19 (18.6)	10 (19.2)	9 (17.6)	0.4587
Number (%) of patients censored	86 (86.0)	83 (81.4)	42 (80.8)	42 (82.4)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	NC (11.170 to NC)	13.14 (8.444 to NC)	NC (1.446 to NC)	14.95 (8.641 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.949 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.949 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5469		0.6076	
Hazard ratio (95% CI) vs Pd	-	1.24 (0.62 to 2.47)		0.79 (0.32 to 1.95)	
P-value	-	0.5476		0.6084	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (39.0)	39 (38.2)	18 (34.6)	20 (39.2)	0.6757
Number (%) of patients censored	61 (61.0)	63 (61.8)	34 (65.4)	31 (60.8)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	3.06 (1.051 to 5.651)	4.80 (3.318 to 9.495)	3.65 (1.610 to 9.331)	3.94 (1.084 to 9.495)	
Median (95% CI)	NC (8.378 to NC)	15.67 (11.663 to NC)	NC (9.331 to NC)	NC (8.838 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.671 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5482		0.9428	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.56 to 1.36)		1.02 (0.54 to 1.94)	
P-value	-	0.5473		0.9429	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (50.0)	6 (42.9)	71 (49.7)	76 (54.3)	0.4848
Number (%) of patients censored	5 (50.0)	8 (57.1)	72 (50.3)	64 (45.7)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.94 (0.953 to 3.811)	1.91 (0.986 to NC)	1.12 (1.051 to 1.971)	1.45 (1.084 to 1.971)	
Median (95% CI)	3.81 (0.953 to NC)	NC (1.084 to NC)	6.87 (3.778 to NC)	4.99 (2.891 to NC)	
75% quantile (95% CI)	NC (2.661 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5600		0.7833	
Hazard ratio (95% CI) vs Pd	-	0.70 (0.21 to 2.32)		1.05 (0.76 to 1.45)	
P-value	-	0.5620		0.7834	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (50.0)	13 (92.9)	99 (69.2)	101 (72.1)	0.6910
Number (%) of patients censored	5 (50.0)	1 (7.1)	44 (30.8)	39 (27.9)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.02 (0.920 to 3.055)	1.08 (0.986 to 2.661)	1.15 (1.018 to 1.873)	1.08 (1.018 to 1.248)	
Median (95% CI)	3.06 (0.920 to NC)	2.78 (1.051 to 3.844)	2.83 (1.971 to 3.745)	2.20 (1.906 to 3.778)	
75% quantile (95% CI)	NC (1.741 to NC)	3.84 (2.661 to 13.864)	9.30 (4.830 to NC)	8.84 (5.552 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8826		0.8162	
Hazard ratio (95% CI) vs Pd	-	1.08 (0.37 to 3.15)		1.03 (0.78 to 1.36)	
P-value	-	0.8826		0.8162	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (20.0)	2 (14.3)	22 (15.4)	26 (18.6)	0.3470
Number (%) of patients censored	8 (80.0)	12 (85.7)	121 (84.6)	114 (81.4)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	NC (0.953 to NC)	NC (4.041 to NC)	NC (11.170 to NC)	14.95 (9.823 to NC)	
Median (95% CI)	NC (0.953 to NC)	NC (8.444 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3854		0.6417	
Hazard ratio (95% CI) vs Pd	-	0.42 (0.06 to 3.13)		1.14 (0.65 to 2.02)	
P-value	-	0.3987		0.6428	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (30.0)	9 (64.3)	55 (38.5)	50 (35.7)	0.5678
Number (%) of patients censored	7 (70.0)	5 (35.7)	88 (61.5)	90 (64.3)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	3.06 (0.920 to NC)	1.84 (1.051 to 8.411)	3.15 (1.873 to 5.585)	4.93 (3.318 to 10.021)	
Median (95% CI)	NC (0.920 to NC)	8.51 (1.117 to NC)	NC (9.331 to NC)	15.67 (12.747 to NC)	
75% quantile (95% CI)	NC (3.055 to NC)	NC (8.411 to NC)	NC (NC to NC)	NC (15.671 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9239		0.3852	
Hazard ratio (95% CI) vs Pd	-	1.07 (0.27 to 4.30)		0.84 (0.57 to 1.24)	
P-value	-	0.9239		0.3854	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_detpl_mri_de_i_t_x.rtf (08APR2021 14:42)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (52.1)	48 (55.2)	25 (51.0)	30 (54.5)	0.7471
Number (%) of patients censored	46 (47.9)	39 (44.8)	24 (49.0)	25 (45.5)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.12 (1.018 to 2.004)	1.45 (1.084 to 2.070)	1.12 (0.986 to 1.938)	1.91 (1.051 to 2.760)	
Median (95% CI)	6.87 (2.891 to NC)	4.01 (2.793 to NC)	4.07 (1.938 to NC)	5.32 (2.760 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9194		0.7318	
Hazard ratio (95% CI) vs Pd	-	1.02 (0.69 to 1.52)		0.91 (0.54 to 1.55)	
P-value	-	0.9193		0.7319	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_impl_crcl_de_i_t_x.rtf (08APR2021 14:41)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	64 (66.7)	67 (77.0)	35 (71.4)	43 (78.2)	0.4106
Number (%) of patients censored	32 (33.3)	20 (23.0)	14 (28.6)	12 (21.8)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.15 (1.018 to 1.938)	1.08 (0.986 to 1.248)	1.02 (0.986 to 1.938)	1.05 (0.986 to 1.380)	
Median (95% CI)	2.86 (1.971 to 4.830)	2.07 (1.840 to 3.713)	2.86 (1.906 to 3.745)	2.66 (1.380 to 4.731)	
75% quantile (95% CI)	12.02 (6.637 to NC)	7.98 (4.041 to NC)	4.70 (3.745 to NC)	7.69 (4.731 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2431		0.7895	
Hazard ratio (95% CI) vs Pd	-	1.23 (0.87 to 1.73)		0.94 (0.60 to 1.47)	
P-value	-	0.2439		0.7888	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (18.8)	17 (19.5)	6 (12.2)	8 (14.5)	0.9210
Number (%) of patients censored	78 (81.3)	70 (80.5)	43 (87.8)	47 (85.5)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	11.47 (9.331 to NC)	13.14 (8.838 to NC)	NC (6.242 to NC)	NC (8.641 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.949 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8873		0.8844	
Hazard ratio (95% CI) vs Pd	-	0.95 (0.49 to 1.85)		1.08 (0.37 to 3.12)	
P-value	-	0.8873		0.8849	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (33.3)	32 (36.8)	21 (42.9)	26 (47.3)	0.8448
Number (%) of patients censored	64 (66.7)	55 (63.2)	28 (57.1)	29 (52.7)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	3.65 (1.610 to 9.331)	4.83 (2.628 to 10.875)	3.81 (0.986 to 5.585)	3.58 (1.117 to 8.411)	
Median (95% CI)	NC (10.973 to NC)	NC (11.663 to NC)	8.80 (4.435 to NC)	13.67 (8.115 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	15.67 (13.667 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9039		0.7415	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.63 to 1.68)		0.91 (0.51 to 1.62)	
P-value	-	0.9038		0.7416	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	2 (100.0)	75 (49.7)	80 (52.6)	0.4164
Number (%) of patients censored	1 (50.0)	0 (0.0)	76 (50.3)	72 (47.4)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	1.91 (1.906 to 1.971)	1.12 (1.051 to 1.938)	1.45 (1.084 to 2.070)	
Median (95% CI)	NC (1.281 to NC)	1.94 (1.906 to 1.971)	6.87 (3.778 to NC)	5.32 (2.924 to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	1.97 (1.906 to 1.971)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6949		0.9893	
Hazard ratio (95% CI) vs Pd	-	1.62 (0.14 to 18.31)		1.00 (0.73 to 1.37)	
P-value	-	0.6975		0.9893	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	2 (100.0)	103 (68.2)	112 (73.7)	0.5296
Number (%) of patients censored	1 (50.0)	0 (0.0)	48 (31.8)	40 (26.3)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	2.10 (2.103 to NC)	0.99 (0.986 to 7.688)	1.12 (1.018 to 1.610)	1.08 (1.018 to 1.216)	
Median (95% CI)	NC (2.103 to NC)	4.34 (0.986 to 7.688)	2.83 (1.971 to 3.745)	2.27 (1.906 to 3.581)	
75% quantile (95% CI)	NC (2.103 to NC)	7.69 (0.986 to 7.688)	9.30 (4.830 to NC)	8.61 (4.928 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.7079	
Hazard ratio (95% CI) vs Pd	-	1.41 (0.08 to 23.57)		1.05 (0.81 to 1.38)	
P-value	-	0.8092		0.7081	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	23 (15.2)	27 (17.8)	0.5545
Number (%) of patients censored	1 (50.0)	1 (50.0)	128 (84.8)	125 (82.2)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	10.45 (10.448 to NC)	NC (11.170 to NC)	14.95 (9.823 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (10.448 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (10.448 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.7684	
Hazard ratio (95% CI) vs Pd	-			1.09 (0.62 to 1.90)	
P-value	-	0.9984		0.7690	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	58 (38.4)	59 (38.8)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	93 (61.6)	93 (61.2)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	3.06 (1.873 to 5.585)	4.73 (2.628 to 8.115)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.331 to NC)	14.39 (11.663 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.5978	
Hazard ratio (95% CI) vs Pd	-			0.91 (0.63 to 1.30)	
P-value	-			0.5972	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	56 (48.7)	67 (56.8)	20 (52.6)	15 (41.7)	0.2610
Number (%) of patients censored	59 (51.3)	51 (43.2)	18 (47.4)	21 (58.3)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.15 (1.051 to 2.004)	1.51 (1.084 to 1.971)	1.12 (0.986 to 2.530)	1.25 (1.018 to 4.271)	
Median (95% CI)	6.87 (3.778 to NC)	3.78 (2.793 to 9.626)	8.41 (1.938 to NC)	NC (3.253 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5387		0.3331	
Hazard ratio (95% CI) vs Pd	-	1.12 (0.78 to 1.59)		0.72 (0.37 to 1.41)	
P-value	-	0.5401		0.3353	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	73 (63.5)	88 (74.6)	31 (81.6)	26 (72.2)	0.3598
Number (%) of patients censored	42 (36.5)	30 (25.4)	7 (18.4)	10 (27.8)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.08 (1.018 to 1.347)	1.07 (1.018 to 1.150)	1.61 (0.986 to 1.971)	1.08 (0.986 to 1.873)	
Median (95% CI)	2.86 (1.971 to 3.975)	2.63 (1.906 to 3.811)	2.46 (1.938 to 3.055)	2.14 (1.478 to 4.041)	
75% quantile (95% CI)	NC (5.191 to NC)	8.61 (5.552 to NC)	5.39 (2.957 to NC)	6.11 (3.417 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3855		0.6364	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.84 to 1.57)		0.88 (0.52 to 1.49)	
P-value	-	0.3859		0.6376	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (16.5)	23 (19.5)	5 (13.2)	5 (13.9)	0.9851
Number (%) of patients censored	96 (83.5)	95 (80.5)	33 (86.8)	31 (86.1)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	NC (10.251 to NC)	14.95 (9.823 to NC)	NC (6.407 to NC)	NC (6.637 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.949 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8742		0.9613	
Hazard ratio (95% CI) vs Pd	-	1.05 (0.57 to 1.93)		1.03 (0.30 to 3.56)	
P-value	-	0.8744		0.9613	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_imppl_refr4_de_i_t_x.rtf (08APR2021 14:42)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (36.5)	45 (38.1)	16 (42.1)	14 (38.9)	0.9018
Number (%) of patients censored	73 (63.5)	73 (61.9)	22 (57.9)	22 (61.1)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	3.65 (1.873 to 5.651)	4.83 (2.628 to 8.608)	2.46 (1.051 to 8.542)	3.94 (0.986 to 11.663)	
Median (95% CI)	NC (9.331 to NC)	15.67 (12.747 to NC)	NC (4.435 to NC)	14.39 (8.115 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.390 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6056		0.8481	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.59 to 1.36)		0.93 (0.45 to 1.91)	
P-value	-	0.6044		0.8483	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	72 (50.0)	77 (52.4)	4 (44.4)	5 (71.4)	0.2128
Number (%) of patients censored	72 (50.0)	70 (47.6)	5 (55.6)	2 (28.6)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.12 (1.051 to 1.938)	1.71 (1.084 to 2.136)	2.07 (0.986 to NC)	1.05 (1.018 to 1.938)	
Median (95% CI)	6.87 (3.745 to NC)	5.32 (3.187 to NC)	NC (0.986 to NC)	1.94 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.768 to NC)	NC (1.117 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8437		0.2606	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.70 to 1.34)		2.11 (0.56 to 7.97)	
P-value	-	0.8436		0.2710	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	96 (66.7)	111 (75.5)	8 (88.9)	3 (42.9)	0.0517
Number (%) of patients censored	48 (33.3)	36 (24.5)	1 (11.1)	4 (57.1)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.15 (1.018 to 1.873)	1.08 (1.018 to 1.150)	0.99 (0.986 to 3.088)	1.45 (1.018 to NC)	
Median (95% CI)	2.83 (1.971 to 3.745)	2.14 (1.906 to 3.417)	3.09 (0.986 to 6.637)	NC (1.018 to NC)	
75% quantile (95% CI)	9.33 (5.191 to NC)	7.69 (4.830 to NC)	4.73 (1.018 to NC)	NC (4.928 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3635		0.0652	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.86 to 1.49)		0.30 (0.08 to 1.16)	
P-value	-	0.3647		0.0806	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (16.7)	25 (17.0)	0 (0.0)	3 (42.9)	0.9850
Number (%) of patients censored	120 (83.3)	122 (83.0)	9 (100.0)	4 (57.1)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	NC (10.251 to NC)	14.95 (10.448 to NC)	NC (NC to NC)	1.12 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.938 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7128		0.0328	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.51 to 1.58)			
P-value	-	0.7121		0.9972	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	55 (38.2)	57 (38.8)	3 (33.3)	2 (28.6)	0.9606
Number (%) of patients censored	89 (61.8)	90 (61.2)	6 (66.7)	5 (71.4)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	3.06 (1.873 to 5.585)	4.73 (2.628 to 8.411)	8.80 (0.986 to NC)	4.93 (1.018 to NC)	
Median (95% CI)	NC (9.331 to NC)	15.67 (11.663 to NC)	NC (0.986 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5346		0.8563	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.61 to 1.29)		0.85 (0.14 to 5.11)	
P-value	-	0.5335		0.8565	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (50.0)	45 (48.4)	32 (49.2)	37 (60.7)	0.8428
Number (%) of patients censored	44 (50.0)	48 (51.6)	33 (50.8)	24 (39.3)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.25 (1.018 to 2.891)	1.91 (1.084 to 2.234)	1.08 (0.986 to 1.971)	1.45 (1.051 to 2.070)	
Median (95% CI)	8.41 (3.778 to NC)	6.08 (2.891 to NC)	6.64 (1.971 to NC)	3.78 (2.168 to 9.626)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9375		0.8593	
Hazard ratio (95% CI) vs Pd	-	0.98 (0.65 to 1.49)		1.04 (0.65 to 1.68)	
P-value	-	0.9374		0.8595	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_impl_llen_de_i_t_x.rtf (08APR2021 14:41)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	65 (73.9)	69 (74.2)	39 (60.0)	45 (73.8)	0.4810
Number (%) of patients censored	23 (26.1)	24 (25.8)	26 (40.0)	16 (26.2)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.08 (0.986 to 1.873)	1.08 (1.018 to 1.380)	1.17 (1.018 to 2.070)	1.08 (0.986 to 1.150)	
Median (95% CI)	2.04 (1.938 to 2.858)	2.07 (1.873 to 3.055)	3.88 (2.070 to 5.388)	3.52 (1.281 to 5.552)	
75% quantile (95% CI)	5.59 (3.745 to NC)	6.70 (3.778 to NC)	NC (5.388 to NC)	10.64 (5.552 to 13.864)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9346		0.4409	
Hazard ratio (95% CI) vs Pd	-	0.99 (0.70 to 1.38)		1.18 (0.77 to 1.82)	
P-value	-	0.9346		0.4421	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_detl_llen_de_i_t_x.rtf (08APR2021 14:41)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (17.0)	14 (15.1)	9 (13.8)	14 (23.0)	0.3711
Number (%) of patients censored	73 (83.0)	79 (84.9)	56 (86.2)	47 (77.0)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	NC (9.331 to NC)	14.95 (10.448 to NC)	NC (7.031 to NC)	13.14 (3.318 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.949 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6558		0.3620	
Hazard ratio (95% CI) vs Pd	-	0.85 (0.41 to 1.76)		1.47 (0.64 to 3.40)	
P-value	-	0.6556		0.3650	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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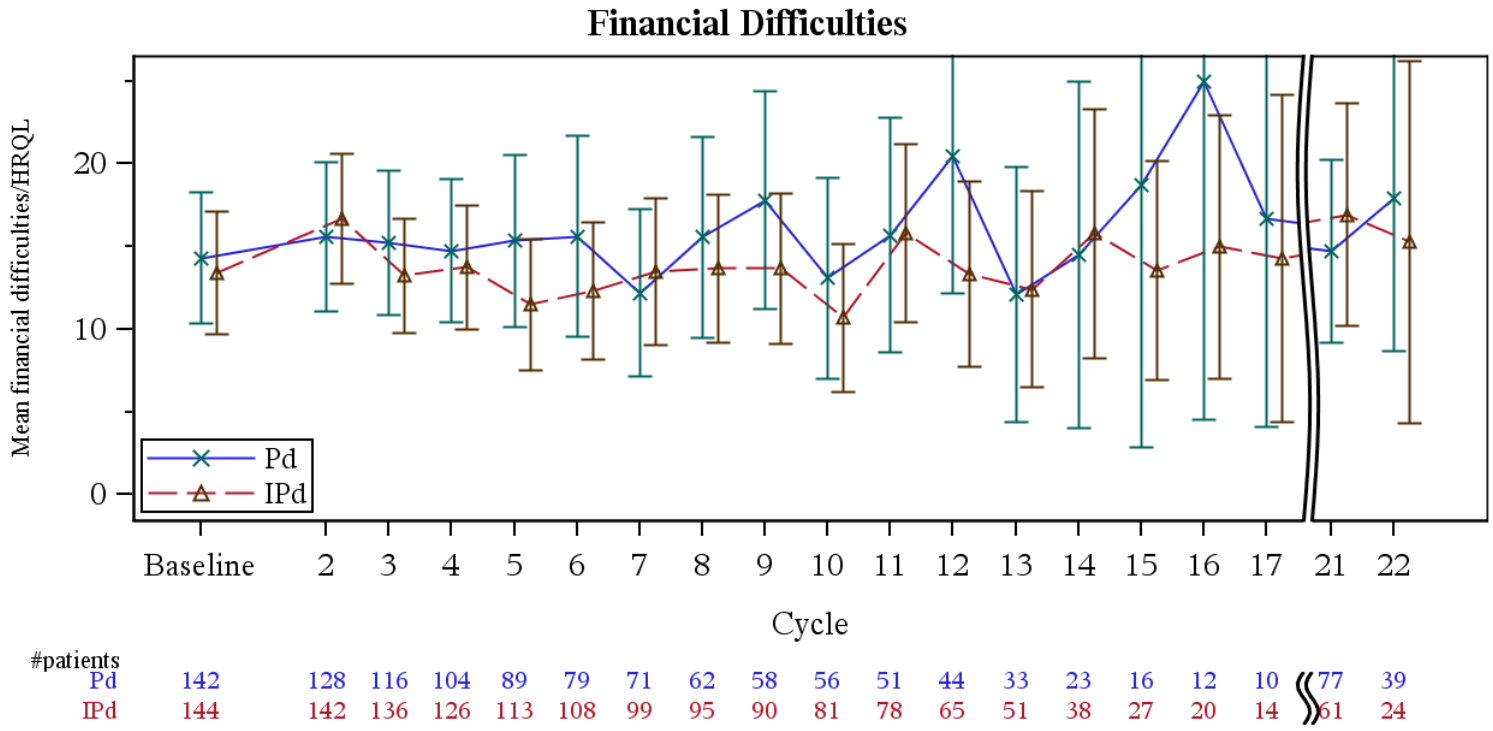
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Fatigue
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (45.5)	32 (34.4)	18 (27.7)	27 (44.3)	0.0502
Number (%) of patients censored	48 (54.5)	61 (65.6)	47 (72.3)	34 (55.7)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	2.46 (1.150 to 5.191)	5.68 (1.906 to 10.021)	4.83 (1.347 to NC)	4.70 (1.117 to 6.965)	
Median (95% CI)	9.33 (5.651 to NC)	14.39 (11.663 to NC)	NC (10.973 to NC)	15.67 (6.965 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.671 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0905		0.2596	
Hazard ratio (95% CI) vs Pd	-	0.67 (0.42 to 1.07)		1.41 (0.77 to 2.56)	
P-value	-	0.0927		0.2619	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_detpl_llen_de_i_t_x.rtf (08APR2021 14:42)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Financial difficulties
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-C30 - Mean and 95% CI for financial difficulties score over time (LOCF) - ITT population



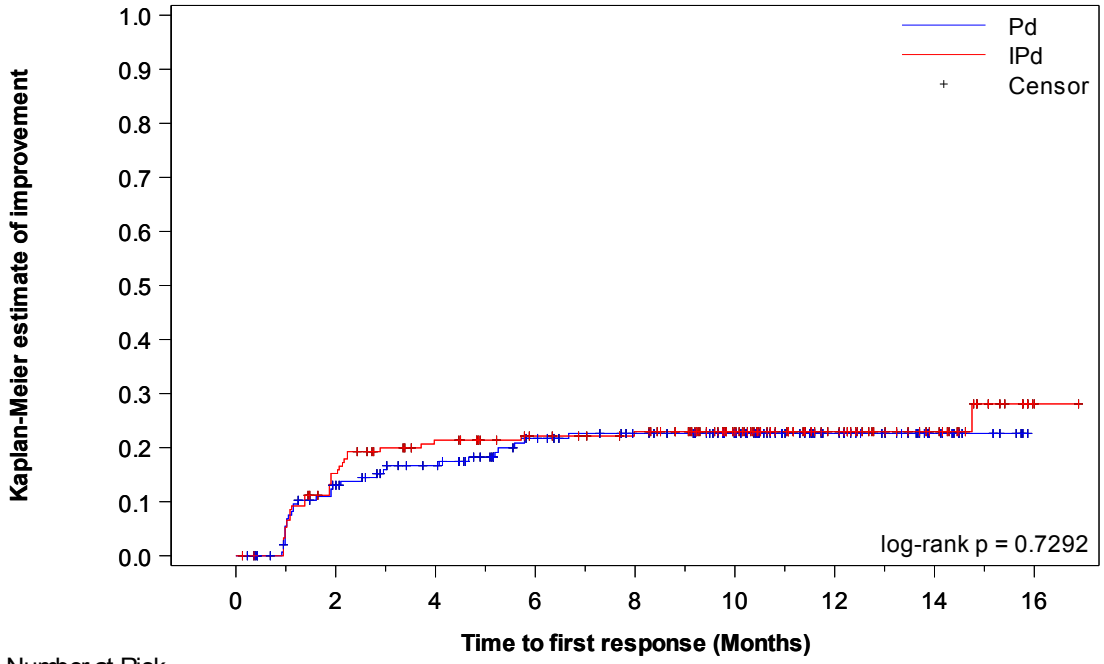
A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_line_i_f.sas OUT=REPORT/OUTPUT/eff_qlq_line_c30_fin_de_i_f_x.rtf (12FEB2021 17:15)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Financial difficulties
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-C30 - Time to first improvement by 15 pt in financial difficulties (LOCF) - ITT population

First improvement 15 points Financial difficulties (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	31 (20.3)	35 (22.7)
Number (%) of patients censored	122 (79.7)	119 (77.3)
Kaplan-Meier estimates of financial difficulties in months		
25% quantile (95% CI)	NC (4.665 to NC)	14.75 (2.168 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.7292
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.09 (0.67 to 1.77)
P-value	-	0.7296
Probability (95% CI)[c]		
2 Months	0.13 (0.082 to 0.191)	0.15 (0.100 to 0.214)
4 Months	0.17 (0.111 to 0.232)	0.21 (0.152 to 0.283)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_imp15l_de_i_t_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Financial difficulties
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-C30 - Time to first improvement by 15 pt in financial difficulties - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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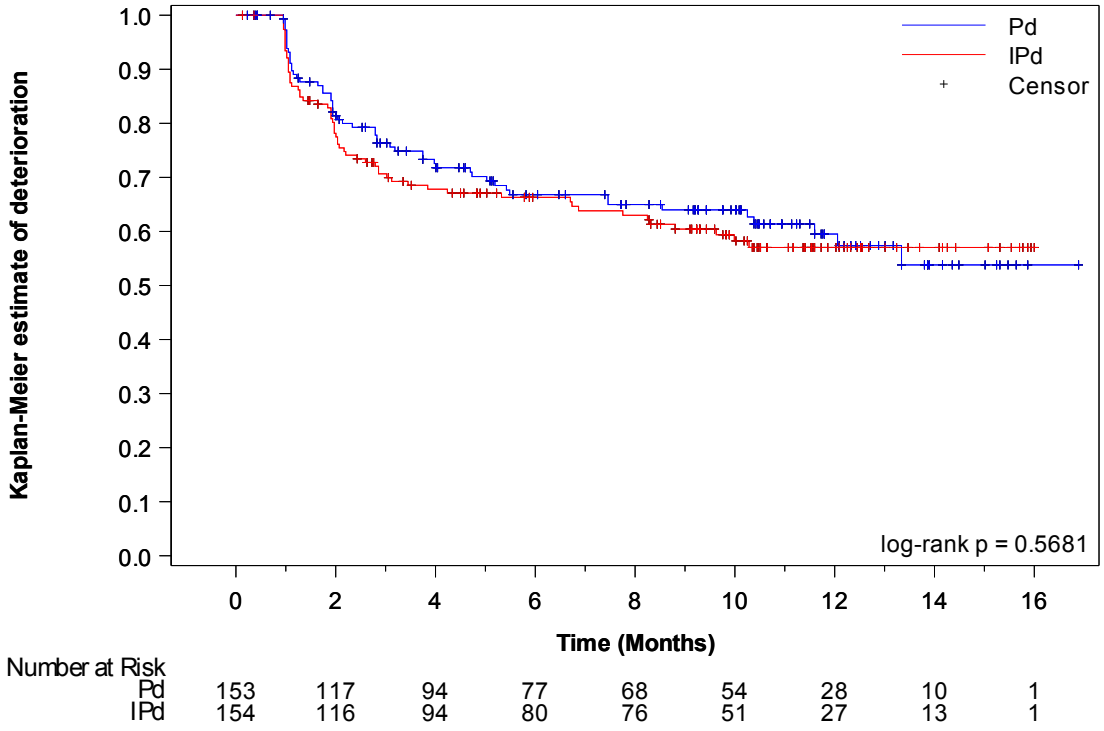
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Financial difficulties
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-C30 - Time to first deterioration by 15 pt in financial difficulties (LOCF) - ITT population

First deterioration 15 points Financial difficulties (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	54 (35.3)	60 (39.0)
Number (%) of patients censored	99 (64.7)	94 (61.0)
Kaplan-Meier estimates of financial difficulties in months		
25% quantile (95% CI)	3.19 (1.938 to 5.421)	2.17 (1.906 to 3.844)
Median (95% CI)	NC (11.598 to NC)	NC (9.988 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5681
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.11 (0.77 to 1.61)
P-value	-	0.5686
Probability (95% CI)[c]		
2 Months	0.82 (0.748 to 0.874)	0.78 (0.707 to 0.839)
4 Months	0.73 (0.644 to 0.792)	0.68 (0.596 to 0.747)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_det15l_de_i_t_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Financial difficulties
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-C30 - Time to first deterioration by 15 pt in financial difficulties - Kaplan-Meier curve (LOCF) - ITT population



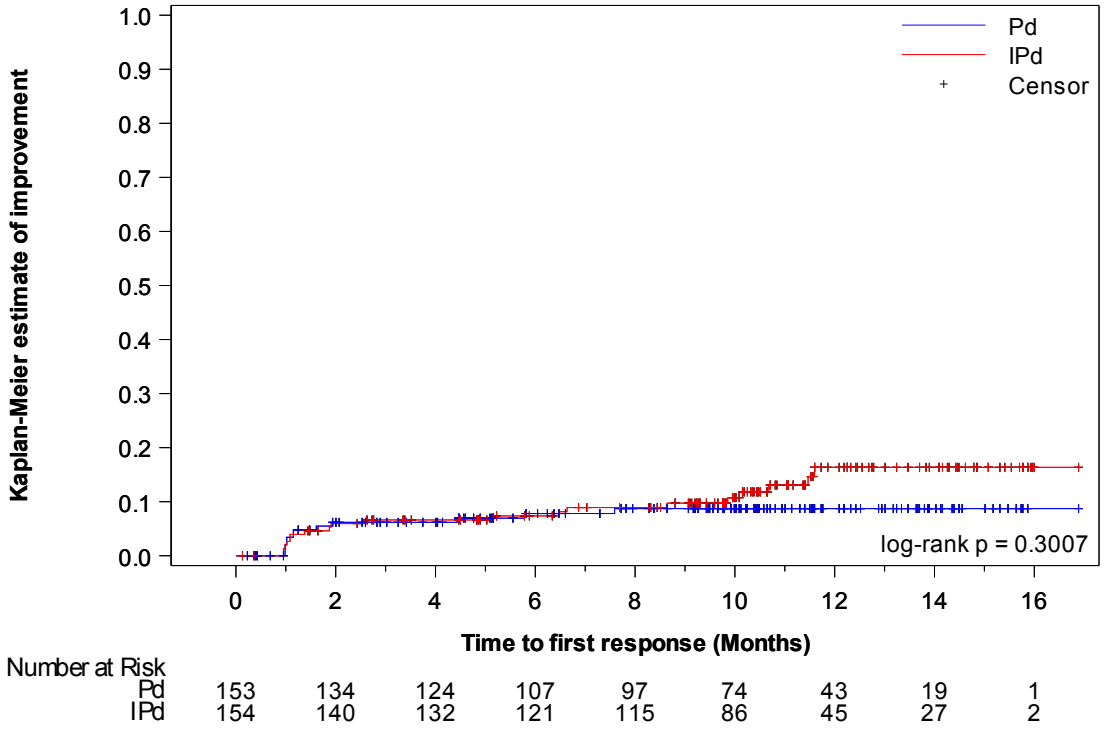
A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_det15l_de_i_f_x.rtf (08APR2021 15:33)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Financial difficulties
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in financial difficulties (LOCF) - ITT population

First permanent improvement 15 points Financial difficulties (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	12 (7.8)	19 (12.3)
Number (%) of patients censored	141 (92.2)	135 (87.7)
Kaplan-Meier estimates of financial difficulties in months		
25% quantile (95% CI)	NC (NC to NC)	NC (11.598 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3007
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.46 (0.71 to 3.01)
P-value	-	0.3036
Probability (95% CI)[c]		
2 Months	0.06 (0.030 to 0.109)	0.06 (0.029 to 0.105)
4 Months	0.06 (0.030 to 0.109)	0.07 (0.034 to 0.113)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_imp15pl_de_i_t_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Financial difficulties
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-C30 - Time until permanent improvement by 15 pt in financial difficulties - Kaplan-Meier curve (LOCF) - ITT population



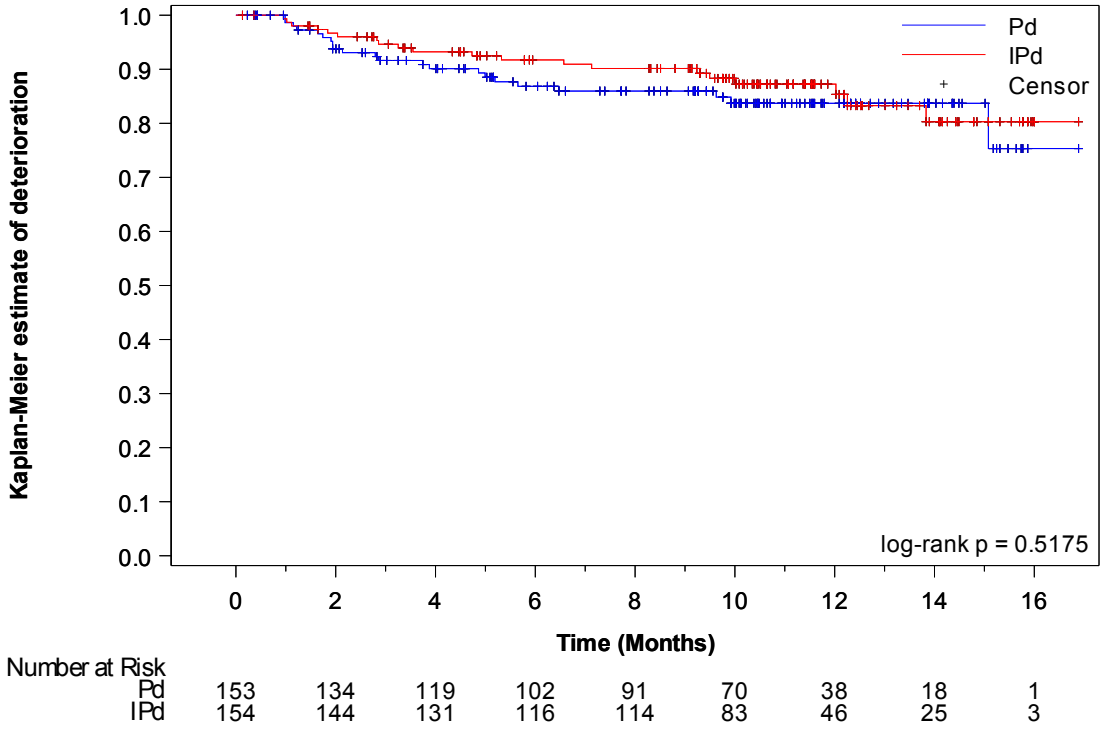
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_imp15pl_de_i_f_x.rtf (08APR2021 15:33)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Financial difficulties
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in financial difficulties (LOCF) - ITT population

First permanent deterioration 15 points Financial difficulties (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	22 (14.4)	20 (13.0)
Number (%) of patients censored	131 (85.6)	134 (87.0)
Kaplan-Meier estimates of financial difficulties in months		
25% quantile (95% CI)	NC (15.080 to NC)	NC (12.255 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5175
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.82 (0.45 to 1.50)
P-value	-	0.5175
Probability (95% CI)[c]		
2 Months	0.94 (0.884 to 0.967)	0.97 (0.922 to 0.986)
4 Months	0.90 (0.839 to 0.940)	0.93 (0.878 to 0.963)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_det15pl_de_i_t_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Financial difficulties
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-C30 - Time until permanent deterioration by 15 pt in financial difficulties - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_det15pl_de_i_f_x.rtf (08APR2021 15:33)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (27.1)	11 (20.4)	9 (16.7)	16 (23.5)	3 (10.3)	8 (25.0)	0.1947
Number (%) of patients censored	51 (72.9)	43 (79.6)	45 (83.3)	52 (76.5)	26 (89.7)	24 (75.0)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	5.26 (1.150 to NC)	14.75 (1.873 to NC)	NC (2.957 to NC)	NC (1.906 to NC)	NC (1.117 to NC)	2.89 (1.117 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.752 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2979		0.3679		0.2001	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.32 to 1.42)		1.45 (0.64 to 3.29)		2.32 (0.62 to 8.76)	
P-value	-	0.3010		0.3707		0.2134	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_impl_age_de_i_t_x.rtf (08APR2021 14:56)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (35.7)	22 (40.7)	15 (27.8)	28 (41.2)	14 (48.3)	10 (31.3)	0.0826
Number (%) of patients censored	45 (64.3)	32 (59.3)	39 (72.2)	40 (58.8)	15 (51.7)	22 (68.8)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	3.75 (1.938 to 10.382)	1.97 (1.018 to 2.858)	4.01 (1.741 to NC)	3.02 (1.906 to 8.246)	1.91 (1.018 to 4.698)	3.14 (1.051 to NC)	
Median (95% CI)	NC (10.382 to NC)	NC (2.858 to NC)	NC (NC to NC)	NC (8.312 to NC)	5.49 (1.938 to NC)	NC (6.702 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.487 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4240		0.1898		0.1042	
Hazard ratio (95% CI) vs Pd	-	1.26 (0.71 to 2.24)		1.52 (0.81 to 2.84)		0.51 (0.23 to 1.16)	
P-value	-	0.4250		0.1930		0.1105	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_detl_age_de_i_t_x.rtf (08APR2021 14:55)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (11.4)	5 (9.3)	2 (3.7)	9 (13.2)	2 (6.9)	5 (15.6)	0.2594
Number (%) of patients censored	62 (88.6)	49 (90.7)	52 (96.3)	59 (86.8)	27 (93.1)	27 (84.4)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.466 to NC)	NC (5.782 to NC)	NC (6.637 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6243		0.0864		0.4538	
Hazard ratio (95% CI) vs Pd	-	0.76 (0.25 to 2.31)		3.51 (0.76 to 16.26)		1.85 (0.36 to 9.59)	
P-value	-	0.6254		0.1081		0.4611	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (15.7)	11 (20.4)	7 (13.0)	7 (10.3)	4 (13.8)	2 (6.3)	0.3734
Number (%) of patients censored	59 (84.3)	43 (79.6)	47 (87.0)	61 (89.7)	25 (86.2)	30 (93.8)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	NC (4.994 to NC)	NC (2.858 to NC)	15.08 (9.626 to NC)	NC (12.025 to NC)	NC (2.858 to NC)	NC (12.255 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.255 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5344		0.4562		0.2394	
Hazard ratio (95% CI) vs Pd	-	1.30 (0.56 to 3.00)		0.67 (0.24 to 1.92)		0.38 (0.07 to 2.05)	
P-value	-	0.5356		0.4591		0.2580	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_detpl_age_de_i_t_x.rtf (08APR2021 14:56)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (20.8)	22 (21.6)	10 (19.2)	13 (25.0)	0.7574
Number (%) of patients censored	80 (79.2)	80 (78.4)	42 (80.8)	39 (75.0)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (3.023 to NC)	NC (2.037 to NC)	NC (1.610 to NC)	14.75 (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.752 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.752 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9274		0.6648	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.57 to 1.87)		1.20 (0.53 to 2.74)	
P-value	-	0.9274		0.6652	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_impl_plne_de_i_t_x.rtf (08APR2021 14:56)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	33 (32.7)	38 (37.3)	21 (40.4)	22 (42.3)	0.6700
Number (%) of patients censored	68 (67.3)	64 (62.7)	31 (59.6)	30 (57.7)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	4.01 (1.938 to 10.382)	2.60 (1.906 to 5.322)	2.83 (1.150 to 5.487)	1.97 (1.084 to 6.867)	
Median (95% CI)	NC (12.057 to NC)	NC (9.626 to NC)	11.60 (5.027 to NC)	NC (6.702 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5055		0.9820	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.73 to 1.87)		0.99 (0.55 to 1.81)	
P-value	-	0.5065		0.9820	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_detl_plne_de_i_t_x.rtf (08APR2021 14:56)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (5.0)	14 (13.7)	7 (13.5)	5 (9.6)	0.0561
Number (%) of patients censored	96 (95.0)	88 (86.3)	45 (86.5)	47 (90.4)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.466 to NC)	NC (1.938 to NC)	NC (10.678 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0476		0.3916	
Hazard ratio (95% CI) vs Pd	-	2.69 (0.97 to 7.48)		0.61 (0.19 to 1.92)	
P-value	-	0.0571		0.3968	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_imppl_plne_de_i_t_x.rtf (08APR2021 14:57)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (14.9)	13 (12.7)	7 (13.5)	7 (13.5)	0.8155
Number (%) of patients censored	86 (85.1)	89 (87.3)	45 (86.5)	45 (86.5)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (9.626 to NC)	NC (12.025 to NC)	15.08 (4.994 to NC)	NC (10.021 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4935		0.8747	
Hazard ratio (95% CI) vs Pd	-	0.77 (0.37 to 1.62)		0.92 (0.32 to 2.62)	
P-value	-	0.4947		0.8746	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (14.3)	19 (21.3)	21 (25.3)	16 (24.6)	0.3669
Number (%) of patients censored	60 (85.7)	70 (78.7)	62 (74.7)	49 (75.4)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (5.191 to NC)	14.75 (2.168 to NC)	5.59 (1.906 to NC)	7.98 (1.380 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3404		0.8169	
Hazard ratio (95% CI) vs Pd	-	1.45 (0.67 to 3.12)		0.93 (0.48 to 1.78)	
P-value	-	0.3431		0.8177	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (37.1)	38 (42.7)	28 (33.7)	22 (33.8)	0.5269
Number (%) of patients censored	44 (62.9)	51 (57.3)	55 (66.3)	43 (66.2)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	2.83 (1.741 to 5.191)	2.04 (1.281 to 3.121)	4.73 (1.906 to 11.598)	2.60 (1.281 to 8.805)	
Median (95% CI)	NC (7.458 to NC)	NC (5.322 to NC)	NC (11.598 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4772		0.8147	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.73 to 1.97)		0.94 (0.54 to 1.64)	
P-value	-	0.4778		0.8153	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (2.9)	11 (12.4)	10 (12.0)	8 (12.3)	0.0859
Number (%) of patients censored	68 (97.1)	78 (87.6)	73 (88.0)	57 (87.7)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.466 to NC)	NC (NC to NC)	NC (10.152 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0372		0.8480	
Hazard ratio (95% CI) vs Pd	-	4.34 (0.96 to 19.56)		0.91 (0.36 to 2.32)	
P-value	-	0.0564		0.8486	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (20.0)	12 (13.5)	8 (9.6)	8 (12.3)	0.3882
Number (%) of patients censored	56 (80.0)	77 (86.5)	75 (90.4)	57 (87.7)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	15.08 (4.994 to NC)	NC (12.255 to NC)	NC (NC to NC)	NC (12.025 to NC)	
Median (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2370		0.8644	
Hazard ratio (95% CI) vs Pd	-	0.63 (0.29 to 1.36)		1.09 (0.41 to 2.91)	
P-value	-	0.2412		0.8643	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (19.0)	31 (26.3)	6 (31.6)	4 (16.7)	0.1493
Number (%) of patients censored	102 (81.0)	87 (73.7)	13 (68.4)	20 (83.3)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (4.665 to NC)	5.72 (1.906 to NC)	2.96 (0.986 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.957 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3068		0.2604	
Hazard ratio (95% CI) vs Pd	-	1.32 (0.77 to 2.25)		0.49 (0.14 to 1.74)	
P-value	-	0.3083		0.2704	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (34.9)	45 (38.1)	9 (47.4)	13 (54.2)	0.8025
Number (%) of patients censored	82 (65.1)	73 (61.9)	10 (52.6)	11 (45.8)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	2.83 (1.938 to 5.487)	2.20 (1.347 to 3.450)	3.09 (1.018 to 10.251)	2.04 (0.953 to 6.735)	
Median (95% CI)	NC (12.057 to NC)	NC (9.626 to NC)	10.25 (3.088 to NC)	8.80 (2.037 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.251 to NC)	NC (9.988 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7560		0.7410	
Hazard ratio (95% CI) vs Pd	-	1.07 (0.70 to 1.62)		1.15 (0.49 to 2.72)	
P-value	-	0.7559		0.7412	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_detl_race_de_i_t_x.rtf (08APR2021 14:56)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (7.1)	18 (15.3)	3 (15.8)	1 (4.2)	0.0712
Number (%) of patients censored	117 (92.9)	100 (84.7)	16 (84.2)	23 (95.8)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.466 to NC)	NC (0.986 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0823		0.2071	
Hazard ratio (95% CI) vs Pd	-	2.00 (0.90 to 4.46)		0.26 (0.03 to 2.49)	
P-value	-	0.0886		0.2418	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (13.5)	13 (11.0)	5 (26.3)	7 (29.2)	0.5449
Number (%) of patients censored	109 (86.5)	105 (89.0)	14 (73.7)	17 (70.8)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	NC (13.832 to NC)	15.08 (1.906 to 15.080)	12.02 (0.953 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	15.08 (NC to NC)	NC (12.025 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	15.08 (NC to NC)	NC (12.255 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3801		0.9897	
Hazard ratio (95% CI) vs Pd	-	0.72 (0.35 to 1.49)		1.01 (0.31 to 3.23)	
P-value	-	0.3822		0.9897	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	2 (50.0)	30 (22.4)	33 (25.4)	0.9956
Number (%) of patients censored	2 (66.7)	2 (50.0)	104 (77.6)	97 (74.6)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	5.26 (NC to NC)	3.37 (1.018 to NC)	NC (2.957 to NC)	7.98 (2.037 to NC)	
Median (95% CI)	5.26 (NC to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	5.26 (NC to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5151		0.7424	
Hazard ratio (95% CI) vs Pd	-	0.41 (0.03 to 6.62)		1.09 (0.66 to 1.78)	
P-value	-	0.5287		0.7426	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_impl_ethn_de_i_t_x.rtf (08APR2021 14:56)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (25.0)	51 (38.1)	54 (41.5)	0.9860
Number (%) of patients censored	3 (100.0)	3 (75.0)	83 (61.9)	76 (58.5)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	NC (1.018 to NC)	2.83 (1.906 to 4.731)	2.17 (1.840 to 3.844)	
Median (95% CI)	NC (NC to NC)	NC (1.018 to NC)	NC (10.251 to NC)	NC (8.805 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.7279	
Hazard ratio (95% CI) vs Pd	-			1.07 (0.73 to 1.57)	
P-value	-	0.9985		0.7280	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (50.0)	12 (9.0)	17 (13.1)	0.9897
Number (%) of patients censored	3 (100.0)	2 (50.0)	122 (91.0)	113 (86.9)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	11.53 (11.466 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (11.466 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (11.466 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.4024	
Hazard ratio (95% CI) vs Pd	-			1.37 (0.65 to 2.87)	
P-value	-			0.4043	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_imppl_ethn_de_i_t_x.rtf (08APR2021 14:57)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	22 (16.4)	19 (14.6)	0.9999
Number (%) of patients censored	3 (100.0)	4 (100.0)	112 (83.6)	111 (85.4)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	15.08 (9.626 to NC)	NC (12.025 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.4621	
Hazard ratio (95% CI) vs Pd	-			0.79 (0.43 to 1.47)	
P-value	-			0.4629	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	8 (10.5)	7 (12.7)	6 (30.0)	10 (35.7)	2 (40.0)	4 (57.1)	4 (26.7)	3 (14.3)	11 (29.7)	11 (25.6)	0.6089
Number (%) of patients censored	68 (89.5)	48 (87.3)	14 (70.0)	18 (64.3)	3 (60.0)	3 (42.9)	11 (73.3)	18 (85.7)	26 (70.3)	32 (74.4)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (NC to NC)	NC (5.717 to NC)	2.83 (0.953 to NC)	1.99 (0.953 to NC)	5.26 (2.957 to NC)	0.95 (0.953 to 1.084)	3.02 (0.986 to NC)	NC (1.084 to NC)	4.67 (1.248 to NC)	14.75 (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.825 to NC)	NC (2.168 to NC)	NC (2.957 to NC)	1.08 (0.953 to NC)	NC (1.150 to NC)	NC (NC to NC)	NC (5.191 to NC)	NC (14.752 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.957 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.7887		0.7285		0.3694		0.3666		0.3711	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.42 to 3.17)		1.20 (0.43 to 3.29)		2.16 (0.39 to 11.99)		0.51 (0.11 to 2.27)		0.68 (0.29 to 1.59)	
P-value	-	0.7888		0.7289		0.3804		0.3757		0.3739	
Improvement probability (95% CI)[b]											
2 Months	0.070 (0.026 to 0.145)	0.093 (0.034 to 0.189)	0.211 (0.066 to 0.410)	0.250 (0.111 to 0.418)		0.571 (0.172 to 0.837)	0.200 (0.049 to 0.424)	0.048 (0.003 to 0.197)	0.197 (0.087 to 0.340)	0.144 (0.058 to 0.267)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	23 (30.3)	15 (27.3)	9 (45.0)	12 (42.9)	1 (20.0)	4 (57.1)	9 (60.0)	11 (52.4)	12 (32.4)	18 (41.9)	0.6574
Number (%) of patients censored	53 (69.7)	40 (72.7)	11 (55.0)	16 (57.1)	4 (80.0)	3 (42.9)	6 (40.0)	10 (47.6)	25 (67.6)	25 (58.1)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	4.70 (1.741 to 12.057)	6.70 (1.643 to NC)	1.64 (0.986 to 8.542)	2.55 (1.018 to 8.312)	NC (0.986 to NC)	2.79 (1.248 to 3.450)	2.00 (1.018 to 5.191)	2.04 (0.953 to 8.805)	3.75 (2.037 to NC)	1.35 (1.018 to 2.858)	
Median (95% CI)	NC (12.057 to NC)	NC (NC to NC)	8.54 (1.643 to NC)	NC (4.238 to NC)	NC (0.986 to NC)	3.45 (1.248 to NC)	5.42 (1.906 to 10.251)	9.99 (2.037 to NC)	NC (7.458 to NC)	NC (2.168 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (2.858 to NC)	10.25 (5.421 to 10.251)	NC (9.988 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.7034		0.7459		0.3068		0.4954		0.3102	
Hazard ratio (95% CI) vs Pd	-	0.88 (0.46 to 1.69)		0.87 (0.37 to 2.06)		2.98 (0.33 to 26.83)		0.73 (0.29 to 1.81)		1.46 (0.70 to 3.03)	
P-value	-	0.7036		0.7461		0.3302		0.4971		0.3131	
Deterioration probability (95% CI)[b]											

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	4 (5.3)	3 (5.5)	3 (15.0)	6 (21.4)	0 (0.0)	3 (42.9)	2 (13.3)	1 (4.8)	3 (8.1)	6 (14.0)	0.8336
Number (%) of patients censored	72 (94.7)	52 (94.5)	17 (85.0)	22 (78.6)	5 (100.0)	4 (57.1)	13 (86.7)	20 (95.2)	34 (91.9)	37 (86.0)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (NC to NC)	NC (11.466 to NC)	NC (0.986 to NC)	10.68 (0.986 to NC)	NC (NC to NC)	2.63 (1.084 to NC)	NC (1.150 to NC)	NC (1.084 to NC)	NC (7.589 to NC)	NC (8.641 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.678 to NC)	NC (NC to NC)	11.60 (1.084 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.598 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.9994		0.5836		0.1538		0.3963		0.6252	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.22 to 4.47)		1.47 (0.37 to 5.91)				0.37 (0.03 to 4.07)		1.41 (0.35 to 5.68)	
P-value	-	0.9994		0.5859		0.9973		0.4156		0.6269	
Improvement probability (95% CI)[b]											
2 Months	0.042 (0.011 to 0.108)	0.037 (0.007 to 0.114)	0.105 (0.018 to 0.284)	0.107 (0.027 to 0.251)		0.143 (0.007 to 0.465)	0.133 (0.022 to 0.346)	0.048 (0.003 to 0.197)	0.057 (0.010 to 0.167)	0.048 (0.009 to 0.144)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	9 (11.8)	5 (9.1)	4 (20.0)	2 (7.1)	1 (20.0)	2 (28.6)	5 (33.3)	6 (28.6)	3 (8.1)	5 (11.6)	0.8054
Number (%) of patients censored	67 (88.2)	50 (90.9)	16 (80.0)	26 (92.9)	4 (80.0)	5 (71.4)	10 (66.7)	15 (71.4)	34 (91.9)	38 (88.4)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (9.922 to NC)	NC (NC to NC)	NC (1.216 to NC)	NC (5.322 to NC)	NC (0.986 to NC)	7.13 (2.858 to NC)	5.19 (1.906 to 15.080)	12.02 (0.953 to NC)	NC (3.745 to NC)	NC (10.021 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.626 to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (2.858 to NC)	15.08 (4.994 to 15.080)	NC (12.025 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (7.129 to NC)	15.08 (NC to NC)	NC (12.255 to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_detpl_greg_de_i_t_x.rtf (08APR2021 14:56)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.5471		0.1584		0.7913		0.5818		0.7638	
Hazard ratio (95% CI) vs Pd	-	0.72 (0.24 to 2.14)		0.31 (0.06 to 1.72)		1.38 (0.12 to 15.32)		0.71 (0.21 to 2.43)		1.25 (0.30 to 5.24)	
P-value	-	0.5490		0.1819		0.7922		0.5834		0.7642	
Deterioration probability (95% CI)[b]											
2 Months	0.943 (0.856 to 0.978)	0.963 (0.859 to 0.991)	0.895 (0.641 to 0.973)	1.000 (1.000 to 1.000)	0.800 (0.204 to 0.969)	1.000 (1.000 to 1.000)	0.933 (0.613 to 0.990)	0.952 (0.707 to 0.993)	0.971 (0.814 to 0.996)	0.952 (0.823 to 0.988)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (14.4)	14 (18.2)	17 (30.4)	21 (27.3)	0.4764
Number (%) of patients censored	83 (85.6)	63 (81.8)	39 (69.6)	56 (72.7)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (5.782 to NC)	14.75 (2.136 to NC)	3.02 (1.150 to NC)	3.71 (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.752 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6614		0.6354	
Hazard ratio (95% CI) vs Pd	-	1.18 (0.56 to 2.48)		0.86 (0.45 to 1.62)	
P-value	-	0.6617		0.6357	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (27.8)	25 (32.5)	27 (48.2)	35 (45.5)	0.6882
Number (%) of patients censored	70 (72.2)	52 (67.5)	29 (51.8)	42 (54.5)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	5.03 (1.906 to 13.339)	2.79 (1.281 to NC)	2.83 (1.906 to 4.731)	2.00 (1.347 to 3.844)	
Median (95% CI)	NC (13.339 to NC)	NC (NC to NC)	10.25 (4.008 to NC)	10.28 (5.322 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6258		0.9074	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.66 to 1.97)		0.97 (0.59 to 1.60)	
P-value	-	0.6261		0.9072	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (6.2)	7 (9.1)	6 (10.7)	12 (15.6)	0.9606
Number (%) of patients censored	91 (93.8)	70 (90.9)	50 (89.3)	65 (84.4)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.598 to NC)	NC (NC to NC)	NC (9.856 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5782		0.5074	
Hazard ratio (95% CI) vs Pd	-	1.36 (0.46 to 4.05)		1.39 (0.52 to 3.71)	
P-value	-	0.5797		0.5093	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (11.3)	11 (14.3)	11 (19.6)	9 (11.7)	0.2144
Number (%) of patients censored	86 (88.7)	66 (85.7)	45 (80.4)	68 (88.3)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	NC (9.298 to NC)	15.08 (3.877 to NC)	NC (12.025 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7306		0.1491	
Hazard ratio (95% CI) vs Pd	-	1.16 (0.50 to 2.67)		0.53 (0.22 to 1.28)	
P-value	-	0.7308		0.1560	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (20.4)	31 (22.5)	3 (18.8)	4 (25.0)	0.6547
Number (%) of patients censored	109 (79.6)	107 (77.5)	13 (81.3)	12 (75.0)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (4.665 to NC)	14.75 (2.234 to NC)	NC (0.986 to NC)	1.87 (0.953 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.906 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8912		0.5967	
Hazard ratio (95% CI) vs Pd	-	1.04 (0.62 to 1.73)		1.49 (0.33 to 6.69)	
P-value	-	0.8913		0.5991	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	47 (34.3)	56 (40.6)	7 (43.8)	4 (25.0)	0.1189
Number (%) of patients censored	90 (65.7)	82 (59.4)	9 (56.3)	12 (75.0)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	3.98 (2.037 to 7.458)	2.17 (1.643 to 3.450)	1.08 (0.953 to 3.745)	9.63 (1.906 to NC)	
Median (95% CI)	NC (12.057 to NC)	NC (8.805 to NC)	NC (1.051 to NC)	NC (1.971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.745 to NC)	NC (9.626 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3324		0.1690	
Hazard ratio (95% CI) vs Pd	-	1.21 (0.82 to 1.78)		0.42 (0.12 to 1.49)	
P-value	-	0.3343		0.1810	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (7.3)	16 (11.6)	2 (12.5)	3 (18.8)	0.9451
Number (%) of patients censored	127 (92.7)	122 (88.4)	14 (87.5)	13 (81.3)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	11.60 (1.873 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.598 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3282		0.7143	
Hazard ratio (95% CI) vs Pd	-	1.48 (0.67 to 3.26)		1.40 (0.23 to 8.36)	
P-value	-	0.3313		0.7156	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (13.9)	20 (14.5)	3 (18.8)	0 (0.0)	0.9853
Number (%) of patients censored	118 (86.1)	118 (85.5)	13 (81.3)	16 (100.0)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (15.080 to NC)	NC (12.255 to NC)	9.92 (2.793 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.472 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.922 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8675		0.0484	
Hazard ratio (95% CI) vs Pd	-	0.95 (0.51 to 1.78)			
P-value	-	0.8674		0.9972	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (23.5)	14 (21.9)	12 (21.4)	11 (20.8)	7 (16.3)	10 (29.4)	0.6880
Number (%) of patients censored	39 (76.5)	50 (78.1)	44 (78.6)	42 (79.2)	36 (83.7)	24 (70.6)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	NC (2.530 to NC)	14.75 (1.873 to NC)	NC (1.938 to NC)	NC (1.906 to NC)	NC (1.117 to NC)	3.71 (1.380 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.752 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.975 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8848		0.9121		0.3405	
Hazard ratio (95% CI) vs Pd	-	0.94 (0.44 to 2.04)		0.95 (0.42 to 2.16)		1.59 (0.61 to 4.19)	
P-value	-	0.8846		0.9121		0.3448	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (41.2)	25 (39.1)	18 (32.1)	26 (49.1)	15 (34.9)	9 (26.5)	0.1461
Number (%) of patients censored	30 (58.8)	39 (60.9)	38 (67.9)	27 (50.9)	28 (65.1)	25 (73.5)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	2.79 (1.117 to 7.458)	3.12 (1.347 to 8.246)	4.70 (1.643 to NC)	1.94 (1.084 to 2.201)	3.75 (1.741 to 11.598)	5.32 (1.051 to NC)	
Median (95% CI)	NC (5.421 to NC)	NC (8.312 to NC)	NC (8.542 to NC)	9.63 (2.201 to NC)	12.06 (3.975 to NC)	NC (6.702 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.057 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9280		0.0772		0.2703	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.54 to 1.74)		1.71 (0.94 to 3.12)		0.63 (0.27 to 1.44)	
P-value	-	0.9279		0.0807		0.2744	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (9.8)	9 (14.1)	5 (8.9)	5 (9.4)	2 (4.7)	5 (14.7)	0.5916
Number (%) of patients censored	46 (90.2)	55 (85.9)	51 (91.1)	48 (90.6)	41 (95.3)	29 (85.3)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	NC (NC to NC)	NC (10.152 to NC)	NC (NC to NC)	NC (11.466 to NC)	NC (NC to NC)	NC (1.380 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4509		0.9701		0.1951	
Hazard ratio (95% CI) vs Pd	-	1.52 (0.51 to 4.53)		0.98 (0.28 to 3.38)		2.83 (0.55 to 14.60)	
P-value	-	0.4542		0.9701		0.2151	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (21.6)	9 (14.1)	8 (14.3)	8 (15.1)	3 (7.0)	3 (8.8)	0.8320
Number (%) of patients censored	40 (78.4)	55 (85.9)	48 (85.7)	45 (84.9)	40 (93.0)	31 (91.2)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	15.08 (4.862 to NC)	13.83 (12.025 to NC)	NC (5.191 to NC)	NC (7.129 to NC)	NC (4.994 to NC)	NC (5.322 to NC)	
Median (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3936		0.9877		0.9175	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.28 to 1.65)		0.99 (0.37 to 2.64)		1.09 (0.22 to 5.41)	
P-value	-	0.3965		0.9877		0.9175	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (22.6)	7 (17.9)	23 (23.5)	23 (23.2)	1 (4.2)	5 (31.3)	0.1642
Number (%) of patients censored	24 (77.4)	32 (82.1)	75 (76.5)	76 (76.8)	23 (95.8)	11 (68.8)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	NC (1.051 to NC)	14.75 (1.084 to NC)	6.67 (1.938 to NC)	NC (2.070 to NC)	NC (1.906 to NC)	2.04 (0.953 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.752 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.873 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5335		0.8951		0.0294	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.25 to 2.07)		0.96 (0.54 to 1.71)		7.57 (0.88 to 64.85)	
P-value	-	0.5353		0.8951		0.0647	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (51.6)	13 (33.3)	31 (31.6)	44 (44.4)	7 (29.2)	3 (18.8)	0.0194
Number (%) of patients censored	15 (48.4)	26 (66.7)	67 (68.4)	55 (55.6)	17 (70.8)	13 (81.3)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	1.22 (0.986 to 3.187)	3.84 (1.347 to NC)	5.03 (2.333 to 10.382)	1.97 (1.117 to 2.793)	2.83 (0.986 to 12.057)	6.70 (1.018 to NC)	
Median (95% CI)	7.46 (1.906 to NC)	NC (9.988 to NC)	NC (13.339 to NC)	NC (5.322 to NC)	11.60 (2.825 to NC)	NC (6.702 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	12.06 (11.598 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0928		0.0411		0.2496	
Hazard ratio (95% CI) vs Pd	-	0.54 (0.26 to 1.12)		1.61 (1.02 to 2.55)		0.46 (0.12 to 1.79)	
P-value	-	0.0980		0.0430		0.2609	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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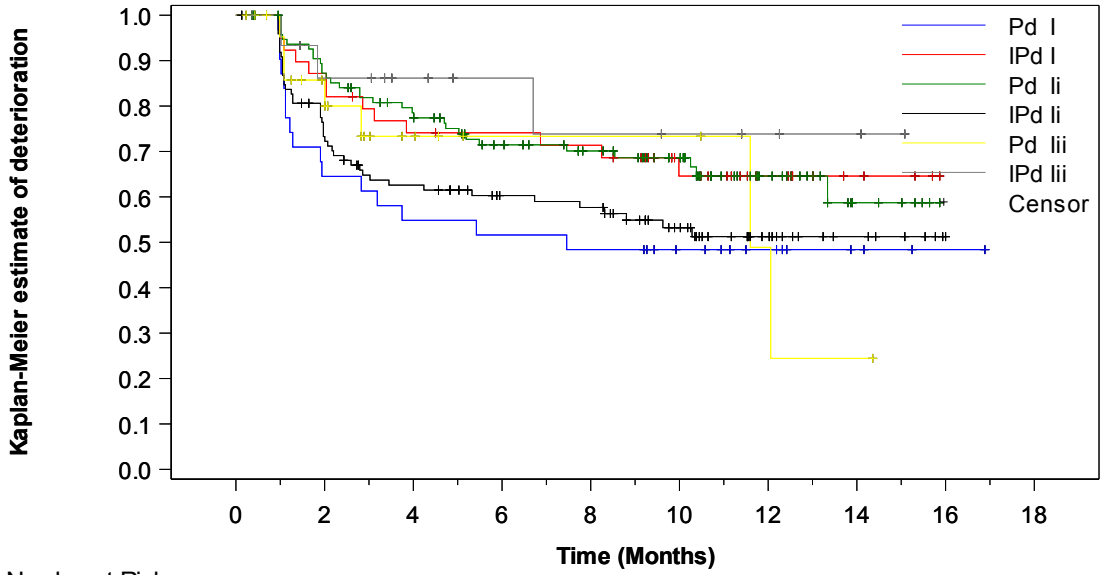
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to R-ISS stage (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd I	31	19	16	15	7	2	0
IPd I	39	30	27	24	9	3	0
Pd Ii	98	75	57	46	19	5	0
IPd Ii	99	59	46	37	15	5	0
Pd Iii	24	9	4	4	2	0	0
IPd Iii	16	12	7	6	3	1	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (6.5)	5 (12.8)	9 (9.2)	12 (12.1)	1 (4.2)	2 (12.5)	0.7767
Number (%) of patients censored	29 (93.5)	34 (87.2)	89 (90.8)	87 (87.9)	23 (95.8)	14 (87.5)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	NC (NC to NC)	NC (9.856 to NC)	NC (NC to NC)	NC (11.466 to NC)	NC (4.435 to NC)	NC (0.953 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.435 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3799		0.6312		0.4294	
Hazard ratio (95% CI) vs Pd	-	2.05 (0.40 to 10.59)		1.24 (0.52 to 2.93)		2.55 (0.23 to 28.35)	
P-value	-	0.3901		0.6318		0.4458	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.7 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (29.0)	5 (12.8)	12 (12.2)	13 (13.1)	1 (4.2)	2 (12.5)	0.2596
Number (%) of patients censored	22 (71.0)	34 (87.2)	86 (87.8)	86 (86.9)	23 (95.8)	14 (87.5)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	9.63 (1.216 to NC)	NC (12.255 to NC)	15.08 (15.080 to NC)	NC (12.025 to NC)	NC (4.994 to NC)	NC (1.018 to NC)	
Median (95% CI)	NC (9.922 to NC)	NC (13.832 to NC)	NC (15.080 to NC)	NC (NC to NC)	NC (4.994 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0813		0.9983		0.3868	
Hazard ratio (95% CI) vs Pd	-	0.39 (0.13 to 1.17)		1.00 (0.46 to 2.19)		2.76 (0.25 to 30.49)	
P-value	-	0.0927		0.9983		0.4069	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (17.4)	1 (7.1)	17 (17.9)	30 (25.4)	0.2685
Number (%) of patients censored	19 (82.6)	13 (92.9)	78 (82.1)	88 (74.6)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	5.78 (0.953 to NC)	NC (1.084 to NC)	NC (4.665 to NC)	7.98 (2.037 to NC)	
Median (95% CI)	NC (5.782 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3714		0.2638	
Hazard ratio (95% CI) vs Pd	-	0.38 (0.04 to 3.42)		1.40 (0.77 to 2.55)	
P-value	-	0.3896		0.2661	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (21.7)	7 (50.0)	35 (36.8)	48 (40.7)	0.0843
Number (%) of patients censored	18 (78.3)	7 (50.0)	60 (63.2)	70 (59.3)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	12.06 (1.051 to NC)	1.97 (0.953 to 2.858)	3.75 (1.906 to 5.421)	2.04 (1.281 to 3.844)	
Median (95% CI)	NC (4.008 to NC)	2.86 (1.840 to NC)	NC (10.251 to NC)	NC (9.626 to NC)	
75% quantile (95% CI)	NC (12.057 to NC)	7.75 (2.858 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0189		0.6315	
Hazard ratio (95% CI) vs Pd	-	3.97 (1.15 to 13.74)		1.11 (0.72 to 1.72)	
P-value	-	0.0293		0.6317	
Hazard ratio inverted (95% CI) vs IPd		-		0.90 (0.58 to 1.39)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (8.7)	0 (0.0)	8 (8.4)	18 (15.3)	0.9883
Number (%) of patients censored	21 (91.3)	14 (100.0)	87 (91.6)	100 (84.7)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (1.610 to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.466 to NC)	
Median (95% CI)	NC (5.782 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2325		0.2066	
Hazard ratio (95% CI) vs Pd	-			1.70 (0.74 to 3.91)	
P-value	-	0.9978		0.2120	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (4.3)	3 (21.4)	16 (16.8)	15 (12.7)	0.0654
Number (%) of patients censored	22 (95.7)	11 (78.6)	79 (83.2)	103 (87.3)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (1.938 to NC)	9.30 (1.840 to NC)	15.08 (9.626 to NC)	NC (12.255 to NC)	
Median (95% CI)	NC (NC to NC)	NC (2.858 to NC)	NC (15.080 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (9.298 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0825		0.2694	
Hazard ratio (95% CI) vs Pd	-	5.95 (0.61 to 58.07)		0.67 (0.33 to 1.36)	
P-value	-	0.1250		0.2725	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (16.7)	2 (8.3)	15 (19.2)	28 (27.2)	0.2475
Number (%) of patients censored	30 (83.3)	22 (91.7)	63 (80.8)	75 (72.8)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (1.610 to NC)	NC (1.084 to NC)	NC (2.530 to NC)	5.72 (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.752 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3480		0.3435	
Hazard ratio (95% CI) vs Pd	-	0.47 (0.10 to 2.35)		1.35 (0.72 to 2.54)	
P-value	-	0.3592		0.3453	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (25.0)	10 (41.7)	29 (37.2)	43 (41.7)	0.2814
Number (%) of patients censored	27 (75.0)	14 (58.3)	49 (62.8)	60 (58.3)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	4.73 (1.938 to NC)	1.97 (0.953 to 7.754)	3.75 (1.906 to 7.458)	2.04 (1.281 to 4.238)	
Median (95% CI)	NC (12.057 to NC)	8.80 (1.971 to NC)	NC (10.251 to NC)	NC (8.312 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (8.805 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1139		0.6028	
Hazard ratio (95% CI) vs Pd	-	2.06 (0.83 to 5.12)		1.13 (0.71 to 1.82)	
P-value	-	0.1216		0.6030	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (8.3)	1 (4.2)	7 (9.0)	16 (15.5)	0.3307
Number (%) of patients censored	33 (91.7)	23 (95.8)	71 (91.0)	87 (84.5)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (5.782 to NC)	NC (6.637 to NC)	NC (NC to NC)	NC (10.678 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4486		0.2762	
Hazard ratio (95% CI) vs Pd	-	0.43 (0.04 to 4.12)		1.63 (0.67 to 3.96)	
P-value	-	0.4620		0.2811	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (5.6)	6 (25.0)	14 (17.9)	12 (11.7)	0.0134
Number (%) of patients censored	34 (94.4)	18 (75.0)	64 (82.1)	91 (88.3)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	10.02 (1.018 to NC)	15.08 (6.472 to NC)	NC (13.832 to NC)	
Median (95% CI)	NC (NC to NC)	12.02 (9.298 to NC)	NC (15.080 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.025 to NC)	NC (15.080 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0189		0.1481	
Hazard ratio (95% CI) vs Pd	-	5.60 (1.12 to 28.15)		0.57 (0.26 to 1.23)	
P-value	-	0.0364		0.1535	
Hazard ratio inverted (95% CI) vs IPd		-		1.76 (0.81 to 3.81)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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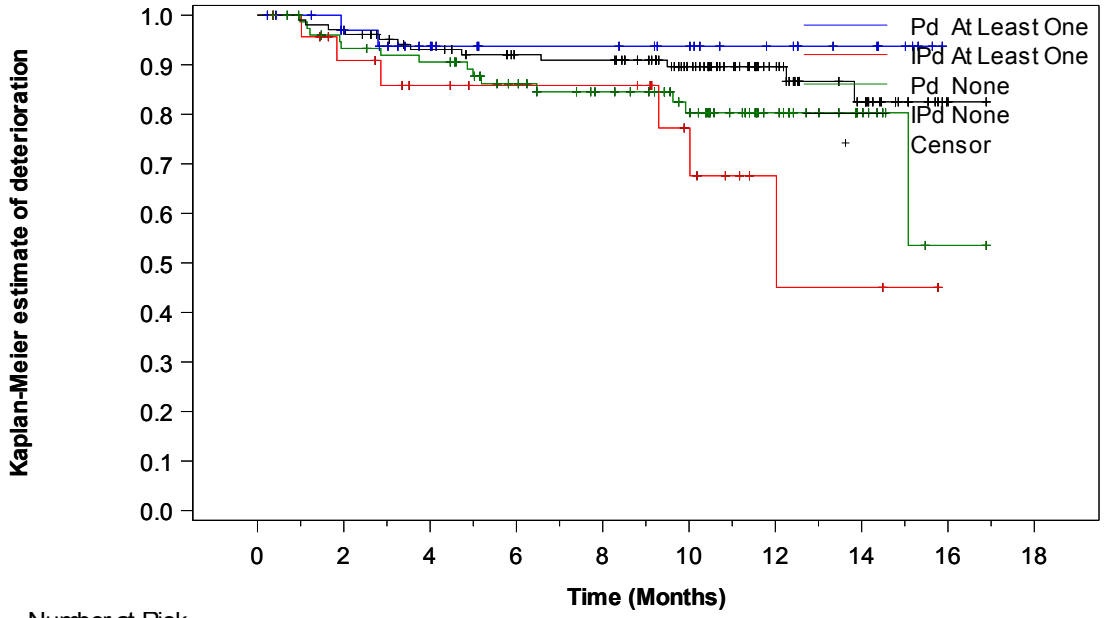
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.7 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to cytogenetic abnormality (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd At Least One	36	28	19	18	11	5	0
IPd At Least One	24	17	13	12	3	1	0
Pd None	78	67	55	46	20	3	0
IPd None	103	95	83	76	34	9	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (22.2)	17 (20.5)	11 (17.5)	18 (25.4)	0.5238
Number (%) of patients censored	70 (77.8)	66 (79.5)	52 (82.5)	53 (74.6)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (4.074 to NC)	14.75 (1.906 to NC)	NC (1.150 to NC)	7.98 (2.037 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.752 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7967		0.4873	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.48 to 1.76)		1.30 (0.62 to 2.76)	
P-value	-	0.7972		0.4886	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (32.2)	34 (41.0)	25 (39.7)	26 (36.6)	0.1244
Number (%) of patients censored	61 (67.8)	49 (59.0)	38 (60.3)	45 (63.4)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	4.73 (1.938 to 12.057)	2.07 (1.117 to 3.121)	2.83 (1.117 to 4.698)	3.02 (1.906 to 8.805)	
Median (95% CI)	NC (13.339 to NC)	NC (6.867 to NC)	11.60 (4.698 to NC)	NC (9.626 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1745		0.3993	
Hazard ratio (95% CI) vs Pd	-	1.41 (0.86 to 2.31)		0.79 (0.46 to 1.37)	
P-value	-	0.1766		0.4003	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (7.8)	9 (10.8)	5 (7.9)	10 (14.1)	0.9795
Number (%) of patients censored	83 (92.2)	74 (89.2)	58 (92.1)	61 (85.9)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.466 to NC)	NC (NC to NC)	NC (10.678 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4830		0.5219	
Hazard ratio (95% CI) vs Pd	-	1.42 (0.53 to 3.82)		1.42 (0.48 to 4.16)	
P-value	-	0.4853		0.5240	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (15.6)	13 (15.7)	8 (12.7)	7 (9.9)	0.4531
Number (%) of patients censored	76 (84.4)	70 (84.3)	55 (87.3)	64 (90.1)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	15.08 (9.922 to NC)	NC (9.298 to NC)	NC (5.191 to NC)	NC (12.255 to NC)	
Median (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9974		0.3225	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.47 to 2.13)		0.60 (0.22 to 1.66)	
P-value	-	0.9974		0.3276	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	30 (19.9)	35 (23.0)	0.9817
Number (%) of patients censored	1 (50.0)	2 (100.0)	121 (80.1)	117 (77.0)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	1.94 (1.938 to NC)	NC (NC to NC)	NC (4.665 to NC)	14.75 (2.168 to NC)	
Median (95% CI)	NC (1.938 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.938 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.6648	
Hazard ratio (95% CI) vs Pd	-			1.11 (0.68 to 1.81)	
P-value	-	0.9990		0.6656	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	2 (100.0)	53 (35.1)	58 (38.2)	0.2645
Number (%) of patients censored	1 (50.0)	0 (0.0)	98 (64.9)	94 (61.8)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	3.19 (3.187 to NC)	1.12 (1.117 to 2.037)	3.75 (1.938 to 5.487)	2.43 (1.906 to 4.238)	
Median (95% CI)	NC (3.187 to NC)	1.58 (1.117 to 2.037)	NC (11.598 to NC)	NC (10.283 to NC)	
75% quantile (95% CI)	NC (3.187 to NC)	2.04 (1.117 to 2.037)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.6907	
Hazard ratio (95% CI) vs Pd	-			1.08 (0.74 to 1.57)	
P-value	-	0.9985		0.6910	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	11 (7.3)	19 (12.5)	0.9908
Number (%) of patients censored	1 (50.0)	2 (100.0)	140 (92.7)	133 (87.5)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	1.94 (1.938 to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.598 to NC)	
Median (95% CI)	NC (1.938 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.938 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.2096	
Hazard ratio (95% CI) vs Pd	-			1.60 (0.76 to 3.37)	
P-value	-	0.9990		0.2138	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (100.0)	22 (14.6)	18 (11.8)	0.9871
Number (%) of patients censored	2 (100.0)	0 (0.0)	129 (85.4)	134 (88.2)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	1.12 (1.117 to 2.037)	NC (15.080 to NC)	NC (12.255 to NC)	
Median (95% CI)	NC (NC to NC)	1.58 (1.117 to 2.037)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	2.04 (1.117 to 2.037)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.3088	
Hazard ratio (95% CI) vs Pd	-			0.72 (0.39 to 1.35)	
P-value	-	0.9991		0.3103	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (19.8)	26 (25.0)	10 (24.4)	6 (18.2)	0.5370
Number (%) of patients censored	81 (80.2)	78 (75.0)	31 (75.6)	27 (81.8)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (4.665 to NC)	14.75 (2.070 to NC)	5.26 (1.117 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.752 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4865		0.4812	
Hazard ratio (95% CI) vs Pd	-	1.23 (0.69 to 2.20)		0.70 (0.25 to 1.92)	
P-value	-	0.4873		0.4836	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (41.6)	40 (38.5)	7 (17.1)	14 (42.4)	0.0728
Number (%) of patients censored	59 (58.4)	64 (61.5)	34 (82.9)	19 (57.6)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	2.83 (1.938 to 5.027)	2.43 (1.281 to 6.702)	NC (1.741 to NC)	2.04 (1.084 to 6.735)	
Median (95% CI)	12.06 (7.458 to NC)	NC (9.626 to NC)	NC (NC to NC)	NC (2.201 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6336		0.0280	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.58 to 1.39)		2.66 (1.07 to 6.60)	
P-value	-	0.6336		0.0346	
Hazard ratio inverted (95% CI) vs IPd		-		0.38 (0.15 to 0.93)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (8.9)	13 (12.5)	2 (4.9)	4 (12.1)	0.8359
Number (%) of patients censored	92 (91.1)	91 (87.5)	39 (95.1)	29 (87.9)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.466 to NC)	NC (NC to NC)	NC (6.637 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5467		0.3202	
Hazard ratio (95% CI) vs Pd	-	1.30 (0.55 to 3.04)		2.31 (0.42 to 12.61)	
P-value	-	0.5478		0.3342	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (15.8)	12 (11.5)	3 (7.3)	5 (15.2)	0.4279
Number (%) of patients censored	85 (84.2)	92 (88.5)	38 (92.7)	28 (84.8)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	15.08 (6.472 to NC)	NC (12.255 to NC)	NC (9.626 to NC)	13.83 (9.495 to NC)	
Median (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.025 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.832 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2683		0.3786	
Hazard ratio (95% CI) vs Pd	-	0.66 (0.31 to 1.39)		1.89 (0.45 to 7.92)	
P-value	-	0.2722		0.3865	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (20.0)	25 (24.5)	11 (21.2)	10 (19.6)	0.5318
Number (%) of patients censored	80 (80.0)	77 (75.5)	41 (78.8)	41 (80.4)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (4.665 to NC)	14.75 (2.070 to NC)	NC (1.150 to NC)	NC (1.380 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.752 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5632		0.7728	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.66 to 2.14)		0.88 (0.37 to 2.08)	
P-value	-	0.5637		0.7730	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (41.0)	39 (38.2)	12 (23.1)	21 (41.2)	0.0936
Number (%) of patients censored	59 (59.0)	63 (61.8)	40 (76.9)	30 (58.8)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	2.83 (1.938 to 5.191)	2.25 (1.281 to 6.702)	5.42 (1.281 to NC)	2.17 (1.347 to 4.238)	
Median (95% CI)	12.06 (8.542 to NC)	NC (9.626 to NC)	NC (NC to NC)	NC (3.450 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6755		0.0924	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.59 to 1.41)		1.82 (0.90 to 3.71)	
P-value	-	0.6755		0.0974	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (9.0)	12 (11.8)	3 (5.8)	7 (13.7)	0.4536
Number (%) of patients censored	91 (91.0)	90 (88.2)	49 (94.2)	44 (86.3)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.598 to NC)	NC (NC to NC)	NC (8.641 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6678		0.2386	
Hazard ratio (95% CI) vs Pd	-	1.21 (0.51 to 2.87)		2.21 (0.57 to 8.54)	
P-value	-	0.6683		0.2511	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (16.0)	12 (11.8)	6 (11.5)	8 (15.7)	0.3283
Number (%) of patients censored	84 (84.0)	90 (88.2)	46 (88.5)	43 (84.3)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	15.08 (6.472 to NC)	NC (12.255 to NC)	NC (9.626 to NC)	13.83 (9.495 to NC)	
Median (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.832 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2778		0.6778	
Hazard ratio (95% CI) vs Pd	-	0.66 (0.31 to 1.40)		1.25 (0.43 to 3.61)	
P-value	-	0.2812		0.6784	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	5 (35.7)	30 (21.0)	30 (21.4)	0.2962
Number (%) of patients censored	9 (90.0)	9 (64.3)	113 (79.0)	110 (78.6)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (1.018 to NC)	1.91 (1.084 to NC)	NC (4.074 to NC)	14.75 (2.234 to NC)	
Median (95% CI)	NC (1.018 to NC)	NC (1.380 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2556		0.9425	
Hazard ratio (95% CI) vs Pd	-	3.25 (0.38 to 27.81)		0.98 (0.59 to 1.63)	
P-value	-	0.2828		0.9425	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (30.0)	6 (42.9)	51 (35.7)	54 (38.6)	0.9131
Number (%) of patients censored	7 (70.0)	8 (57.1)	92 (64.3)	86 (61.4)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	3.75 (1.741 to NC)	1.84 (0.986 to NC)	3.19 (1.938 to 5.487)	2.20 (1.906 to 3.844)	
Median (95% CI)	NC (1.741 to NC)	NC (1.117 to NC)	NC (11.598 to NC)	NC (9.988 to NC)	
75% quantile (95% CI)	NC (3.745 to NC)	NC (7.754 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8593		0.6453	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.28 to 4.66)		1.09 (0.75 to 1.60)	
P-value	-	0.8594		0.6454	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	3 (21.4)	11 (7.7)	16 (11.4)	0.9094
Number (%) of patients censored	9 (90.0)	11 (78.6)	132 (92.3)	124 (88.6)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (1.018 to NC)	NC (1.380 to NC)	NC (NC to NC)	NC (11.598 to NC)	
Median (95% CI)	NC (1.018 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6715		0.3889	
Hazard ratio (95% CI) vs Pd	-	1.63 (0.17 to 15.79)		1.40 (0.65 to 3.02)	
P-value	-	0.6747		0.3911	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (20.0)	3 (21.4)	20 (14.0)	17 (12.1)	0.8383
Number (%) of patients censored	8 (80.0)	11 (78.6)	123 (86.0)	123 (87.9)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	3.75 (1.741 to NC)	NC (1.117 to NC)	NC (15.080 to NC)	NC (12.255 to NC)	
Median (95% CI)	NC (1.741 to NC)	NC (9.495 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (3.745 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6970		0.4968	
Hazard ratio (95% CI) vs Pd	-	0.69 (0.11 to 4.43)		0.80 (0.42 to 1.53)	
P-value	-	0.6984		0.4980	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (20.8)	21 (24.1)	10 (20.4)	14 (25.5)	0.9399
Number (%) of patients censored	76 (79.2)	66 (75.9)	39 (79.6)	41 (74.5)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (2.957 to NC)	NC (1.906 to NC)	NC (1.610 to NC)	14.75 (2.037 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.752 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6329		0.9167	
Hazard ratio (95% CI) vs Pd	-	1.16 (0.63 to 2.14)		1.04 (0.46 to 2.38)	
P-value	-	0.6326		0.9169	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (35.4)	35 (40.2)	19 (38.8)	23 (41.8)	0.6419
Number (%) of patients censored	62 (64.6)	52 (59.8)	30 (61.2)	32 (58.2)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	4.01 (2.136 to 8.542)	2.43 (1.906 to 7.754)	1.94 (1.051 to 3.975)	1.97 (1.051 to 3.450)	
Median (95% CI)	NC (12.057 to NC)	NC (8.805 to NC)	NC (2.793 to NC)	NC (3.450 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5244		0.9744	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.73 to 1.87)		0.99 (0.54 to 1.82)	
P-value	-	0.5237		0.9744	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (7.3)	12 (13.8)	5 (10.2)	7 (12.7)	0.4908
Number (%) of patients censored	89 (92.7)	75 (86.2)	44 (89.8)	48 (87.3)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.598 to NC)	NC (NC to NC)	NC (10.678 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2019		0.9102	
Hazard ratio (95% CI) vs Pd	-	1.82 (0.72 to 4.62)		1.07 (0.34 to 3.37)	
P-value	-	0.2087		0.9106	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (16.7)	11 (12.6)	6 (12.2)	9 (16.4)	0.5288
Number (%) of patients censored	80 (83.3)	76 (87.4)	43 (87.8)	46 (83.6)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	15.08 (9.626 to NC)	NC (12.025 to NC)	NC (4.994 to NC)	13.83 (10.021 to NC)	
Median (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.832 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3668		0.8436	
Hazard ratio (95% CI) vs Pd	-	0.70 (0.33 to 1.52)		1.11 (0.39 to 3.13)	
P-value	-	0.3692		0.8437	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	30 (19.9)	34 (22.4)	0.9244
Number (%) of patients censored	1 (50.0)	1 (50.0)	121 (80.1)	118 (77.6)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	2.10 (2.103 to NC)	1.91 (1.906 to NC)	NC (4.665 to NC)	14.75 (2.234 to NC)	
Median (95% CI)	NC (2.103 to NC)	NC (1.906 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (2.103 to NC)	NC (1.906 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.7606	
Hazard ratio (95% CI) vs Pd	-	1.41 (0.08 to 23.57)		1.08 (0.66 to 1.76)	
P-value	-	0.8092		0.7610	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_impl_prmab_de_i_t_x.rtf (08APR2021 14:56)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	54 (35.8)	59 (38.8)	0.9785
Number (%) of patients censored	2 (100.0)	1 (50.0)	97 (64.2)	93 (61.2)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	0.99 (0.986 to NC)	3.19 (1.938 to 5.421)	2.20 (1.906 to 3.844)	
Median (95% CI)	NC (NC to NC)	NC (0.986 to NC)	NC (11.598 to NC)	NC (9.988 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.6757	
Hazard ratio (95% CI) vs Pd	-			1.08 (0.75 to 1.56)	
P-value	-	0.9990		0.6760	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	12 (7.9)	18 (11.8)	0.9899
Number (%) of patients censored	2 (100.0)	1 (50.0)	139 (92.1)	134 (88.2)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	5.09 (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.3665	
Hazard ratio (95% CI) vs Pd	-			1.40 (0.67 to 2.90)	
P-value	-	0.9991		0.3687	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	22 (14.6)	20 (13.2)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	129 (85.4)	132 (86.8)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (12.255 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.5212	
Hazard ratio (95% CI) vs Pd	-			0.82 (0.45 to 1.50)	
P-value	-			0.5211	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (17.4)	30 (25.4)	11 (28.9)	5 (13.9)	0.0549
Number (%) of patients censored	95 (82.6)	88 (74.6)	27 (71.1)	31 (86.1)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (5.585 to NC)	7.98 (1.906 to NC)	3.02 (1.117 to NC)	NC (2.037 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2294		0.1183	
Hazard ratio (95% CI) vs Pd	-	1.41 (0.80 to 2.49)		0.44 (0.15 to 1.27)	
P-value	-	0.2317		0.1288	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (33.9)	49 (41.5)	15 (39.5)	11 (30.6)	0.3381
Number (%) of patients censored	76 (66.1)	69 (58.5)	23 (60.5)	25 (69.4)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	2.83 (1.938 to 5.487)	1.97 (1.281 to 3.844)	4.73 (1.117 to 12.057)	2.86 (1.840 to NC)	
Median (95% CI)	NC (11.598 to NC)	NC (8.312 to NC)	13.34 (7.458 to NC)	NC (8.246 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.339 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3609		0.6150	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.80 to 1.85)		0.82 (0.37 to 1.79)	
P-value	-	0.3617		0.6156	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (8.7)	15 (12.7)	2 (5.3)	4 (11.1)	0.6156
Number (%) of patients censored	105 (91.3)	103 (87.3)	36 (94.7)	32 (88.9)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.466 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.598 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4778		0.3471	
Hazard ratio (95% CI) vs Pd	-	1.34 (0.60 to 2.97)		2.21 (0.40 to 12.09)	
P-value	-	0.4793		0.3597	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (14.8)	14 (11.9)	5 (13.2)	6 (16.7)	0.2775
Number (%) of patients censored	98 (85.2)	104 (88.1)	33 (86.8)	30 (83.3)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (9.922 to NC)	NC (13.832 to NC)	15.08 (5.651 to NC)	12.25 (2.858 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (12.255 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2961		0.4791	
Hazard ratio (95% CI) vs Pd	-	0.69 (0.34 to 1.40)		1.54 (0.46 to 5.10)	
P-value	-	0.2989		0.4823	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (19.4)	34 (23.1)	3 (33.3)	1 (14.3)	0.3190
Number (%) of patients censored	116 (80.6)	113 (76.9)	6 (66.7)	6 (85.7)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (5.191 to NC)	14.75 (2.168 to NC)	1.25 (0.986 to NC)	NC (2.037 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (2.037 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5879		0.3443	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.70 to 1.90)		0.35 (0.04 to 3.39)	
P-value	-	0.5882		0.3658	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	52 (36.1)	57 (38.8)	2 (22.2)	3 (42.9)	0.3828
Number (%) of patients censored	92 (63.9)	90 (61.2)	7 (77.8)	4 (57.1)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	3.19 (1.938 to 5.421)	2.17 (1.906 to 3.844)	NC (1.906 to NC)	1.97 (0.986 to NC)	
Median (95% CI)	NC (11.598 to NC)	NC (9.988 to NC)	NC (1.906 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.322 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7779		0.3967	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.72 to 1.54)		2.13 (0.36 to 12.77)	
P-value	-	0.7780		0.4078	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (6.9)	19 (12.9)	2 (22.2)	0 (0.0)	0.9856
Number (%) of patients censored	134 (93.1)	128 (87.1)	7 (77.8)	7 (100.0)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.598 to NC)	NC (1.018 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.018 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1555		0.2165	
Hazard ratio (95% CI) vs Pd	-	1.73 (0.80 to 3.72)			
P-value	-	0.1608		0.9978	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (14.6)	17 (11.6)	1 (11.1)	3 (42.9)	0.1030
Number (%) of patients censored	123 (85.4)	130 (88.4)	8 (88.9)	4 (57.1)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	15.08 (9.922 to NC)	NC (13.832 to NC)	NC (1.906 to NC)	5.32 (3.548 to NC)	
Median (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (1.906 to NC)	NC (3.548 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.298 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2724		0.1738	
Hazard ratio (95% CI) vs Pd	-	0.70 (0.37 to 1.33)		4.27 (0.44 to 41.45)	
P-value	-	0.2749		0.2110	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (18.2)	19 (20.4)	15 (23.1)	16 (26.2)	0.8387
Number (%) of patients censored	72 (81.8)	74 (79.6)	50 (76.9)	45 (73.8)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (4.074 to NC)	NC (2.891 to NC)	6.67 (1.906 to NC)	14.75 (1.873 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.752 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7089		0.9732	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.58 to 2.21)		1.01 (0.50 to 2.05)	
P-value	-	0.7099		0.9732	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (39.8)	34 (36.6)	19 (29.2)	26 (42.6)	0.2137
Number (%) of patients censored	53 (60.2)	59 (63.4)	46 (70.8)	35 (57.4)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	2.83 (1.938 to 7.458)	2.86 (2.004 to 7.754)	3.75 (1.741 to NC)	1.91 (1.051 to 3.450)	
Median (95% CI)	13.34 (10.251 to NC)	NC (9.988 to NC)	NC (NC to NC)	NC (4.238 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7116		0.2041	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.57 to 1.47)		1.46 (0.81 to 2.65)	
P-value	-	0.7115		0.2068	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (5.7)	9 (9.7)	7 (10.8)	10 (16.4)	0.7716
Number (%) of patients censored	83 (94.3)	84 (90.3)	58 (89.2)	51 (83.6)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.598 to NC)	NC (NC to NC)	NC (6.637 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3656		0.5350	
Hazard ratio (95% CI) vs Pd	-	1.65 (0.55 to 4.92)		1.36 (0.52 to 3.57)	
P-value	-	0.3706		0.5366	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Financial difficulties
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (17.0)	10 (10.8)	7 (10.8)	10 (16.4)	0.2347
Number (%) of patients censored	73 (83.0)	83 (89.2)	58 (89.2)	51 (83.6)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	15.08 (6.472 to NC)	NC (12.255 to NC)	NC (9.626 to NC)	NC (7.129 to NC)	
Median (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2125		0.5910	
Hazard ratio (95% CI) vs Pd	-	0.60 (0.27 to 1.35)		1.30 (0.50 to 3.42)	
P-value	-	0.2173		0.5921	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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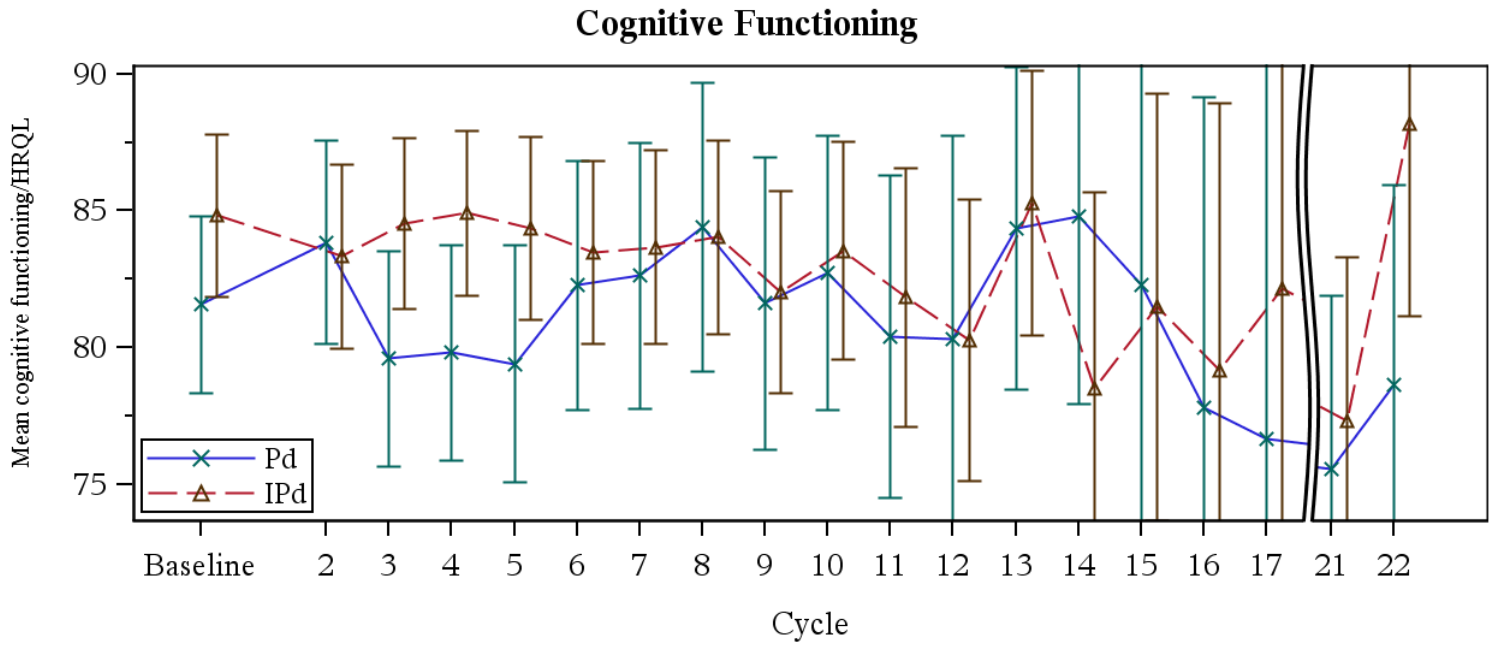
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Cognitive functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-C30 - Mean and 95% CI for cognitive functioning score over time (LOCF) - ITT population



A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Cognitive functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-C30 - Time to first improvement by 15 pt in cognitive functioning (LOCF) - ITT population

First improvement 15 points Cognitive functioning (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	57 (37.3)	55 (35.7)
Number (%) of patients censored	96 (62.7)	99 (64.3)
Kaplan-Meier estimates of cognitive functioning in months		
25% quantile (95% CI)	1.15 (1.018 to 2.168)	1.97 (1.216 to 2.990)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4271
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.86 (0.59 to 1.25)
P-value	-	0.4265
Probability (95% CI)[c]		
2 Months	0.31 (0.236 to 0.385)	0.25 (0.185 to 0.323)
4 Months	0.37 (0.289 to 0.446)	0.33 (0.260 to 0.410)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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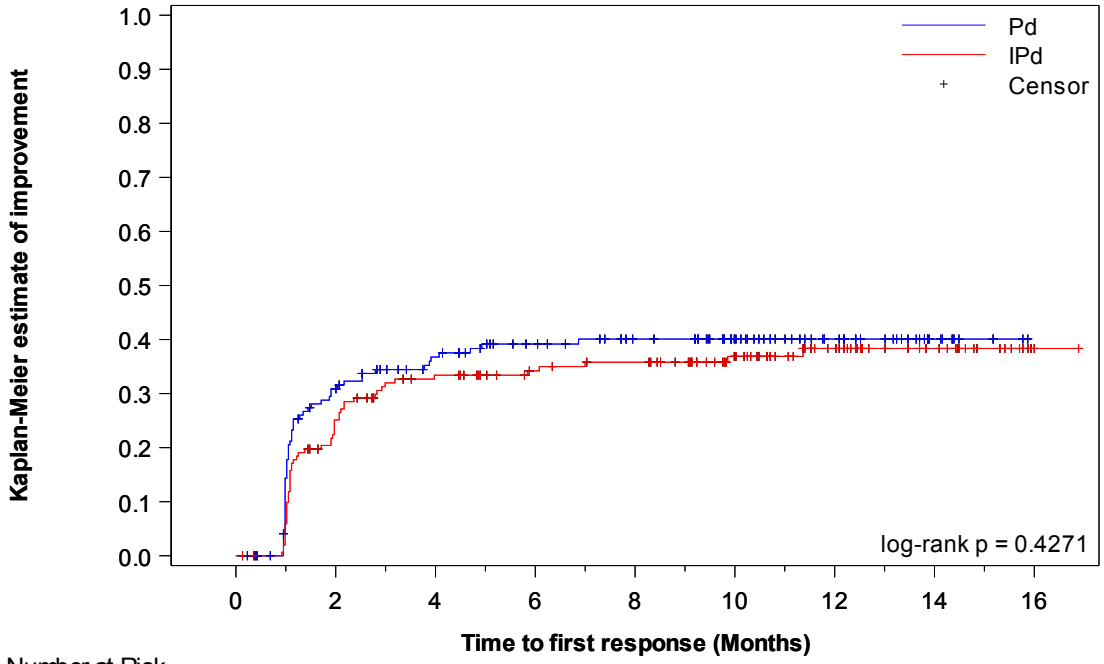
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Cognitive functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-C30 - Time to first improvement by 15 pt in cognitive functioning - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Cognitive functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-C30 - Time to first deterioration by 15 pt in cognitive functioning (LOCF) - ITT population

First deterioration 15 points Cognitive functioning (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	80 (52.3)	86 (55.8)
Number (%) of patients censored	73 (47.7)	68 (44.2)
Kaplan-Meier estimates of cognitive functioning in months		
25% quantile (95% CI)	2.07 (1.873 to 2.793)	1.97 (1.413 to 2.825)
Median (95% CI)	6.05 (3.811 to 10.546)	5.68 (3.778 to 9.659)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9989
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.00 (0.74 to 1.36)
P-value	-	1.0000
Probability (95% CI)[c]		
2 Months	0.77 (0.688 to 0.827)	0.75 (0.671 to 0.810)
4 Months	0.58 (0.489 to 0.653)	0.57 (0.484 to 0.644)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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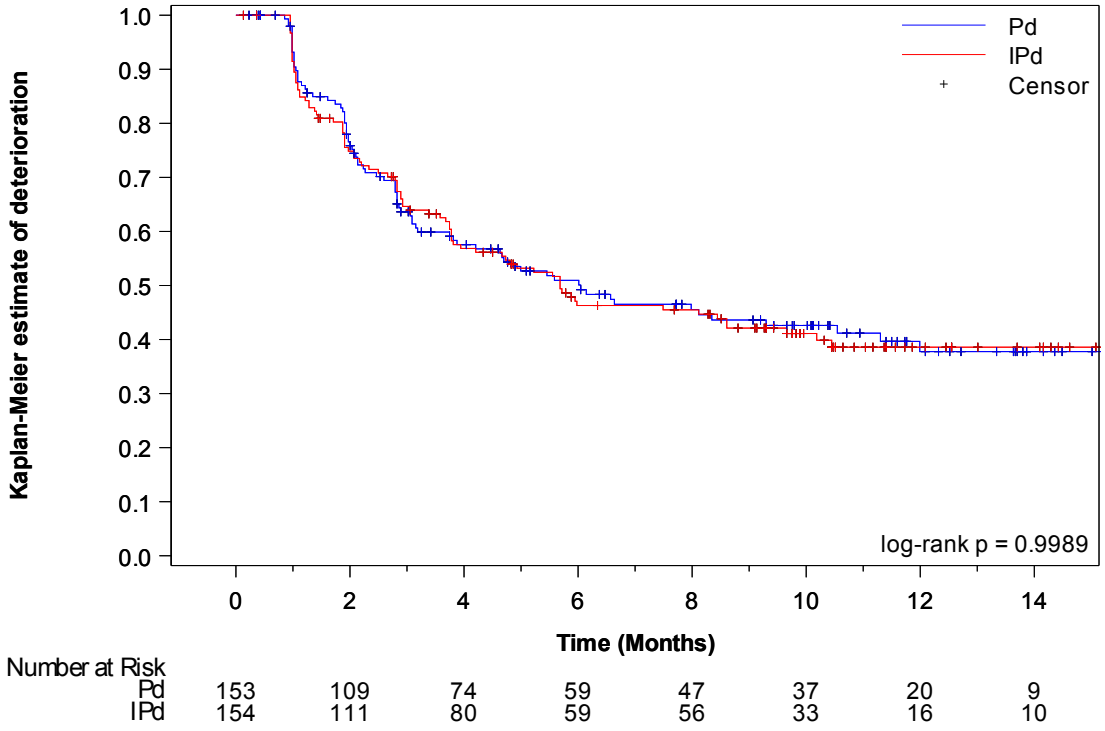
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Cognitive functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-C30 - Time to first deterioration by 15 pt in cognitive functioning - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_det15l_de_i_f_x.rtf (08APR2021 15:31)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Cognitive functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in cognitive functioning (LOCF) - ITT population

First permanent improvement 15 points Cognitive functioning (%)	Pd (N=153)	IPd (N=154)
Number (%) of events	23 (15.0)	23 (14.9)
Number (%) of patients censored	130 (85.0)	131 (85.1)
Kaplan-Meier estimates of cognitive functioning in months		
25% quantile (95% CI)	NC (10.645 to NC)	NC (11.138 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6955
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.89 (0.50 to 1.59)
P-value	-	0.6951
Probability (95% CI)[c]		
2 Months	0.11 (0.066 to 0.166)	0.05 (0.025 to 0.096)
4 Months	0.12 (0.071 to 0.175)	0.07 (0.039 to 0.122)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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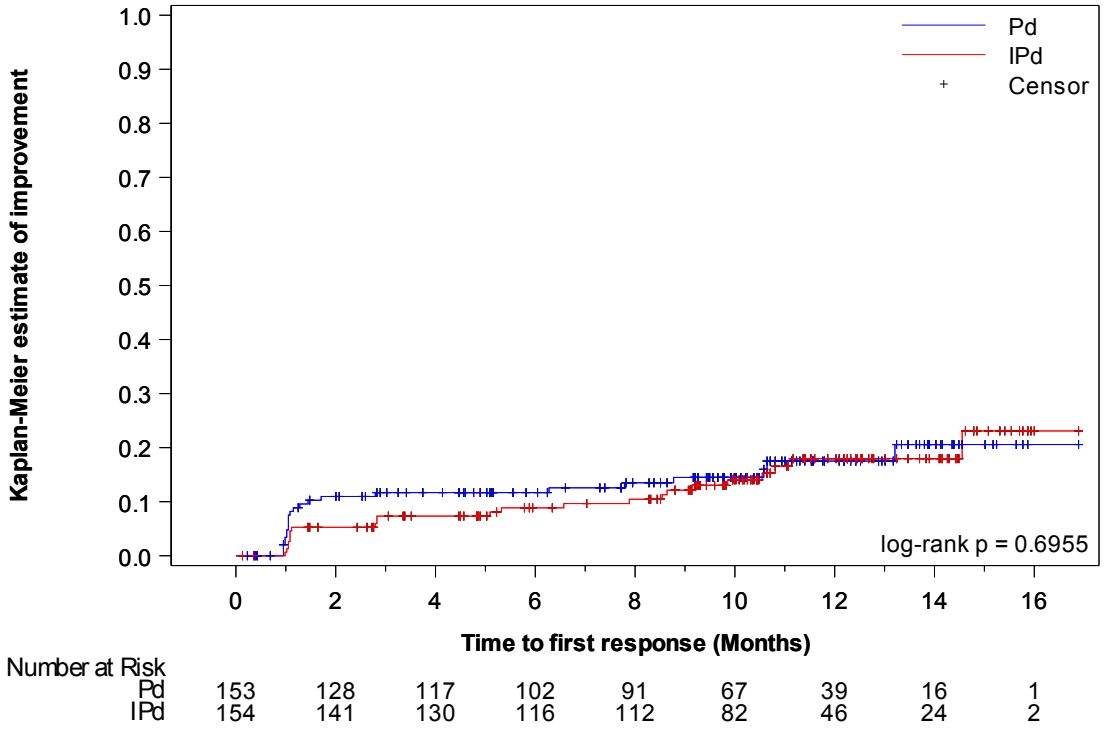
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Cognitive functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-C30 - Time until permanent improvement by 15 pt in cognitive functioning - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Cognitive functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in cognitive functioning (LOCF) - ITT population

First permanent deterioration 15 points Cognitive functioning (%)	Pd (N=153)	IPd (N=154)
Number (%) of events	37 (24.2)	37 (24.0)
Number (%) of patients censored	116 (75.8)	117 (76.0)
Kaplan-Meier estimates of cognitive functioning in months		
25% quantile (95% CI)	9.53 (4.830 to NC)	9.33 (7.097 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6958
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.91 (0.58 to 1.44)
P-value	-	0.6955
Probability (95% CI)[c]		
2 Months	0.93 (0.876 to 0.962)	0.92 (0.865 to 0.954)
4 Months	0.86 (0.789 to 0.907)	0.87 (0.799 to 0.911)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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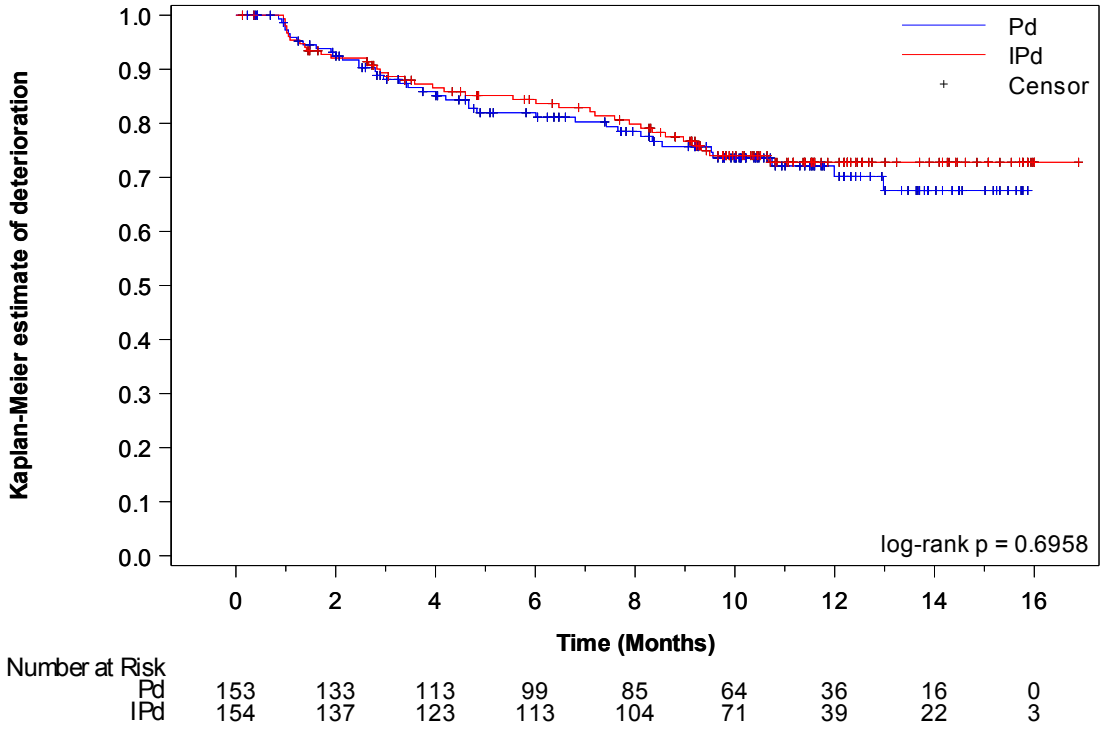
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Cognitive functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-C30 - Time until permanent deterioration by 15 pt in cognitive functioning - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_det15pl_de_i_f_x.rtf (08APR2021 15:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (38.6)	19 (35.2)	20 (37.0)	22 (32.4)	10 (34.5)	14 (43.8)	0.8505
Number (%) of patients censored	43 (61.4)	35 (64.8)	34 (63.0)	46 (67.6)	19 (65.5)	18 (56.3)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	1.13 (0.986 to 2.168)	1.71 (1.018 to 11.368)	1.51 (0.986 to 4.074)	2.79 (1.084 to NC)	1.12 (0.986 to NC)	2.12 (1.117 to 3.975)	
Median (95% CI)	NC (3.910 to NC)	NC (11.368 to NC)	NC (3.877 to NC)	NC (NC to NC)	NC (1.281 to NC)	NC (2.366 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5492		0.4737		0.8937	
Hazard ratio (95% CI) vs Pd	-	0.84 (0.46 to 1.50)		0.80 (0.44 to 1.47)		1.06 (0.47 to 2.39)	
P-value	-	0.5497		0.4746		0.8942	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (45.7)	23 (42.6)	31 (57.4)	41 (60.3)	17 (58.6)	22 (68.8)	0.7352
Number (%) of patients censored	38 (54.3)	31 (57.4)	23 (42.6)	27 (39.7)	12 (41.4)	10 (31.3)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	2.14 (1.906 to 2.825)	2.20 (1.117 to 5.552)	2.60 (1.610 to 3.877)	1.91 (1.084 to 2.891)	1.08 (0.986 to 2.037)	1.89 (1.018 to 2.924)	
Median (95% CI)	11.30 (2.858 to NC)	NC (3.778 to NC)	6.05 (3.745 to 10.546)	4.93 (3.055 to 9.659)	3.06 (1.347 to 8.115)	3.94 (1.971 to 8.608)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.298 to NC)	NC (9.659 to NC)	NC (4.665 to NC)	NC (5.224 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6045		0.6526		0.7352	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.51 to 1.48)		1.11 (0.70 to 1.78)		0.90 (0.48 to 1.69)	
P-value	-	0.6048		0.6528		0.7353	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (21.4)	8 (14.8)	6 (11.1)	10 (14.7)	2 (6.9)	5 (15.6)	0.4131
Number (%) of patients censored	55 (78.6)	46 (85.2)	48 (88.9)	58 (85.3)	27 (93.1)	27 (84.4)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	NC (1.446 to NC)	NC (7.885 to NC)	NC (10.579 to NC)	NC (9.856 to NC)	NC (1.281 to NC)	NC (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.207 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2864		0.8186		0.4360	
Hazard ratio (95% CI) vs Pd	-	0.63 (0.27 to 1.49)		1.13 (0.41 to 3.12)		1.90 (0.37 to 9.83)	
P-value	-	0.2907		0.8187		0.4437	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (22.9)	15 (27.8)	13 (24.1)	17 (25.0)	8 (27.6)	5 (15.6)	0.2414
Number (%) of patients censored	54 (77.1)	39 (72.2)	41 (75.9)	51 (75.0)	21 (72.4)	27 (84.4)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	10.74 (4.008 to NC)	7.10 (2.891 to NC)	9.56 (3.745 to NC)	9.33 (4.600 to NC)	4.67 (0.986 to NC)	NC (2.661 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (NC to NC)	NC (4.665 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5473		0.9319		0.1227	
Hazard ratio (95% CI) vs Pd	-	1.24 (0.61 to 2.51)		0.97 (0.47 to 2.00)		0.42 (0.14 to 1.30)	
P-value	-	0.5481		0.9318		0.1340	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	41 (40.6)	35 (34.3)	16 (30.8)	20 (38.5)	0.3276
Number (%) of patients censored	60 (59.4)	67 (65.7)	36 (69.2)	32 (61.5)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.15 (1.018 to 2.037)	1.97 (1.150 to 5.848)	1.91 (0.986 to NC)	2.07 (1.084 to 6.998)	
Median (95% CI)	NC (3.910 to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.924 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2325		0.7508	
Hazard ratio (95% CI) vs Pd	-	0.76 (0.48 to 1.19)		1.11 (0.58 to 2.15)	
P-value	-	0.2340		0.7509	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (50.5)	56 (54.9)	29 (55.8)	30 (57.7)	0.6026
Number (%) of patients censored	50 (49.5)	46 (45.1)	23 (44.2)	22 (42.3)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.23 (1.906 to 2.825)	2.07 (1.708 to 2.825)	1.94 (1.018 to 2.891)	1.59 (1.018 to 3.581)	
Median (95% CI)	7.98 (3.811 to NC)	5.68 (3.745 to 10.448)	4.83 (2.136 to 11.992)	5.95 (3.581 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.637 to NC)	NC (8.608 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6947		0.7265	
Hazard ratio (95% CI) vs Pd	-	1.08 (0.74 to 1.58)		0.91 (0.55 to 1.52)	
P-value	-	0.6950		0.7260	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (18.8)	13 (12.7)	4 (7.7)	10 (19.2)	0.0408
Number (%) of patients censored	82 (81.2)	89 (87.3)	48 (92.3)	42 (80.8)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (7.786 to NC)	NC (10.809 to NC)	NC (13.207 to NC)	NC (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1213		0.1147	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.28 to 1.17)		2.47 (0.77 to 7.89)	
P-value	-	0.1260		0.1272	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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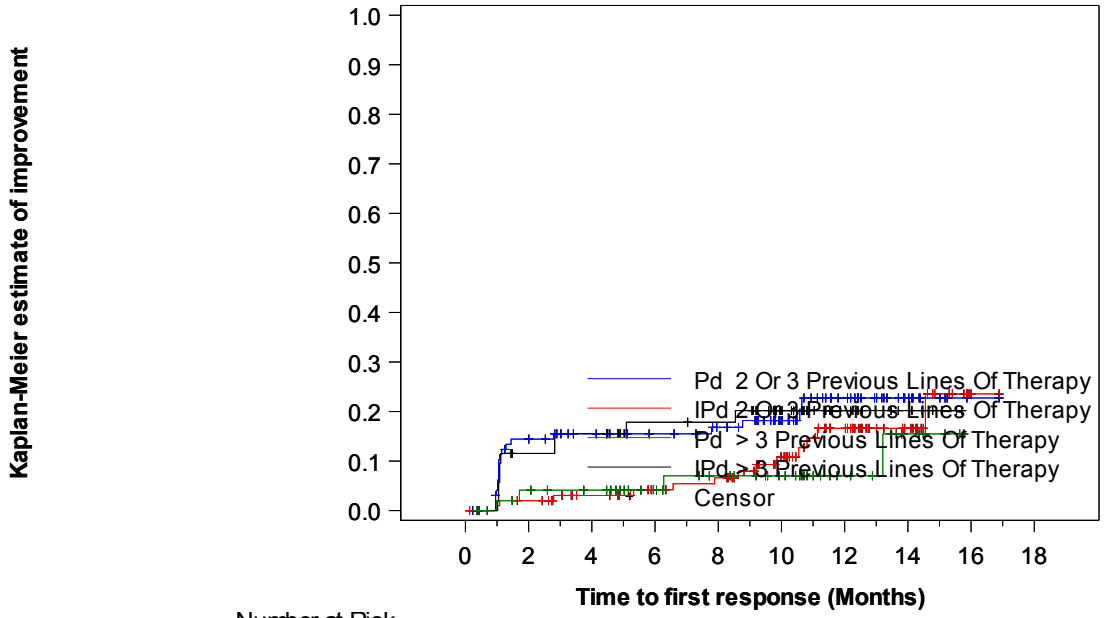
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to nb of prior lines (IRT) (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd 2 Or 3 Previous Lines Of Therapy	101	77	67	59	26	5	0
IPd 2 Or 3 Previous Lines Of Therapy	102	92	80	69	34	8	0
Pd > 3 Previous Lines Of Therapy	52	44	35	27	13	3	0
IPd > 3 Previous Lines Of Therapy	52	42	36	34	12	3	0

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_imppl_plne_de_i_f_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.7 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (23.8)	22 (21.6)	13 (25.0)	15 (28.8)	0.6552
Number (%) of patients censored	77 (76.2)	80 (78.4)	39 (75.0)	37 (71.2)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	9.56 (4.665 to NC)	NC (7.589 to NC)	8.54 (3.285 to NC)	9.23 (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5482		0.8841	
Hazard ratio (95% CI) vs Pd	-	0.84 (0.47 to 1.49)		1.06 (0.50 to 2.22)	
P-value	-	0.5482		0.8843	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (35.7)	32 (36.0)	32 (38.6)	23 (35.4)	0.7058
Number (%) of patients censored	45 (64.3)	57 (64.0)	51 (61.4)	42 (64.6)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.71 (1.018 to 4.698)	1.97 (1.084 to 6.078)	1.12 (0.986 to 2.530)	1.97 (1.051 to 9.856)	
Median (95% CI)	NC (4.928 to NC)	NC (11.368 to NC)	NC (3.778 to NC)	NC (9.856 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7682		0.4497	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.55 to 1.56)		0.81 (0.48 to 1.39)	
P-value	-	0.7683		0.4505	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_impl_sex_de_i_t_x.rtf (08APR2021 14:38)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (48.6)	55 (61.8)	46 (55.4)	31 (47.7)	0.0452
Number (%) of patients censored	36 (51.4)	34 (38.2)	37 (44.6)	34 (52.3)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.14 (1.906 to 2.891)	1.91 (1.051 to 2.793)	1.97 (1.084 to 2.825)	2.33 (1.281 to 4.665)	
Median (95% CI)	10.55 (3.088 to NC)	3.94 (2.891 to 5.979)	5.59 (3.088 to 8.345)	8.61 (4.665 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (9.659 to NC)	NC (9.298 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1553		0.1425	
Hazard ratio (95% CI) vs Pd	-	1.36 (0.89 to 2.09)		0.71 (0.45 to 1.12)	
P-value	-	0.1569		0.1444	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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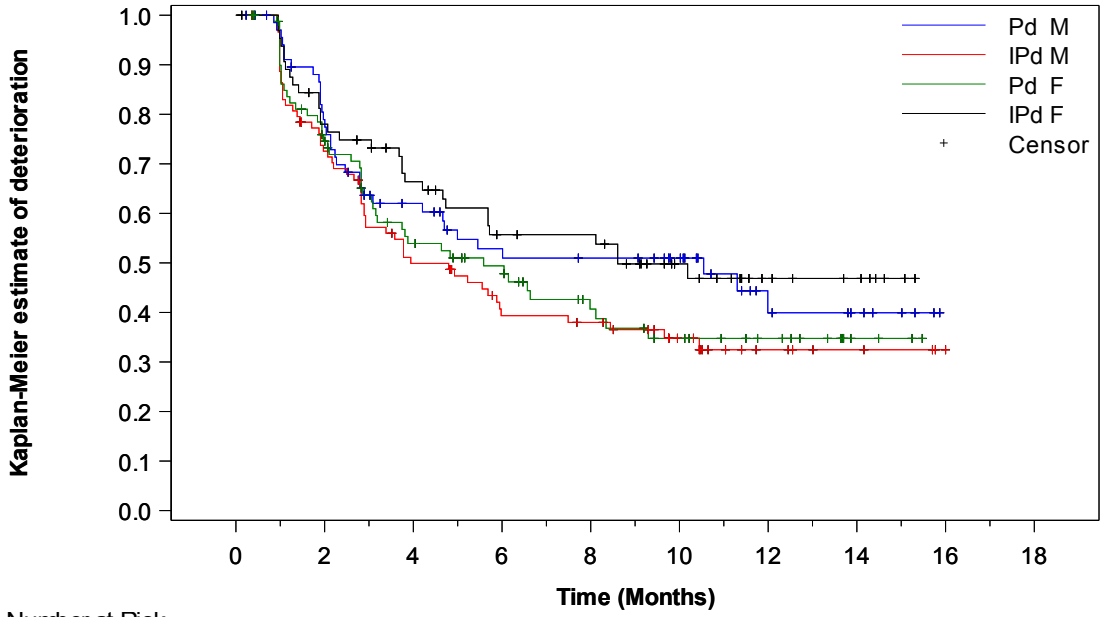
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to gender (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd M	70	40	28	26	9	4	0
IPd M	89	48	29	24	7	3	0
Pd F	83	46	31	19	11	2	0
IPd F	65	46	30	24	9	2	0

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (12.9)	13 (14.6)	14 (16.9)	10 (15.4)	0.5585
Number (%) of patients censored	61 (87.1)	76 (85.4)	69 (83.1)	55 (84.6)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (10.579 to NC)	NC (8.641 to NC)	NC (1.446 to NC)	NC (10.546 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8969		0.5250	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.45 to 2.48)		0.77 (0.34 to 1.73)	
P-value	-	0.8974		0.5262	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.7 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (22.9)	25 (28.1)	21 (25.3)	12 (18.5)	0.1642
Number (%) of patients censored	54 (77.1)	64 (71.9)	62 (74.7)	53 (81.5)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	11.99 (4.665 to NC)	7.20 (3.581 to NC)	8.54 (3.745 to NC)	NC (8.608 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.977 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5583		0.1656	
Hazard ratio (95% CI) vs Pd	-	1.21 (0.64 to 2.26)		0.61 (0.30 to 1.24)	
P-value	-	0.5588		0.1699	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (36.5)	43 (36.4)	10 (52.6)	11 (45.8)	0.9156
Number (%) of patients censored	80 (63.5)	75 (63.6)	9 (47.4)	13 (54.2)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.35 (1.018 to 2.530)	2.07 (1.150 to 3.975)	1.12 (0.953 to 2.037)	1.17 (0.986 to 2.168)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	4.07 (1.117 to NC)	NC (1.248 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.074 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5544		0.6715	
Hazard ratio (95% CI) vs Pd	-	0.88 (0.58 to 1.34)		0.83 (0.35 to 1.96)	
P-value	-	0.5545		0.6719	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	68 (54.0)	65 (55.1)	10 (52.6)	17 (70.8)	0.2729
Number (%) of patients censored	58 (46.0)	53 (44.9)	9 (47.4)	7 (29.2)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.00 (1.741 to 2.793)	1.91 (1.216 to 2.891)	3.09 (1.018 to 4.994)	2.33 (0.986 to 3.384)	
Median (95% CI)	6.01 (3.088 to 10.546)	5.72 (3.778 to 10.448)	5.59 (3.088 to NC)	4.80 (2.661 to 8.444)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.585 to NC)	NC (4.928 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7254		0.2488	
Hazard ratio (95% CI) vs Pd	-	0.94 (0.67 to 1.32)		1.58 (0.72 to 3.46)	
P-value	-	0.7254		0.2529	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (12.7)	20 (16.9)	6 (31.6)	3 (12.5)	0.0825
Number (%) of patients censored	110 (87.3)	98 (83.1)	13 (68.4)	21 (87.5)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (13.207 to NC)	14.55 (10.546 to NC)	6.28 (0.953 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.275 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5773		0.0955	
Hazard ratio (95% CI) vs Pd	-	1.21 (0.62 to 2.33)		0.32 (0.08 to 1.31)	
P-value	-	0.5778		0.1126	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (25.4)	25 (21.2)	5 (26.3)	9 (37.5)	0.2560
Number (%) of patients censored	94 (74.6)	93 (78.8)	14 (73.7)	15 (62.5)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	9.53 (4.008 to NC)	NC (8.115 to NC)	7.66 (1.051 to NC)	7.10 (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.655 to NC)	NC (7.195 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2558		0.4130	
Hazard ratio (95% CI) vs Pd	-	0.74 (0.44 to 1.25)		1.57 (0.53 to 4.70)	
P-value	-	0.2576		0.4170	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	1 (25.0)	50 (37.3)	49 (37.7)	0.6254
Number (%) of patients censored	2 (66.7)	3 (75.0)	84 (62.7)	81 (62.3)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (1.018 to NC)	1.15 (1.018 to 2.530)	1.97 (1.117 to 2.924)	
Median (95% CI)	NC (1.281 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6949		0.6868	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.04 to 9.30)		0.92 (0.62 to 1.37)	
P-value	-	0.6985		0.6867	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_impl_ethn_de_i_t_x.rtf (08APR2021 14:38)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	2 (50.0)	72 (53.7)	75 (57.7)	0.8004
Number (%) of patients censored	2 (66.7)	2 (50.0)	62 (46.3)	55 (42.3)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.27 (2.267 to NC)	1.76 (1.018 to NC)	2.04 (1.873 to 2.793)	1.97 (1.380 to 2.891)	
Median (95% CI)	NC (2.267 to NC)	NC (1.018 to NC)	5.45 (3.187 to 10.546)	5.68 (3.778 to 8.608)	
75% quantile (95% CI)	NC (2.267 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9835		0.9396	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.09 to 10.98)		1.01 (0.73 to 1.40)	
P-value	-	0.9834		0.9396	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	1 (25.0)	20 (14.9)	19 (14.6)	0.4605
Number (%) of patients censored	2 (66.7)	3 (75.0)	114 (85.1)	111 (85.4)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (10.546 to NC)	NC (10.645 to NC)	NC (14.554 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (10.546 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (10.546 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.6811	
Hazard ratio (95% CI) vs Pd	-			0.88 (0.47 to 1.64)	
P-value	-	0.9985		0.6809	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (25.0)	34 (25.4)	31 (23.8)	0.9846
Number (%) of patients censored	3 (100.0)	3 (75.0)	100 (74.6)	99 (76.2)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (3.055 to NC)	9.53 (4.665 to NC)	9.49 (7.195 to NC)	
Median (95% CI)	NC (NC to NC)	NC (3.055 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (3.055 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.5381	
Hazard ratio (95% CI) vs Pd	-			0.86 (0.53 to 1.40)	
P-value	-	0.9985		0.5383	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_detpl_ethn_de_i_t_x.rtf (08APR2021 14:38)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	22 (28.9)	14 (25.5)	7 (35.0)	11 (39.3)	2 (40.0)	5 (71.4)	7 (46.7)	8 (38.1)	19 (51.4)	17 (39.5)	0.6234
Number (%) of patients censored	54 (71.1)	41 (74.5)	13 (65.0)	17 (60.7)	3 (60.0)	2 (28.6)	8 (53.3)	13 (61.9)	18 (48.6)	26 (60.5)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	2.17 (1.051 to NC)	2.37 (1.051 to NC)	0.99 (0.953 to NC)	1.05 (0.986 to NC)	4.93 (1.906 to NC)	1.25 (1.150 to 1.938)	1.15 (0.986 to 4.074)	1.97 (0.986 to NC)	1.03 (0.986 to 1.511)	2.83 (1.906 to 9.856)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (1.084 to NC)	NC (1.906 to NC)	1.94 (1.150 to NC)	NC (1.117 to NC)	NC (1.971 to NC)	2.53 (1.150 to NC)	NC (3.975 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.906 to NC)	NC (1.708 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_impl_greg_de_i_t_x.rtf (08APR2021 14:38)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.5264		0.9797		0.2551		0.7004		0.0811	
Hazard ratio (95% CI) vs Pd	-	0.81 (0.41 to 1.57)		0.99 (0.38 to 2.55)		2.52 (0.49 to 13.07)		0.82 (0.30 to 2.26)		0.56 (0.29 to 1.08)	
P-value	-	0.5272		0.9797		0.2715		0.7009		0.0853	
Improvement probability (95% CI)[b]											
2 Months	0.240 (0.148 to 0.343)	0.204 (0.109 to 0.320)	0.316 (0.129 to 0.522)	0.321 (0.161 to 0.493)	0.200 (0.008 to 0.582)	0.571 (0.172 to 0.837)	0.333 (0.122 to 0.564)	0.289 (0.118 to 0.487)	0.448 (0.282 to 0.601)	0.193 (0.091 to 0.324)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_impl_greg_de_i_t_x.rtf (08APR2021 14:38)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Number (%) of events	32 (42.1)	26 (47.3)	16 (80.0)	13 (46.4)	4 (80.0)	5 (71.4)	9 (60.0)	16 (76.2)	19 (51.4)	26 (60.5)	0.2764
Number (%) of patients censored	44 (57.9)	29 (52.7)	4 (20.0)	15 (53.6)	1 (20.0)	2 (28.6)	6 (40.0)	5 (23.8)	18 (48.6)	17 (39.5)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	2.23 (1.906 to 3.187)	2.20 (1.216 to 4.731)	1.22 (0.986 to 2.825)	2.04 (0.953 to 5.684)	2.60 (2.267 to 3.877)	1.02 (0.953 to 2.924)	1.91 (1.018 to 4.830)	2.33 (0.986 to 2.924)	2.00 (1.248 to 2.825)	1.38 (0.986 to 2.891)	
Median (95% CI)	9.30 (3.745 to NC)	9.66 (3.943 to NC)	3.81 (1.216 to 8.345)	NC (3.055 to NC)	2.79 (2.267 to NC)	2.92 (0.953 to NC)	4.99 (1.084 to NC)	4.21 (2.333 to 8.444)	5.45 (2.464 to NC)	3.81 (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	8.34 (3.811 to NC)	NC (NC to NC)	3.88 (2.267 to NC)	NC (2.793 to NC)	NC (4.994 to NC)	8.61 (4.205 to NC)	NC (11.302 to NC)	NC (8.608 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.8498		0.0498		0.8914		0.3208		0.6806	
Hazard ratio (95% CI) vs Pd	-	1.05 (0.63 to 1.76)		0.49 (0.23 to 1.01)		0.91 (0.24 to 3.42)		1.51 (0.66 to 3.43)		1.13 (0.63 to 2.05)	
P-value	-	0.8494		0.0547		0.8915		0.3242		0.6808	
Deterioration probability (95% CI)[b]											
2 Months	0.788 (0.673 to 0.866)	0.795 (0.661 to 0.881)	0.632 (0.379 to 0.804)	0.750 (0.546 to 0.872)	1.000 (1.000 to 1.000)	0.714 (0.258 to 0.920)	0.733 (0.436 to 0.891)	0.754 (0.506 to 0.890)	0.775 (0.600 to 0.881)	0.689 (0.525 to 0.806)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_detl_greg_de_i_t_x.rtf (08APR2021 14:38)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	11 (14.5)	4 (7.3)	2 (10.0)	8 (28.6)	1 (20.0)	0 (0.0)	3 (20.0)	1 (4.8)	6 (16.2)	10 (23.3)	0.2198
Number (%) of patients censored	65 (85.5)	51 (92.7)	18 (90.0)	20 (71.4)	4 (80.0)	7 (100.0)	12 (80.0)	20 (95.2)	31 (83.8)	33 (76.7)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (6.275 to NC)	NC (NC to NC)	NC (0.953 to NC)	7.89 (1.051 to NC)	10.58 (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (1.084 to NC)	NC (1.446 to NC)	11.14 (8.542 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.546 to NC)	10.58 (NC to NC)	NC (NC to NC)	NC (8.772 to NC)	NC (NC to NC)	NC (13.207 to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	10.58 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.1763		0.1387		0.1573		0.1627		0.8824	
Hazard ratio (95% CI) vs Pd	-	0.46 (0.15 to 1.45)		3.05 (0.65 to 14.39)				0.23 (0.02 to 2.20)		1.08 (0.39 to 2.99)	
P-value	-	0.1870		0.1593		1.0000		0.2015		0.8825	
Improvement probability (95% CI)[b]											
2 Months	0.113 (0.053 to 0.198)	0.056 (0.015 to 0.139)	0.053 (0.004 to 0.214)	0.107 (0.027 to 0.251)			0.133 (0.022 to 0.346)	0.048 (0.003 to 0.197)	0.140 (0.051 to 0.272)	0.024 (0.002 to 0.108)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_imppl_greg_de_i_t_x.rtf (08APR2021 14:39)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Number (%) of events	13 (17.1)	9 (16.4)	8 (40.0)	4 (14.3)	0 (0.0)	2 (28.6)	5 (33.3)	9 (42.9)	11 (29.7)	13 (30.2)	0.5078
Number (%) of patients censored	63 (82.9)	46 (83.6)	12 (60.0)	24 (85.7)	5 (100.0)	5 (71.4)	10 (66.7)	12 (57.1)	26 (70.3)	30 (69.8)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (4.665 to NC)	NC (4.172 to NC)	4.67 (0.986 to 11.992)	NC (6.472 to NC)	NC (NC to NC)	3.06 (2.628 to NC)	7.43 (1.051 to NC)	6.55 (1.906 to 8.969)	9.53 (2.004 to NC)	8.61 (1.708 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.665 to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.628 to NC)	NC (4.830 to NC)	NC (6.012 to NC)	NC (9.561 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.8398		0.0528		0.2137		0.5386		0.7049	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.39 to 2.15)		0.32 (0.10 to 1.08)				1.41 (0.47 to 4.20)		0.86 (0.38 to 1.92)	
P-value	-	0.8399		0.0657		0.9978		0.5405		0.7052	
Deterioration probability (95% CI)[b]											
2 Months	0.944 (0.857 to 0.979)	0.907 (0.792 to 0.960)	0.895 (0.641 to 0.973)	0.964 (0.772 to 0.995)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.933 (0.613 to 0.990)	0.950 (0.695 to 0.993)	0.916 (0.761 to 0.972)	0.880 (0.736 to 0.948)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_detpl_greg_de_i_t_x.rtf (08APR2021 14:38)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (30.9)	24 (31.2)	27 (48.2)	31 (40.3)	0.5023
Number (%) of patients censored	67 (69.1)	53 (68.8)	29 (51.8)	46 (59.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.91 (1.084 to 6.867)	2.07 (1.216 to NC)	1.02 (0.986 to 1.150)	1.97 (1.084 to 2.990)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.150 to NC)	NC (5.848 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7584		0.2273	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.54 to 1.57)		0.73 (0.43 to 1.22)	
P-value	-	0.7593		0.2292	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_impl_rreg_de_i_t_x.rtf (08APR2021 14:38)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (46.4)	39 (50.6)	35 (62.5)	47 (61.0)	0.7412
Number (%) of patients censored	52 (53.6)	38 (49.4)	21 (37.5)	30 (39.0)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.23 (1.906 to 2.891)	2.07 (1.216 to 2.924)	1.91 (1.084 to 2.825)	1.91 (1.117 to 2.825)	
Median (95% CI)	7.98 (3.187 to NC)	5.98 (3.745 to NC)	4.99 (2.825 to 10.546)	5.55 (3.384 to 8.608)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	11.99 (8.345 to NC)	NC (8.608 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9084		0.7501	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.67 to 1.57)		0.93 (0.60 to 1.44)	
P-value	-	0.9084		0.7502	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_detl_rreg_de_i_t_x.rtf (08APR2021 14:38)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (14.4)	7 (9.1)	9 (16.1)	16 (20.8)	0.2079
Number (%) of patients censored	83 (85.6)	70 (90.9)	47 (83.9)	61 (79.2)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (10.579 to NC)	NC (NC to NC)	13.21 (8.772 to NC)	14.55 (8.641 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2075		0.6813	
Hazard ratio (95% CI) vs Pd	-	0.56 (0.23 to 1.39)		1.19 (0.52 to 2.69)	
P-value	-	0.2139		0.6817	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (17.5)	17 (22.1)	20 (35.7)	20 (26.0)	0.1952
Number (%) of patients censored	80 (82.5)	60 (77.9)	36 (64.3)	57 (74.0)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (6.012 to NC)	NC (3.943 to NC)	6.80 (2.825 to 10.743)	9.23 (6.472 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.561 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5899		0.1482	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.61 to 2.36)		0.64 (0.34 to 1.18)	
P-value	-	0.5904		0.1517	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	47 (34.3)	48 (34.8)	10 (62.5)	7 (43.8)	0.5157
Number (%) of patients censored	90 (65.7)	90 (65.2)	6 (37.5)	9 (56.3)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.45 (1.051 to 3.877)	2.17 (1.380 to 5.848)	0.99 (0.953 to 1.281)	1.02 (0.986 to 1.971)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	1.87 (0.986 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.873 to NC)	NC (1.971 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6428		0.3859	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.61 to 1.36)		0.65 (0.25 to 1.72)	
P-value	-	0.6423		0.3894	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	71 (51.8)	79 (57.2)	9 (56.3)	7 (43.8)	0.4674
Number (%) of patients censored	66 (48.2)	59 (42.8)	7 (43.8)	9 (56.3)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.10 (1.906 to 2.825)	2.07 (1.446 to 2.825)	1.08 (0.986 to 2.891)	1.05 (0.953 to 10.185)	
Median (95% CI)	6.14 (3.811 to 11.302)	5.68 (3.778 to 8.608)	4.83 (1.018 to NC)	10.18 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.830 to NC)	NC (10.185 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7334		0.5545	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.77 to 1.46)		0.74 (0.27 to 2.00)	
P-value	-	0.7337		0.5560	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (13.1)	19 (13.8)	5 (31.3)	4 (25.0)	0.6428
Number (%) of patients censored	119 (86.9)	119 (86.2)	11 (68.8)	12 (75.0)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (13.207 to NC)	NC (14.554 to NC)	1.28 (0.953 to NC)	11.14 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.084 to NC)	NC (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.138 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8259		0.5404	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.49 to 1.77)		0.66 (0.17 to 2.52)	
P-value	-	0.8256		0.5428	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (23.4)	32 (23.2)	5 (31.3)	5 (31.3)	0.8362
Number (%) of patients censored	105 (76.6)	106 (76.8)	11 (68.8)	11 (68.8)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	9.56 (6.012 to NC)	10.68 (7.589 to NC)	4.83 (0.986 to NC)	3.06 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.793 to NC)	NC (2.661 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6676		0.9300	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.55 to 1.47)		1.06 (0.31 to 3.66)	
P-value	-	0.6671		0.9300	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (41.2)	22 (34.4)	18 (32.1)	18 (34.0)	16 (37.2)	14 (41.2)	0.7765
Number (%) of patients censored	30 (58.8)	42 (65.6)	38 (67.9)	35 (66.0)	27 (62.8)	20 (58.8)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	1.05 (0.986 to 2.530)	1.97 (1.084 to 9.856)	2.53 (1.051 to NC)	2.07 (1.084 to NC)	1.08 (0.986 to 3.910)	1.97 (0.986 to 2.924)	
Median (95% CI)	NC (2.037 to NC)	NC (9.856 to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.446 to NC)	NC (2.168 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3701		0.9572		0.8740	
Hazard ratio (95% CI) vs Pd	-	0.76 (0.42 to 1.38)		1.02 (0.53 to 1.96)		0.94 (0.46 to 1.93)	
P-value	-	0.3716		0.9572		0.8742	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (60.8)	33 (51.6)	26 (46.4)	31 (58.5)	22 (51.2)	19 (55.9)	0.2870
Number (%) of patients censored	20 (39.2)	31 (48.4)	30 (53.6)	22 (41.5)	21 (48.8)	15 (44.1)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	1.97 (1.150 to 2.825)	1.91 (1.084 to 3.384)	2.79 (1.248 to 3.745)	2.07 (1.216 to 2.793)	1.91 (1.084 to 2.825)	2.66 (1.018 to 4.928)	
Median (95% CI)	4.83 (2.793 to NC)	5.95 (3.680 to NC)	9.30 (3.187 to NC)	5.68 (2.793 to 10.448)	4.67 (2.103 to 11.302)	7.49 (3.745 to NC)	
75% quantile (95% CI)	NC (10.546 to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.659 to NC)	11.99 (6.144 to NC)	NC (8.115 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4970		0.2249		0.4457	
Hazard ratio (95% CI) vs Pd	-	0.84 (0.52 to 1.38)		1.38 (0.82 to 2.33)		0.79 (0.42 to 1.46)	
P-value	-	0.4975		0.2269		0.4465	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (21.6)	10 (15.6)	7 (12.5)	6 (11.3)	4 (9.3)	7 (20.6)	0.3897
Number (%) of patients censored	40 (78.4)	54 (84.4)	49 (87.5)	47 (88.7)	39 (90.7)	27 (79.4)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	13.21 (2.793 to NC)	14.55 (9.856 to NC)	NC (10.579 to NC)	NC (10.809 to NC)	NC (1.446 to NC)	NC (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4435		0.6484		0.2691	
Hazard ratio (95% CI) vs Pd	-	0.72 (0.30 to 1.69)		0.78 (0.26 to 2.31)		1.97 (0.58 to 6.76)	
P-value	-	0.4456		0.6490		0.2783	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (27.5)	14 (21.9)	10 (17.9)	12 (22.6)	13 (30.2)	9 (26.5)	0.5942
Number (%) of patients censored	37 (72.5)	50 (78.1)	46 (82.1)	41 (77.4)	30 (69.8)	25 (73.5)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	10.74 (3.450 to NC)	NC (6.012 to NC)	NC (4.008 to NC)	9.23 (4.600 to NC)	4.67 (1.347 to 9.528)	8.61 (1.051 to NC)	
Median (95% CI)	NC (12.977 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	11.99 (7.655 to NC)	NC (9.495 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5996		0.6492		0.3225	
Hazard ratio (95% CI) vs Pd	-	0.82 (0.39 to 1.72)		1.21 (0.52 to 2.81)		0.65 (0.28 to 1.53)	
P-value	-	0.6002		0.6497		0.3261	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (41.9)	14 (35.9)	37 (37.8)	36 (36.4)	7 (29.2)	5 (31.3)	0.9605
Number (%) of patients censored	18 (58.1)	25 (64.1)	61 (62.2)	63 (63.6)	17 (70.8)	11 (68.8)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	1.05 (0.986 to 3.877)	2.07 (1.018 to NC)	1.15 (1.018 to 3.778)	1.97 (1.117 to 2.825)	1.45 (0.986 to NC)	2.92 (0.953 to NC)	
Median (95% CI)	NC (2.037 to NC)	NC (5.848 to NC)	NC (6.867 to NC)	NC (11.368 to NC)	NC (1.446 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5378		0.5849		0.8555	
Hazard ratio (95% CI) vs Pd	-	0.79 (0.37 to 1.68)		0.88 (0.56 to 1.39)		0.90 (0.28 to 2.86)	
P-value	-	0.5387		0.5844		0.8556	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (64.5)	19 (48.7)	52 (53.1)	58 (58.6)	8 (33.3)	9 (56.3)	0.2435
Number (%) of patients censored	11 (35.5)	20 (51.3)	46 (46.9)	41 (41.4)	16 (66.7)	7 (43.8)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	1.94 (1.018 to 2.234)	2.83 (1.018 to 4.731)	2.27 (1.840 to 3.088)	1.91 (1.216 to 2.793)	2.46 (0.986 to 6.045)	1.12 (0.986 to 3.943)	
Median (95% CI)	3.88 (1.971 to NC)	NC (3.680 to NC)	6.57 (3.811 to 11.992)	5.55 (3.581 to 9.659)	6.05 (2.464 to NC)	3.94 (1.051 to NC)	
75% quantile (95% CI)	NC (5.585 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.045 to NC)	8.61 (3.943 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1746		0.4525		0.4746	
Hazard ratio (95% CI) vs Pd	-	0.65 (0.35 to 1.22)		1.15 (0.79 to 1.68)		1.42 (0.54 to 3.69)	
P-value	-	0.1780		0.4531		0.4767	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (25.8)	6 (15.4)	11 (11.2)	15 (15.2)	4 (16.7)	2 (12.5)	0.4226
Number (%) of patients censored	23 (74.2)	33 (84.6)	87 (88.8)	84 (84.8)	20 (83.3)	14 (87.5)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	13.21 (1.051 to NC)	14.55 (9.199 to NC)	NC (NC to NC)	NC (10.546 to NC)	NC (1.018 to NC)	NC (0.986 to NC)	
Median (95% CI)	NC (13.207 to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2315		0.5684		0.7005	
Hazard ratio (95% CI) vs Pd	-	0.53 (0.18 to 1.53)		1.25 (0.58 to 2.73)		0.72 (0.13 to 3.92)	
P-value	-	0.2392		0.5692		0.7018	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (19.4)	5 (12.8)	26 (26.5)	26 (26.3)	5 (20.8)	6 (37.5)	0.7016
Number (%) of patients censored	25 (80.6)	34 (87.2)	72 (73.5)	73 (73.7)	19 (79.2)	10 (62.5)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	12.98 (1.906 to NC)	NC (7.195 to NC)	8.54 (4.665 to NC)	8.97 (5.552 to NC)	3.29 (1.084 to NC)	2.83 (0.986 to 9.495)	
Median (95% CI)	NC (12.977 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.825 to NC)	9.49 (2.661 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.495 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5179		0.7521		0.5466	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.21 to 2.22)		0.92 (0.53 to 1.58)		1.44 (0.44 to 4.74)	
P-value	-	0.5205		0.7519		0.5488	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (34.8)	3 (21.4)	38 (40.0)	45 (38.1)	0.5070
Number (%) of patients censored	15 (65.2)	11 (78.6)	57 (60.0)	73 (61.9)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.28 (0.953 to NC)	NC (0.986 to NC)	1.51 (1.018 to 2.793)	2.07 (1.117 to 2.990)	
Median (95% CI)	NC (1.281 to NC)	NC (1.938 to NC)	NC (4.698 to NC)	NC (11.368 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3530		0.5334	
Hazard ratio (95% CI) vs Pd	-	0.54 (0.14 to 2.03)		0.87 (0.57 to 1.34)	
P-value	-	0.3606		0.5337	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (39.1)	6 (42.9)	53 (55.8)	68 (57.6)	0.6901
Number (%) of patients censored	14 (60.9)	8 (57.1)	42 (44.2)	50 (42.4)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.89 (1.150 to 6.571)	2.07 (0.953 to 3.778)	1.91 (1.084 to 2.267)	2.07 (1.446 to 2.891)	
Median (95% CI)	6.57 (2.891 to NC)	3.78 (1.051 to NC)	5.45 (2.825 to 10.546)	5.68 (3.745 to 8.608)	
75% quantile (95% CI)	NC (6.571 to NC)	NC (3.778 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6755		0.8451	
Hazard ratio (95% CI) vs Pd	-	1.25 (0.44 to 3.52)		0.96 (0.67 to 1.38)	
P-value	-	0.6761		0.8448	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (21.7)	1 (7.1)	13 (13.7)	19 (16.1)	0.2997
Number (%) of patients censored	18 (78.3)	13 (92.9)	82 (86.3)	99 (83.9)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (0.953 to NC)	NC (1.084 to NC)	NC (10.579 to NC)	NC (10.546 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2299		0.9084	
Hazard ratio (95% CI) vs Pd	-	0.29 (0.03 to 2.49)		1.04 (0.51 to 2.11)	
P-value	-	0.2595		0.9087	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (21.7)	4 (28.6)	23 (24.2)	28 (23.7)	0.5680
Number (%) of patients censored	18 (78.3)	10 (71.4)	72 (75.8)	90 (76.3)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	8.11 (2.825 to NC)	2.83 (1.018 to NC)	10.74 (3.450 to NC)	9.49 (7.195 to NC)	
Median (95% CI)	NC (8.115 to NC)	NC (2.661 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6061		0.6624	
Hazard ratio (95% CI) vs Pd	-	1.41 (0.38 to 5.27)		0.88 (0.51 to 1.54)	
P-value	-	0.6078		0.6626	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (33.3)	5 (20.8)	32 (41.0)	42 (40.8)	0.4535
Number (%) of patients censored	24 (66.7)	19 (79.2)	46 (59.0)	61 (59.2)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.28 (1.018 to NC)	NC (0.986 to NC)	1.15 (0.986 to 2.793)	1.97 (1.084 to 2.990)	
Median (95% CI)	NC (1.873 to NC)	NC (NC to NC)	NC (3.910 to NC)	NC (9.856 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2948		0.6134	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.20 to 1.64)		0.89 (0.56 to 1.41)	
P-value	-	0.3010		0.6136	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (47.2)	12 (50.0)	42 (53.8)	59 (57.3)	0.8937
Number (%) of patients censored	19 (52.8)	12 (50.0)	36 (46.2)	44 (42.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.83 (1.248 to 3.154)	2.07 (0.953 to 3.778)	1.94 (1.216 to 2.464)	1.91 (1.281 to 2.891)	
Median (95% CI)	3.81 (2.825 to NC)	4.21 (2.070 to NC)	6.14 (2.858 to NC)	5.88 (3.680 to 10.185)	
75% quantile (95% CI)	NC (6.571 to NC)	NC (4.205 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8450		0.9266	
Hazard ratio (95% CI) vs Pd	-	1.08 (0.51 to 2.26)		1.02 (0.69 to 1.51)	
P-value	-	0.8450		0.9267	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (16.7)	2 (8.3)	12 (15.4)	17 (16.5)	0.4542
Number (%) of patients censored	30 (83.3)	22 (91.7)	66 (84.6)	86 (83.5)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (1.150 to NC)	NC (1.084 to NC)	NC (8.772 to NC)	14.55 (10.546 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3415		0.8408	
Hazard ratio (95% CI) vs Pd	-	0.47 (0.09 to 2.32)		0.93 (0.44 to 1.95)	
P-value	-	0.3530		0.8409	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (22.2)	7 (29.2)	19 (24.4)	24 (23.3)	0.4673
Number (%) of patients censored	28 (77.8)	17 (70.8)	59 (75.6)	79 (76.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	9.56 (2.793 to NC)	7.59 (1.018 to NC)	10.74 (3.450 to NC)	10.68 (8.115 to NC)	
Median (95% CI)	NC (9.561 to NC)	NC (7.589 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5511		0.6396	
Hazard ratio (95% CI) vs Pd	-	1.36 (0.49 to 3.76)		0.87 (0.47 to 1.58)	
P-value	-	0.5527		0.6399	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (40.0)	28 (33.7)	21 (33.3)	27 (38.0)	0.6328
Number (%) of patients censored	54 (60.0)	55 (66.3)	42 (66.7)	44 (62.0)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.15 (1.018 to 2.530)	1.97 (1.084 to 11.368)	1.28 (0.986 to 4.698)	2.07 (1.150 to 5.848)	
Median (95% CI)	NC (3.910 to NC)	NC (11.368 to NC)	NC (4.698 to NC)	NC (6.998 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3690		0.9068	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.49 to 1.31)		0.97 (0.55 to 1.71)	
P-value	-	0.3700		0.9066	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (48.9)	40 (48.2)	36 (57.1)	46 (64.8)	0.8313
Number (%) of patients censored	46 (51.1)	43 (51.8)	27 (42.9)	25 (35.2)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.23 (1.840 to 2.858)	2.50 (1.413 to 3.778)	1.94 (1.018 to 2.793)	1.87 (1.084 to 2.825)	
Median (95% CI)	8.34 (3.154 to NC)	8.11 (4.665 to NC)	4.83 (2.793 to 8.115)	4.21 (2.924 to 8.444)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.637 to NC)	NC (8.608 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8629		0.8863	
Hazard ratio (95% CI) vs Pd	-	0.96 (0.63 to 1.48)		1.03 (0.67 to 1.60)	
P-value	-	0.8630		0.8865	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (20.0)	15 (18.1)	5 (7.9)	8 (11.3)	0.6477
Number (%) of patients censored	72 (80.0)	68 (81.9)	58 (92.1)	63 (88.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (1.708 to NC)	14.55 (8.542 to NC)	NC (10.645 to NC)	NC (10.809 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (13.207 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6404		0.8501	
Hazard ratio (95% CI) vs Pd	-	0.85 (0.43 to 1.69)		1.11 (0.36 to 3.43)	
P-value	-	0.6408		0.8502	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (24.4)	21 (25.3)	15 (23.8)	16 (22.5)	0.5280
Number (%) of patients censored	68 (75.6)	62 (74.7)	48 (76.2)	55 (77.5)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	9.53 (4.008 to NC)	8.34 (4.172 to NC)	9.56 (4.205 to NC)	NC (4.600 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9031		0.4709	
Hazard ratio (95% CI) vs Pd	-	1.04 (0.57 to 1.89)		0.77 (0.38 to 1.56)	
P-value	-	0.9030		0.4721	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	57 (37.7)	54 (35.5)	0.9840
Number (%) of patients censored	2 (100.0)	1 (50.0)	94 (62.3)	98 (64.5)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (NC to NC)	1.08 (1.084 to NC)	1.15 (1.018 to 2.037)	2.07 (1.216 to 3.187)	
Median (95% CI)	NC (NC to NC)	NC (1.084 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.084 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.3582	
Hazard ratio (95% CI) vs Pd	-			0.84 (0.58 to 1.22)	
P-value	-	0.9990		0.3588	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	79 (52.3)	85 (55.9)	0.7645
Number (%) of patients censored	1 (50.0)	1 (50.0)	72 (47.7)	67 (44.1)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.07 (2.070 to NC)	5.95 (5.947 to NC)	2.04 (1.873 to 2.793)	1.97 (1.380 to 2.825)	
Median (95% CI)	NC (2.070 to NC)	NC (5.947 to NC)	6.05 (3.811 to 10.546)	5.68 (3.778 to 9.659)	
75% quantile (95% CI)	NC (2.070 to NC)	NC (5.947 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.8727	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		1.03 (0.75 to 1.39)	
P-value	-	0.8092		0.8728	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	23 (15.2)	23 (15.1)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	128 (84.8)	129 (84.9)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.645 to NC)	NC (11.138 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.6677	
Hazard ratio (95% CI) vs Pd	-			0.88 (0.49 to 1.57)	
P-value	-			0.6670	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	37 (24.5)	37 (24.3)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	114 (75.5)	115 (75.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	9.53 (4.830 to NC)	9.33 (7.097 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.6799	
Hazard ratio (95% CI) vs Pd	-			0.91 (0.58 to 1.43)	
P-value	-			0.6796	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (38.6)	37 (35.6)	15 (36.6)	14 (42.4)	0.7433
Number (%) of patients censored	62 (61.4)	67 (64.4)	26 (63.4)	19 (57.6)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.15 (1.018 to 2.168)	1.97 (1.084 to 5.848)	1.45 (0.986 to 4.928)	1.97 (0.986 to 3.975)	
Median (95% CI)	NC (4.698 to NC)	NC (NC to NC)	NC (3.877 to NC)	NC (2.168 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3841		0.7767	
Hazard ratio (95% CI) vs Pd	-	0.82 (0.52 to 1.28)		1.11 (0.54 to 2.30)	
P-value	-	0.3848		0.7760	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_impl_semm_de_i_t_x.rtf (08APR2021 14:38)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	56 (55.4)	58 (55.8)	21 (51.2)	18 (54.5)	0.1541
Number (%) of patients censored	45 (44.6)	46 (44.2)	20 (48.8)	15 (45.5)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.97 (1.216 to 2.825)	2.07 (1.413 to 2.891)	2.00 (1.150 to 3.088)	2.79 (1.084 to 3.811)	
Median (95% CI)	4.70 (3.055 to 9.298)	5.55 (3.778 to 10.185)	7.98 (2.793 to NC)	8.11 (2.924 to NC)	
75% quantile (95% CI)	NC (11.992 to NC)	NC (NC to NC)	NC (10.546 to NC)	NC (10.448 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6352		0.8774	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.63 to 1.32)		0.95 (0.51 to 1.79)	
P-value	-	0.6346		0.8776	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (16.8)	16 (15.4)	4 (9.8)	5 (15.2)	0.6880
Number (%) of patients censored	84 (83.2)	88 (84.6)	37 (90.2)	28 (84.8)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (10.579 to NC)	14.55 (10.546 to NC)	NC (1.446 to NC)	NC (1.117 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4978		0.5825	
Hazard ratio (95% CI) vs Pd	-	0.79 (0.40 to 1.56)		1.44 (0.39 to 5.38)	
P-value	-	0.4987		0.5846	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_imppl_semm_de_i_t_x.rtf (08APR2021 14:39)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (25.7)	25 (24.0)	10 (24.4)	5 (15.2)	0.1207
Number (%) of patients censored	75 (74.3)	79 (76.0)	31 (75.6)	28 (84.8)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	9.56 (4.008 to NC)	9.49 (7.097 to NC)	8.34 (2.464 to NC)	NC (3.943 to NC)	
Median (95% CI)	NC (12.977 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5729		0.2027	
Hazard ratio (95% CI) vs Pd	-	0.85 (0.49 to 1.48)		0.50 (0.17 to 1.48)	
P-value	-	0.5723		0.2115	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (39.0)	35 (34.3)	18 (34.6)	19 (37.3)	0.5748
Number (%) of patients censored	61 (61.0)	67 (65.7)	34 (65.4)	32 (62.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.15 (1.018 to 2.037)	2.02 (1.084 to 9.856)	1.45 (0.986 to 4.928)	2.17 (1.084 to 6.078)	
Median (95% CI)	NC (4.698 to NC)	NC (NC to NC)	NC (4.074 to NC)	NC (6.078 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2825		0.9582	
Hazard ratio (95% CI) vs Pd	-	0.78 (0.49 to 1.23)		0.98 (0.52 to 1.87)	
P-value	-	0.2838		0.9582	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	55 (55.0)	57 (55.9)	24 (46.2)	29 (56.9)	0.3144
Number (%) of patients censored	45 (45.0)	45 (44.1)	28 (53.8)	22 (43.1)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.97 (1.216 to 2.825)	2.02 (1.413 to 2.891)	2.27 (1.741 to 4.830)	1.91 (1.051 to 3.680)	
Median (95% CI)	5.59 (3.055 to 11.302)	5.55 (3.778 to 10.185)	8.34 (4.665 to NC)	5.88 (2.924 to NC)	
75% quantile (95% CI)	NC (11.992 to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.448 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7081		0.3433	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.64 to 1.35)		1.30 (0.76 to 2.23)	
P-value	-	0.7078		0.3451	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (17.0)	15 (14.7)	6 (11.5)	7 (13.7)	0.5949
Number (%) of patients censored	83 (83.0)	87 (85.3)	46 (88.5)	44 (86.3)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	13.21 (10.579 to NC)	14.55 (10.809 to NC)	NC (6.275 to NC)	NC (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4031		0.8570	
Hazard ratio (95% CI) vs Pd	-	0.74 (0.37 to 1.49)		1.11 (0.37 to 3.29)	
P-value	-	0.4048		0.8574	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_imppl_dghc_de_i_t_x.rtf (08APR2021 14:38)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (25.0)	24 (23.5)	11 (21.2)	13 (25.5)	0.6053
Number (%) of patients censored	75 (75.0)	78 (76.5)	41 (78.8)	38 (74.5)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	8.54 (3.745 to NC)	9.33 (6.472 to NC)	9.53 (4.665 to NC)	8.61 (2.825 to NC)	
Median (95% CI)	NC (12.977 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6012		0.8262	
Hazard ratio (95% CI) vs Pd	-	0.86 (0.49 to 1.51)		1.09 (0.49 to 2.44)	
P-value	-	0.6008		0.8267	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	4 (28.6)	56 (39.2)	51 (36.4)	0.3156
Number (%) of patients censored	9 (90.0)	10 (71.4)	87 (60.8)	89 (63.6)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (0.986 to NC)	1.91 (0.986 to NC)	1.15 (1.018 to 1.906)	2.07 (1.150 to 2.990)	
Median (95% CI)	NC (0.986 to NC)	NC (1.906 to NC)	NC (6.867 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3775		0.3545	
Hazard ratio (95% CI) vs Pd	-	2.59 (0.29 to 23.15)		0.84 (0.57 to 1.22)	
P-value	-	0.3953		0.3546	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (30.0)	7 (50.0)	77 (53.8)	79 (56.4)	0.8897
Number (%) of patients censored	7 (70.0)	7 (50.0)	66 (46.2)	61 (43.6)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.94 (0.920 to NC)	1.38 (0.986 to 8.608)	2.07 (1.873 to 2.793)	2.07 (1.446 to 2.891)	
Median (95% CI)	NC (0.920 to NC)	8.61 (1.084 to NC)	6.01 (3.811 to 10.546)	5.68 (3.778 to 8.608)	
75% quantile (95% CI)	NC (NC to NC)	NC (8.608 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6783		0.8905	
Hazard ratio (95% CI) vs Pd	-	1.33 (0.34 to 5.25)		1.02 (0.75 to 1.40)	
P-value	-	0.6793		0.8905	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_detl_mri_de_i_t_x.rtf (08APR2021 14:38)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	4 (28.6)	23 (16.1)	19 (13.6)	0.9888
Number (%) of patients censored	10 (100.0)	10 (71.4)	120 (83.9)	121 (86.4)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (NC to NC)	7.89 (1.084 to NC)	NC (10.645 to NC)	NC (11.138 to NC)	
Median (95% CI)	NC (NC to NC)	NC (7.885 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1972		0.3716	
Hazard ratio (95% CI) vs Pd	-			0.76 (0.41 to 1.39)	
P-value	-	0.9973		0.3734	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	4 (28.6)	36 (25.2)	33 (23.6)	0.5943
Number (%) of patients censored	9 (90.0)	10 (71.4)	107 (74.8)	107 (76.4)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (0.920 to NC)	8.61 (1.084 to NC)	9.53 (4.665 to NC)	9.49 (7.097 to NC)	
Median (95% CI)	NC (0.920 to NC)	NC (2.661 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5726		0.5970	
Hazard ratio (95% CI) vs Pd	-	1.88 (0.20 to 17.48)		0.88 (0.55 to 1.41)	
P-value	-	0.5786		0.5972	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (39.6)	30 (34.5)	18 (36.7)	24 (43.6)	0.4913
Number (%) of patients censored	58 (60.4)	57 (65.5)	31 (63.3)	31 (56.4)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.15 (1.018 to 2.793)	1.97 (1.084 to 9.856)	1.51 (0.986 to 2.530)	1.97 (1.051 to 3.187)	
Median (95% CI)	NC (4.698 to NC)	NC (NC to NC)	NC (2.168 to NC)	NC (3.187 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3326		0.9270	
Hazard ratio (95% CI) vs Pd	-	0.79 (0.49 to 1.27)		1.03 (0.56 to 1.90)	
P-value	-	0.3337		0.9271	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	47 (49.0)	50 (57.5)	31 (63.3)	32 (58.2)	0.1321
Number (%) of patients censored	49 (51.0)	37 (42.5)	18 (36.7)	23 (41.8)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.79 (1.938 to 3.088)	1.91 (1.216 to 2.891)	1.87 (1.018 to 2.037)	2.17 (1.117 to 3.745)	
Median (95% CI)	8.11 (3.877 to NC)	5.55 (3.581 to 10.185)	4.67 (1.938 to 6.571)	5.88 (3.745 to 10.448)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	11.99 (6.144 to NC)	NC (10.448 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3837		0.2377	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.80 to 1.78)		0.74 (0.45 to 1.22)	
P-value	-	0.3832		0.2394	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (19.8)	13 (14.9)	3 (6.1)	10 (18.2)	0.0522
Number (%) of patients censored	77 (80.2)	74 (85.1)	46 (93.9)	45 (81.8)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	13.21 (6.275 to NC)	NC (11.138 to NC)	NC (10.579 to NC)	NC (5.322 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2248		0.1018	
Hazard ratio (95% CI) vs Pd	-	0.65 (0.32 to 1.31)		2.80 (0.77 to 10.19)	
P-value	-	0.2284		0.1173	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (22.9)	22 (25.3)	15 (30.6)	12 (21.8)	0.2386
Number (%) of patients censored	74 (77.1)	65 (74.7)	34 (69.4)	43 (78.2)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	9.56 (6.012 to NC)	9.23 (4.600 to NC)	4.67 (2.464 to 11.992)	10.68 (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.743 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9166		0.1779	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.57 to 1.86)		0.60 (0.28 to 1.28)	
P-value	-	0.9166		0.1827	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	2 (100.0)	56 (37.1)	53 (34.9)	0.4084
Number (%) of patients censored	1 (50.0)	0 (0.0)	95 (62.9)	99 (65.1)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	1.91 (1.906 to 1.971)	1.15 (1.018 to 2.168)	2.07 (1.150 to 3.975)	
Median (95% CI)	NC (1.281 to NC)	1.94 (1.906 to 1.971)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	1.97 (1.906 to 1.971)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6949		0.3727	
Hazard ratio (95% CI) vs Pd	-	1.62 (0.14 to 18.31)		0.84 (0.58 to 1.23)	
P-value	-	0.6975		0.3720	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	2 (100.0)	79 (52.3)	84 (55.3)	0.6361
Number (%) of patients censored	1 (50.0)	0 (0.0)	72 (47.7)	68 (44.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.10 (2.103 to NC)	0.99 (0.986 to 10.448)	2.04 (1.873 to 2.793)	2.07 (1.413 to 2.825)	
Median (95% CI)	NC (2.103 to NC)	5.72 (0.986 to 10.448)	6.05 (3.811 to 10.546)	5.68 (3.778 to 9.659)	
75% quantile (95% CI)	NC (2.103 to NC)	10.45 (0.986 to 10.448)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.9574	
Hazard ratio (95% CI) vs Pd	-	1.41 (0.08 to 23.57)		1.01 (0.74 to 1.37)	
P-value	-	0.8092		0.9574	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	22 (14.6)	22 (14.5)	0.7939
Number (%) of patients censored	1 (50.0)	1 (50.0)	129 (85.4)	130 (85.5)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	5.09 (5.092 to NC)	NC (10.645 to NC)	NC (11.138 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.6879	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		0.89 (0.49 to 1.60)	
P-value	-	0.8092		0.6874	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	37 (24.5)	37 (24.3)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	114 (75.5)	115 (75.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	9.53 (4.830 to NC)	9.33 (7.097 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.7070	
Hazard ratio (95% CI) vs Pd	-			0.92 (0.58 to 1.45)	
P-value	-			0.7068	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (35.7)	44 (37.3)	16 (42.1)	11 (30.6)	0.3859
Number (%) of patients censored	74 (64.3)	74 (62.7)	22 (57.9)	25 (69.4)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.35 (1.018 to 2.793)	1.97 (1.084 to 2.924)	1.12 (0.986 to 3.877)	2.17 (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (11.368 to NC)	NC (1.906 to NC)	NC (3.975 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7896		0.2488	
Hazard ratio (95% CI) vs Pd	-	0.94 (0.62 to 1.44)		0.64 (0.30 to 1.38)	
P-value	-	0.7893		0.2527	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	61 (53.0)	63 (53.4)	19 (50.0)	23 (63.9)	0.2558
Number (%) of patients censored	54 (47.0)	55 (46.6)	19 (50.0)	13 (36.1)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.14 (1.906 to 2.825)	2.07 (1.446 to 2.891)	1.91 (1.018 to 3.088)	1.63 (1.018 to 2.924)	
Median (95% CI)	6.01 (3.745 to 9.298)	5.88 (3.943 to NC)	10.55 (2.037 to NC)	3.81 (2.497 to 8.115)	
75% quantile (95% CI)	NC (11.992 to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.947 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6384		0.2931	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.65 to 1.31)		1.39 (0.75 to 2.55)	
P-value	-	0.6379		0.2952	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (12.2)	21 (17.8)	9 (23.7)	2 (5.6)	0.0375
Number (%) of patients censored	101 (87.8)	97 (82.2)	29 (76.3)	34 (94.4)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (13.207 to NC)	14.55 (10.546 to NC)	10.58 (1.018 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4972		0.0299	
Hazard ratio (95% CI) vs Pd	-	1.26 (0.64 to 2.49)		0.21 (0.05 to 0.99)	
P-value	-	0.4981		0.0488	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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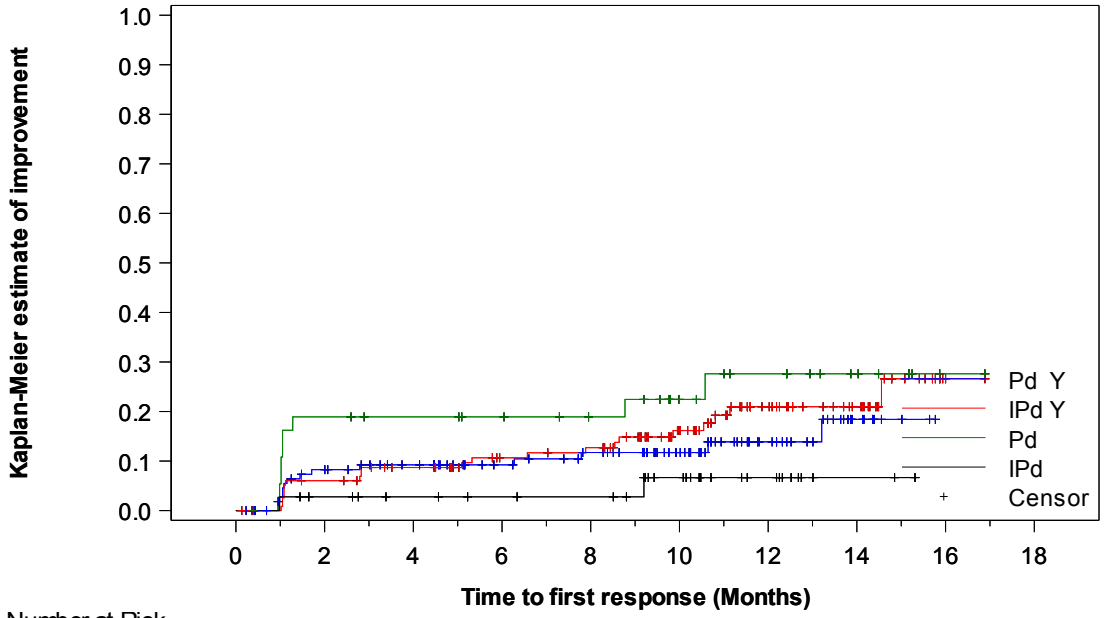
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to refractory to PI status (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd Y	115	93	76	64	27	3	0
IPd Y	118	103	88	78	36	10	0
Pd	38	28	26	22	12	5	0
IPd	36	31	28	25	10	1	0

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.7 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (24.3)	27 (22.9)	9 (23.7)	10 (27.8)	0.4630
Number (%) of patients censored	87 (75.7)	91 (77.1)	29 (76.3)	26 (72.2)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	9.56 (4.665 to NC)	10.68 (6.472 to NC)	9.53 (2.957 to NC)	8.34 (3.055 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.232 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4881		0.6928	
Hazard ratio (95% CI) vs Pd	-	0.83 (0.49 to 1.41)		1.20 (0.49 to 2.95)	
P-value	-	0.4888		0.6930	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	52 (36.1)	50 (34.0)	5 (55.6)	5 (71.4)	0.4624
Number (%) of patients censored	92 (63.9)	97 (66.0)	4 (44.4)	2 (28.6)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.28 (1.051 to 2.530)	2.10 (1.248 to 5.848)	0.99 (0.986 to 2.168)	1.02 (0.986 to 1.971)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	2.17 (0.986 to NC)	1.97 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.906 to NC)	NC (1.051 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3810		0.6790	
Hazard ratio (95% CI) vs Pd	-	0.84 (0.57 to 1.24)		1.30 (0.38 to 4.50)	
P-value	-	0.3816		0.6799	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	74 (51.4)	82 (55.8)	6 (66.7)	4 (57.1)	0.8027
Number (%) of patients censored	70 (48.6)	65 (44.2)	3 (33.3)	3 (42.9)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.07 (1.873 to 2.793)	2.07 (1.380 to 2.825)	1.91 (0.986 to 6.045)	1.45 (1.117 to 4.928)	
Median (95% CI)	6.01 (3.811 to 11.302)	5.68 (3.778 to 9.659)	6.05 (0.986 to NC)	4.93 (1.117 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.088 to NC)	NC (2.825 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8562		0.8058	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.75 to 1.41)		0.85 (0.24 to 3.03)	
P-value	-	0.8563		0.8060	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (14.6)	21 (14.3)	2 (22.2)	2 (28.6)	0.5142
Number (%) of patients censored	123 (85.4)	126 (85.7)	7 (77.8)	5 (71.4)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (10.645 to NC)	NC (11.138 to NC)	13.21 (10.579 to NC)	5.32 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.579 to NC)	NC (1.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.207 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5961		0.3012	
Hazard ratio (95% CI) vs Pd	-	0.85 (0.46 to 1.56)		3.34 (0.30 to 37.43)	
P-value	-	0.5965		0.3289	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (22.9)	37 (25.2)	4 (44.4)	0 (0.0)	0.9853
Number (%) of patients censored	111 (77.1)	110 (74.8)	5 (55.6)	7 (100.0)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	10.74 (4.830 to NC)	9.23 (6.472 to NC)	7.66 (3.450 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.450 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.528 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9978		0.0750	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.63 to 1.60)			
P-value	-	0.9978		0.9968	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (33.0)	29 (31.2)	28 (43.1)	26 (42.6)	0.9020
Number (%) of patients censored	59 (67.0)	64 (68.8)	37 (56.9)	35 (57.4)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.35 (1.051 to 4.698)	2.92 (1.938 to 11.368)	1.12 (0.986 to 2.037)	1.25 (1.018 to 2.366)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.037 to NC)	NC (2.793 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6103		0.5480	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.52 to 1.46)		0.85 (0.50 to 1.45)	
P-value	-	0.6095		0.5479	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (51.1)	54 (58.1)	35 (53.8)	32 (52.5)	0.4981
Number (%) of patients censored	43 (48.9)	39 (41.9)	30 (46.2)	29 (47.5)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.97 (1.248 to 2.793)	2.07 (1.380 to 2.924)	2.14 (1.741 to 3.088)	1.97 (1.084 to 2.924)	
Median (95% CI)	6.57 (3.055 to NC)	5.72 (3.778 to 9.659)	6.01 (3.088 to 11.992)	5.68 (3.581 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.448 to NC)	NC (10.546 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6030		0.6678	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.75 to 1.65)		0.90 (0.56 to 1.45)	
P-value	-	0.6042		0.6681	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (19.3)	11 (11.8)	6 (9.2)	12 (19.7)	0.0513
Number (%) of patients censored	71 (80.7)	82 (88.2)	59 (90.8)	49 (80.3)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (2.793 to NC)	14.55 (11.138 to NC)	NC (10.645 to NC)	NC (5.322 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1130		0.1951	
Hazard ratio (95% CI) vs Pd	-	0.55 (0.26 to 1.17)		1.89 (0.71 to 5.04)	
P-value	-	0.1185		0.2028	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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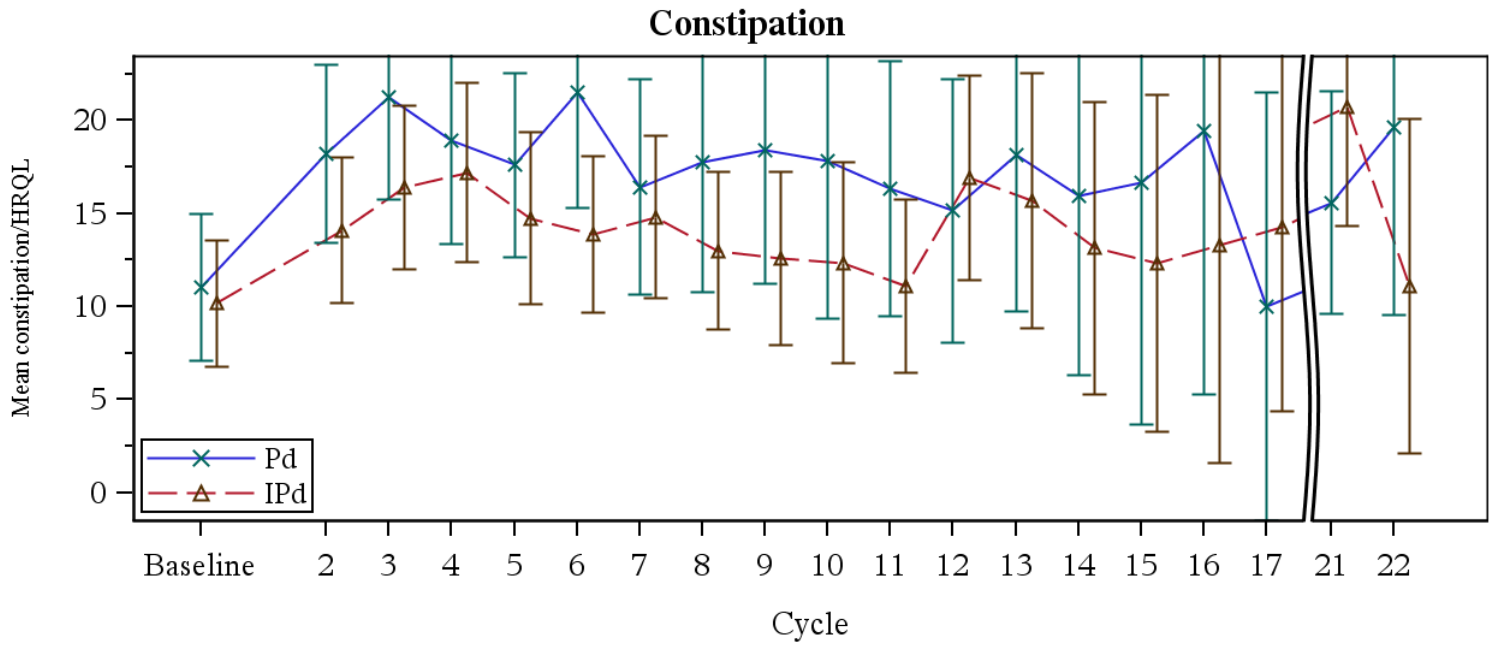
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Cognitive functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (26.1)	24 (25.8)	14 (21.5)	13 (21.3)	0.8285
Number (%) of patients censored	65 (73.9)	69 (74.2)	51 (78.5)	48 (78.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	8.34 (2.957 to NC)	8.61 (3.943 to NC)	9.53 (4.665 to NC)	NC (5.552 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8500		0.6466	
Hazard ratio (95% CI) vs Pd	-	0.95 (0.53 to 1.68)		0.84 (0.39 to 1.78)	
P-value	-	0.8499		0.6464	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_detpl_llen_de_i_t_x.rtf (08APR2021 14:38)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Constipation
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-C30 - Mean and 95% CI for constipation score over time (LOCF) - ITT population



#patients																			
Pd	142	128	116	104	89	79	71	62	58	56	51	44	33	23	16	12	10	77	39
IPd	144	142	136	126	113	108	99	95	90	81	78	65	51	38	27	20	14	61	24

A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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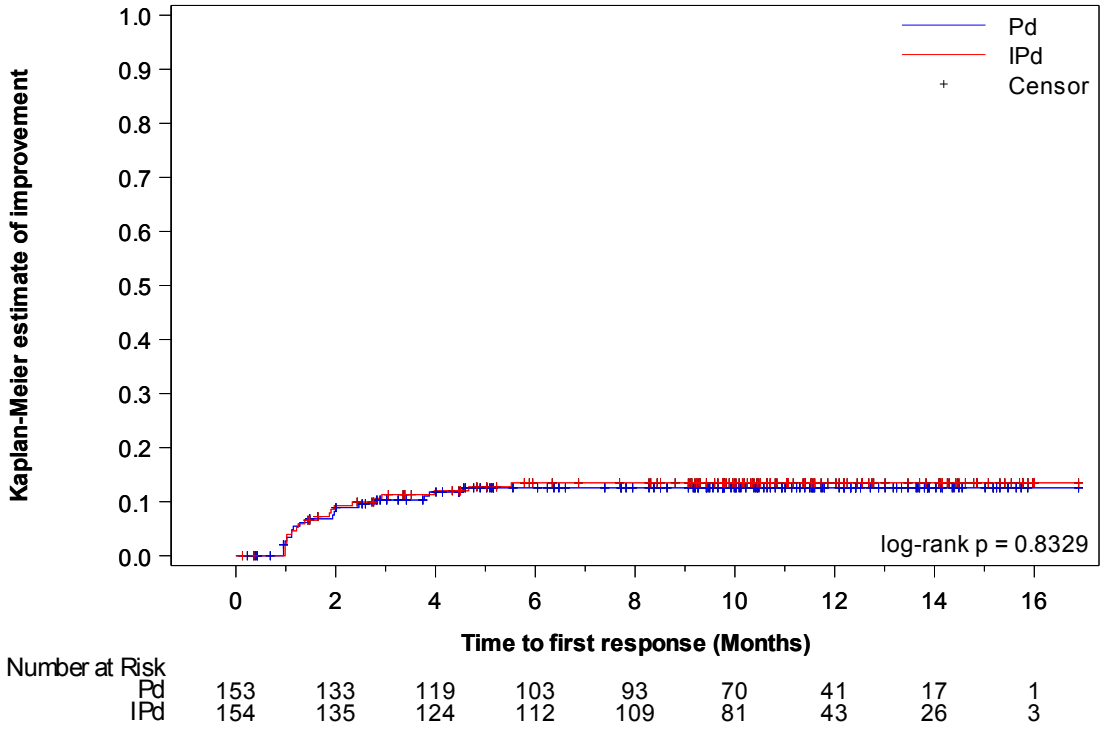
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Constipation
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-C30 - Time to first improvement by 15 pt in constipation (LOCF) - ITT population

First improvement 15 points Constipation (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	18 (11.8)	20 (13.0)
Number (%) of patients censored	135 (88.2)	134 (87.0)
Kaplan-Meier estimates of constipation in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8329
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.07 (0.57 to 2.03)
P-value	-	0.8331
Probability (95% CI)[c]		
2 Months	0.08 (0.045 to 0.134)	0.09 (0.053 to 0.145)
4 Months	0.12 (0.072 to 0.176)	0.12 (0.074 to 0.178)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_imp15l_de_i_t_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Constipation
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-C30 - Time to first improvement by 15 pt in constipation - Kaplan-Meier curve (LOCF) - ITT population



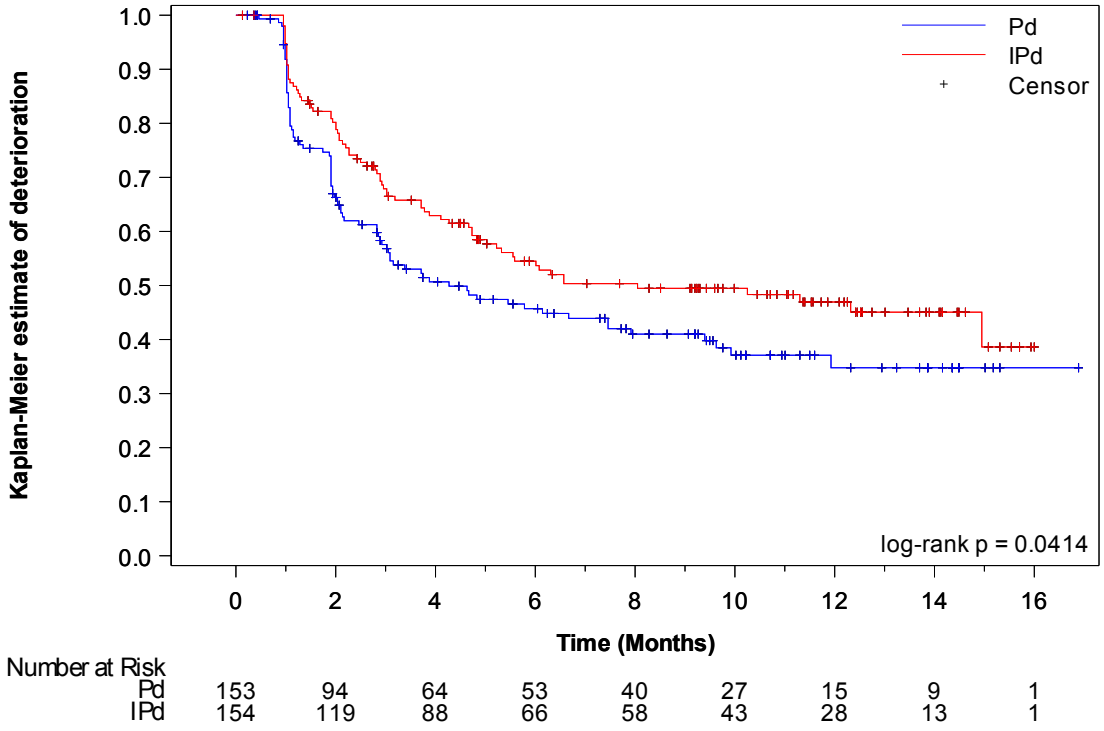
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_con_imp15l_de_i_f_x.rtf (08APR2021 15:33)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Constipation
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-C30 - Time to first deterioration by 15 pt in constipation (LOCF) - ITT population

First deterioration 15 points Constipation (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	85 (55.6)	76 (49.4)
Number (%) of patients censored	68 (44.4)	78 (50.6)
Kaplan-Meier estimates of constipation in months		
25% quantile (95% CI)	1.74 (1.084 to 1.938)	2.27 (1.906 to 2.957)
Median (95% CI)	4.27 (2.891 to 7.918)	8.05 (5.027 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (14.949 to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0414
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.72 (0.53 to 0.99)
P-value	-	0.0423
Probability (95% CI)[c]		
2 Months	0.66 (0.580 to 0.733)	0.80 (0.729 to 0.857)
4 Months	0.51 (0.421 to 0.586)	0.63 (0.546 to 0.702)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_det15l_de_i_t_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Constipation
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-C30 - Time to first deterioration by 15 pt in constipation - Kaplan-Meier curve (LOCF) - ITT population



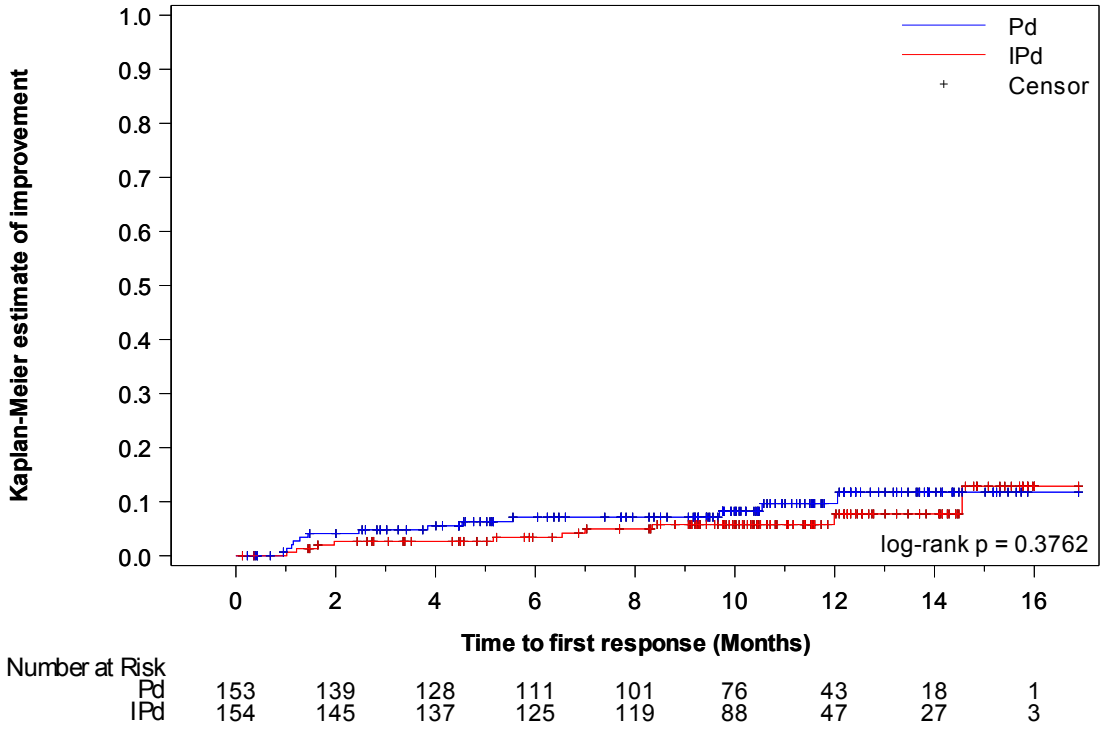
A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_con_det15l_de_i_f_x.rtf (08APR2021 15:33)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Constipation
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in constipation (LOCF) - ITT population

First permanent improvement 15 points Constipation (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	13 (8.5)	10 (6.5)
Number (%) of patients censored	140 (91.5)	144 (93.5)
Kaplan-Meier estimates of constipation in months		
25% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3762
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.69 (0.30 to 1.58)
P-value	-	0.3789
Probability (95% CI)[c]		
2 Months	0.04 (0.017 to 0.082)	0.03 (0.009 to 0.062)
4 Months	0.06 (0.026 to 0.101)	0.03 (0.009 to 0.062)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_imp15pl_de_i_t_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Constipation
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-C30 - Time until permanent improvement by 15 pt in constipation - Kaplan-Meier curve (LOCF) - ITT population



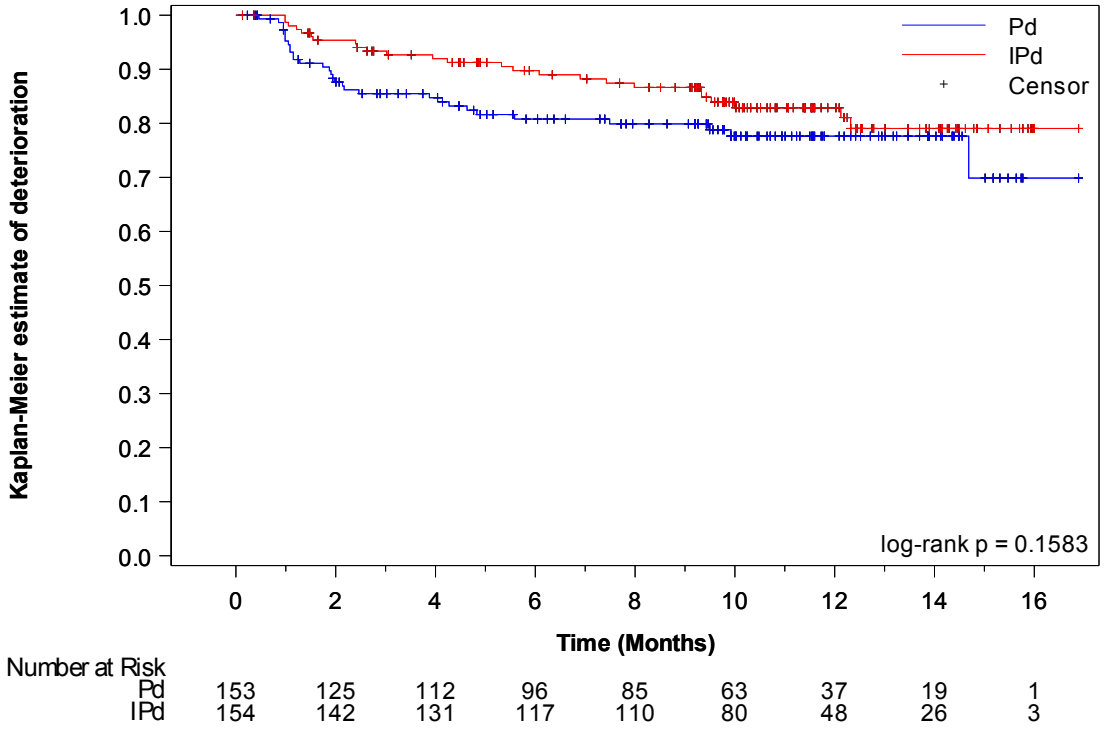
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_con_imp15pl_de_i_f_x.rtf (08APR2021 15:33)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Constipation
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in constipation (LOCF) - ITT population

First permanent deterioration 15 points Constipation (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	31 (20.3)	25 (16.2)
Number (%) of patients censored	122 (79.7)	129 (83.8)
Kaplan-Meier estimates of constipation in months		
25% quantile (95% CI)	14.69 (4.830 to NC)	NC (12.123 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1583
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.69 (0.40 to 1.16)
P-value	-	0.1607
Probability (95% CI)[c]		
2 Months	0.88 (0.811 to 0.920)	0.95 (0.905 to 0.978)
4 Months	0.85 (0.777 to 0.897)	0.92 (0.863 to 0.954)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_det15pl_de_i_t_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Constipation
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-C30 - Time until permanent deterioration by 15 pt in constipation - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (10.0)	8 (14.8)	4 (7.4)	8 (11.8)	7 (24.1)	4 (12.5)	0.2558
Number (%) of patients censored	63 (90.0)	46 (85.2)	50 (92.6)	60 (88.2)	22 (75.9)	28 (87.5)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	NC (NC to NC)	NC (1.643 to NC)	NC (NC to NC)	NC (NC to NC)	4.53 (1.117 to NC)	NC (2.333 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4284		0.4787		0.1916	
Hazard ratio (95% CI) vs Pd	-	1.50 (0.54 to 4.14)		1.54 (0.46 to 5.11)		0.45 (0.13 to 1.54)	
P-value	-	0.4316		0.4821		0.2034	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (57.1)	21 (38.9)	28 (51.9)	33 (48.5)	17 (58.6)	22 (68.8)	0.2639
Number (%) of patients censored	30 (42.9)	33 (61.1)	26 (48.1)	35 (51.5)	12 (41.4)	10 (31.3)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	1.10 (1.018 to 1.906)	2.63 (1.018 to 6.012)	2.10 (1.150 to 3.154)	2.79 (1.906 to 3.713)	1.08 (0.953 to 1.938)	1.76 (1.018 to 2.957)	
Median (95% CI)	2.92 (1.906 to 9.626)	NC (6.012 to NC)	4.83 (3.088 to NC)	6.57 (3.713 to NC)	3.38 (1.183 to 11.926)	4.73 (2.070 to 11.302)	
75% quantile (95% CI)	NC (9.626 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	11.93 (5.782 to NC)	12.32 (5.224 to 14.949)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0222		0.5702		0.5473	
Hazard ratio (95% CI) vs Pd	-	0.54 (0.32 to 0.92)		0.86 (0.52 to 1.43)		0.82 (0.43 to 1.56)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (8.6)	5 (9.3)	2 (3.7)	5 (7.4)	5 (17.2)	0 (0.0)	0.8600
Number (%) of patients censored	64 (91.4)	49 (90.7)	52 (96.3)	63 (92.6)	24 (82.8)	32 (100.0)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	NC (12.057 to NC)	NC (NC to NC)	NC (10.546 to NC)	NC (14.554 to NC)	NC (1.281 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9440		0.5176		0.0096	
Hazard ratio (95% CI) vs Pd	-	1.04 (0.32 to 3.42)		1.71 (0.33 to 8.88)			
P-value	-	0.9439		0.5227		0.9964	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (21.4)	8 (14.8)	9 (16.7)	11 (16.2)	7 (24.1)	6 (18.8)	0.7705
Number (%) of patients censored	55 (78.6)	46 (85.2)	45 (83.3)	57 (83.8)	22 (75.9)	26 (81.3)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	14.69 (1.906 to NC)	NC (5.552 to NC)	NC (4.830 to NC)	NC (9.331 to NC)	9.49 (0.986 to NC)	12.32 (6.078 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.495 to NC)	NC (12.320 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2476		0.7998		0.3691	
Hazard ratio (95% CI) vs Pd	-	0.61 (0.26 to 1.43)		0.89 (0.37 to 2.15)		0.61 (0.20 to 1.82)	
P-value	-	0.2526		0.7999		0.3739	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_detpl_age_de_i_t_x.rtf (08APR2021 14:52)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (12.9)	16 (15.7)	5 (9.6)	4 (7.7)	0.5430
Number (%) of patients censored	88 (87.1)	86 (84.3)	47 (90.4)	48 (92.3)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (5.520 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6358		0.6693	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.57 to 2.48)		0.75 (0.20 to 2.80)	
P-value	-	0.6362		0.6704	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_impl_plne_de_i_t_x.rtf (08APR2021 14:52)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	55 (54.5)	53 (52.0)	30 (57.7)	23 (44.2)	0.3552
Number (%) of patients censored	46 (45.5)	49 (48.0)	22 (42.3)	29 (55.8)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	1.87 (1.051 to 2.037)	2.27 (1.544 to 3.023)	1.15 (1.018 to 1.971)	2.07 (1.051 to 4.731)	
Median (95% CI)	4.63 (2.825 to 9.922)	6.31 (4.107 to NC)	3.38 (1.938 to 9.626)	NC (4.665 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.949 to NC)	11.93 (7.918 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2865		0.0644	
Hazard ratio (95% CI) vs Pd	-	0.81 (0.56 to 1.19)		0.60 (0.35 to 1.04)	
P-value	-	0.2873		0.0672	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	11 (10.9)	8 (7.8)	2 (3.8)	2 (3.8)	0.7948
Number (%) of patients censored	90 (89.1)	94 (92.2)	50 (96.2)	50 (96.2)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (12.057 to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3576		0.8941	
Hazard ratio (95% CI) vs Pd	-	0.65 (0.26 to 1.63)		0.87 (0.12 to 6.24)	
P-value	-	0.3612		0.8939	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (19.8)	17 (16.7)	11 (21.2)	8 (15.4)	0.6739
Number (%) of patients censored	81 (80.2)	85 (83.3)	41 (78.8)	44 (84.6)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	14.69 (4.271 to NC)	NC (9.331 to NC)	NC (1.150 to NC)	NC (9.331 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3828		0.2554	
Hazard ratio (95% CI) vs Pd	-	0.75 (0.39 to 1.43)		0.59 (0.24 to 1.48)	
P-value	-	0.3845		0.2608	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (8.6)	13 (14.6)	12 (14.5)	7 (10.8)	0.1866
Number (%) of patients censored	64 (91.4)	76 (85.4)	71 (85.5)	58 (89.2)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.534 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2680		0.4459	
Hazard ratio (95% CI) vs Pd	-	1.72 (0.65 to 4.51)		0.70 (0.27 to 1.77)	
P-value	-	0.2739		0.4484	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (55.7)	42 (47.2)	46 (55.4)	34 (52.3)	0.4226
Number (%) of patients censored	31 (44.3)	47 (52.8)	37 (44.6)	31 (47.7)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	1.08 (1.018 to 1.906)	2.50 (1.281 to 3.877)	1.94 (1.084 to 2.825)	2.07 (1.248 to 3.187)	
Median (95% CI)	2.92 (1.906 to NC)	11.30 (5.027 to NC)	6.14 (3.154 to 9.626)	5.59 (3.713 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.949 to NC)	NC (9.626 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0650		0.4072	
Hazard ratio (95% CI) vs Pd	-	0.66 (0.43 to 1.03)		0.83 (0.53 to 1.29)	
P-value	-	0.0668		0.4079	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_detl_sex_de_i_t_x.rtf (08APR2021 14:52)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (5.7)	7 (7.9)	9 (10.8)	3 (4.6)	0.1618
Number (%) of patients censored	66 (94.3)	82 (92.1)	74 (89.2)	62 (95.4)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.057 to NC)	NC (14.554 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6364		0.1085	
Hazard ratio (95% CI) vs Pd	-	1.34 (0.39 to 4.59)		0.36 (0.10 to 1.33)	
P-value	-	0.6377		0.1243	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (24.3)	14 (15.7)	14 (16.9)	11 (16.9)	0.3682
Number (%) of patients censored	53 (75.7)	75 (84.3)	69 (83.1)	54 (83.1)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	9.49 (1.906 to NC)	NC (9.528 to NC)	14.69 (7.491 to NC)	NC (6.899 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0909		0.7847	
Hazard ratio (95% CI) vs Pd	-	0.55 (0.27 to 1.11)		0.90 (0.41 to 1.98)	
P-value	-	0.0958		0.7848	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_detpl_sex_de_i_t_x.rtf (08APR2021 14:53)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (12.7)	15 (12.7)	1 (5.3)	5 (20.8)	0.1793
Number (%) of patients censored	110 (87.3)	103 (87.3)	18 (94.7)	19 (79.2)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.150 to NC)	NC (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8753		0.1475	
Hazard ratio (95% CI) vs Pd	-	0.95 (0.47 to 1.91)		4.29 (0.50 to 36.70)	
P-value	-	0.8754		0.1841	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	68 (54.0)	60 (50.8)	13 (68.4)	12 (50.0)	0.3796
Number (%) of patients censored	58 (46.0)	58 (49.2)	6 (31.6)	12 (50.0)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	1.87 (1.084 to 2.103)	2.43 (1.906 to 3.023)	1.08 (0.953 to 1.938)	2.14 (0.953 to 5.322)	
Median (95% CI)	5.45 (3.088 to 9.626)	6.57 (4.731 to NC)	2.04 (1.084 to NC)	8.05 (2.924 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.949 to NC)	NC (2.037 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1660		0.1557	
Hazard ratio (95% CI) vs Pd	-	0.78 (0.55 to 1.11)		0.57 (0.26 to 1.25)	
P-value	-	0.1670		0.1610	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_detl_race_de_i_t_x.rtf (08APR2021 14:52)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (8.7)	10 (8.5)	1 (5.3)	0 (0.0)	0.9912
Number (%) of patients censored	115 (91.3)	108 (91.5)	18 (94.7)	24 (100.0)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (1.150 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7694		0.2611	
Hazard ratio (95% CI) vs Pd	-	0.88 (0.37 to 2.07)			
P-value	-	0.7696		0.9984	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_imppl_race_de_i_t_x.rtf (08APR2021 14:53)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (17.5)	17 (14.4)	6 (31.6)	5 (20.8)	0.7177
Number (%) of patients censored	104 (82.5)	101 (85.6)	13 (68.4)	19 (79.2)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	14.69 (7.491 to NC)	NC (12.123 to NC)	1.94 (0.953 to NC)	NC (1.314 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (1.938 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2751		0.3581	
Hazard ratio (95% CI) vs Pd	-	0.70 (0.37 to 1.33)		0.58 (0.18 to 1.89)	
P-value	-	0.2775		0.3642	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_detpl_race_de_i_t_x.rtf (08APR2021 14:53)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	1 (25.0)	14 (10.4)	18 (13.8)	0.4646
Number (%) of patients censored	2 (66.7)	3 (75.0)	120 (89.6)	112 (86.2)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6949		0.4686	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.04 to 9.30)		1.29 (0.64 to 2.60)	
P-value	-	0.6985		0.4698	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_impl_ethn_de_i_t_x.rtf (08APR2021 14:52)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (25.0)	72 (53.7)	67 (51.5)	0.9837
Number (%) of patients censored	3 (100.0)	3 (75.0)	62 (46.3)	63 (48.5)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (2.497 to NC)	1.91 (1.117 to 2.103)	2.27 (1.511 to 3.023)	
Median (95% CI)	NC (NC to NC)	NC (2.497 to NC)	4.83 (3.088 to 9.922)	6.57 (4.731 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (2.497 to NC)	NC (NC to NC)	NC (14.949 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.2744	
Hazard ratio (95% CI) vs Pd	-			0.83 (0.60 to 1.16)	
P-value	-	0.9985		0.2740	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	1 (25.0)	10 (7.5)	8 (6.2)	0.5407
Number (%) of patients censored	2 (66.7)	3 (75.0)	124 (92.5)	122 (93.8)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (5.158 to NC)	NC (NC to NC)	NC (14.554 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (5.158 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (5.158 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4504		0.5287	
Hazard ratio (95% CI) vs Pd	-	0.35 (0.02 to 5.89)		0.74 (0.29 to 1.88)	
P-value	-	0.4689		0.5302	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	23 (17.2)	21 (16.2)	0.9999
Number (%) of patients censored	3 (100.0)	4 (100.0)	111 (82.8)	109 (83.8)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	14.69 (9.495 to NC)	NC (10.021 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.5334	
Hazard ratio (95% CI) vs Pd	-			0.83 (0.46 to 1.50)	
P-value	-			0.5334	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	11 (14.5)	5 (9.1)	2 (10.0)	3 (10.7)	1 (20.0)	2 (28.6)	1 (6.7)	3 (14.3)	3 (8.1)	7 (16.3)	0.6202
Number (%) of patients censored	65 (85.5)	50 (90.9)	18 (90.0)	25 (89.3)	4 (80.0)	5 (71.4)	14 (93.3)	18 (85.7)	34 (91.9)	36 (83.7)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (3.778 to NC)	NC (NC to NC)	NC (1.117 to NC)	NC (1.018 to NC)	NC (0.986 to NC)	1.25 (1.018 to NC)	NC (1.150 to NC)	NC (0.986 to NC)	NC (NC to NC)	NC (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_impl_greg_de_i_t_x.rtf (08APR2021 14:52)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.3055		0.9373		0.8311		0.4648		0.3110	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.20 to 1.67)		1.07 (0.18 to 6.43)		1.30 (0.12 to 14.35)		2.27 (0.24 to 21.86)		1.98 (0.51 to 7.67)	
P-value	-	0.3117		0.9373		0.8316		0.4771		0.3207	
Improvement probability (95% CI)[b]											
2 Months	0.084 (0.034 to 0.163)	0.056 (0.015 to 0.140)	0.053 (0.004 to 0.214)	0.071 (0.013 to 0.204)	0.200 (0.008 to 0.582)	0.286 (0.041 to 0.612)	0.067 (0.004 to 0.260)	0.095 (0.016 to 0.261)	0.083 (0.021 to 0.201)	0.120 (0.044 to 0.238)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	40 (52.6)	28 (50.9)	10 (50.0)	10 (35.7)	2 (40.0)	4 (57.1)	9 (60.0)	9 (42.9)	24 (64.9)	25 (58.1)	0.8543
Number (%) of patients censored	36 (47.4)	27 (49.1)	10 (50.0)	18 (64.3)	3 (60.0)	3 (42.9)	6 (40.0)	12 (57.1)	13 (35.1)	18 (41.9)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	1.15 (1.018 to 1.906)	1.54 (1.018 to 2.497)	3.02 (0.953 to 6.669)	5.32 (1.051 to NC)	3.71 (2.037 to NC)	2.63 (1.084 to 6.078)	1.12 (1.051 to 1.938)	2.14 (0.953 to 4.665)	1.49 (0.986 to 2.136)	2.89 (1.281 to 3.713)	
Median (95% CI)	5.78 (2.103 to 9.922)	11.30 (2.497 to NC)	11.93 (3.023 to NC)	NC (5.552 to NC)	NC (2.037 to NC)	6.08 (1.084 to NC)	2.10 (1.084 to NC)	NC (2.136 to NC)	2.89 (1.971 to 7.458)	5.03 (3.187 to 10.251)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_detl_greg_de_i_t_x.rtf (08APR2021 14:52)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (9.922 to NC)	14.95 (12.320 to NC)	NC (11.926 to NC)	NC (NC to NC)	NC (2.037 to NC)	NC (2.793 to NC)	NC (2.103 to NC)	NC (NC to NC)	9.40 (3.088 to NC)	NC (8.049 to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.4534		0.2954		0.5955		0.3937		0.1295	
Hazard ratio (95% CI) vs Pd	-	0.83 (0.51 to 1.35)		0.63 (0.26 to 1.51)		1.58 (0.29 to 8.65)		0.67 (0.26 to 1.69)		0.65 (0.37 to 1.14)	
P-value	-	0.4540		0.2997		0.5987		0.3968		0.1324	
Deterioration probability (95% CI)[b]											

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_detl_greg_de_i_t_x.rtf (08APR2021 14:52)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	8 (10.5)	4 (7.3)	1 (5.0)	3 (10.7)	0 (0.0)	1 (14.3)	1 (6.7)	0 (0.0)	3 (8.1)	2 (4.7)	0.8765
Number (%) of patients censored	68 (89.5)	51 (92.7)	19 (95.0)	25 (89.3)	5 (100.0)	6 (85.7)	14 (93.3)	21 (100.0)	34 (91.9)	41 (95.3)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (12.057 to NC)	NC (11.992 to NC)	NC (10.546 to NC)	14.55 (6.538 to NC)	NC (NC to NC)	NC (5.158 to NC)	NC (1.150 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	14.55 (14.554 to NC)	NC (NC to NC)	NC (5.158 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_imppl_greg_de_i_t_x.rtf (08APR2021 14:53)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.5395		0.4475		0.3980		0.2367		0.4492	
Hazard ratio (95% CI) vs Pd	-	0.69 (0.21 to 2.29)		2.35 (0.24 to 22.76)						0.51 (0.08 to 3.05)	
P-value	-	0.5419		0.4609		0.9984		0.9984		0.4577	
Improvement probability (95% CI)[b]											

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	17 (22.4)	14 (25.5)	1 (5.0)	2 (7.1)	0 (0.0)	2 (28.6)	4 (26.7)	3 (14.3)	9 (24.3)	4 (9.3)	0.4107
Number (%) of patients censored	59 (77.6)	41 (74.5)	19 (95.0)	26 (92.9)	5 (100.0)	5 (71.4)	11 (73.3)	18 (85.7)	28 (75.7)	39 (90.7)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	9.92 (3.877 to NC)	9.53 (2.398 to NC)	NC (0.953 to NC)	NC (5.322 to NC)	NC (NC to NC)	6.08 (2.628 to NC)	4.83 (1.051 to NC)	NC (1.314 to NC)	14.69 (1.084 to NC)	NC (10.021 to NC)	
Median (95% CI)	NC (NC to NC)	NC (12.320 to NC)	NC (NC to NC)	NC (12.123 to NC)	NC (NC to NC)	NC (2.628 to NC)	NC (1.938 to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.8762		0.6874		0.2137		0.3571		0.0309	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.52 to 2.15)		1.64 (0.14 to 18.66)				0.50 (0.11 to 2.24)		0.29 (0.09 to 0.96)	
P-value	-	0.8759		0.6902		0.9978		0.3666		0.0421	
Deterioration probability (95% CI)[b]											

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (12.4)	10 (13.0)	6 (10.7)	10 (13.0)	0.7575
Number (%) of patients censored	85 (87.6)	67 (87.0)	50 (89.3)	67 (87.0)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9920		0.7012	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.43 to 2.30)		1.22 (0.44 to 3.35)	
P-value	-	0.9920		0.7017	
Improvement probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	52 (53.6)	41 (53.2)	33 (58.9)	35 (45.5)	0.4402
Number (%) of patients censored	45 (46.4)	36 (46.8)	23 (41.1)	42 (54.5)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	1.15 (1.018 to 1.938)	1.53 (1.051 to 2.628)	1.91 (1.051 to 2.825)	2.92 (2.037 to 4.107)	
Median (95% CI)	3.75 (2.168 to 9.922)	6.57 (2.957 to NC)	4.67 (2.825 to 11.926)	10.25 (4.665 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.949 to NC)	NC (9.396 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4029		0.0668	
Hazard ratio (95% CI) vs Pd	-	0.84 (0.56 to 1.27)		0.64 (0.40 to 1.04)	
P-value	-	0.4035		0.0690	
Deterioration probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (8.2)	6 (7.8)	5 (8.9)	4 (5.2)	0.5580
Number (%) of patients censored	89 (91.8)	71 (92.2)	51 (91.1)	73 (94.8)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.992 to NC)	NC (10.546 to NC)	NC (14.554 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8490		0.3469	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.31 to 2.60)		0.54 (0.14 to 2.00)	
P-value	-	0.8491		0.3546	
Improvement probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (23.7)	18 (23.4)	8 (14.3)	7 (9.1)	0.5350
Number (%) of patients censored	74 (76.3)	59 (76.6)	48 (85.7)	70 (90.9)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	9.49 (2.168 to NC)	10.02 (6.078 to NC)	14.69 (4.830 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6095		0.2792	
Hazard ratio (95% CI) vs Pd	-	0.85 (0.46 to 1.58)		0.58 (0.21 to 1.59)	
P-value	-	0.6099		0.2853	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (10.9)	17 (12.3)	3 (18.8)	3 (18.8)	0.9813
Number (%) of patients censored	122 (89.1)	121 (87.7)	13 (81.3)	13 (81.3)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.281 to NC)	NC (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.004 to NC)	NC (5.520 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8304		0.9386	
Hazard ratio (95% CI) vs Pd	-	1.08 (0.54 to 2.16)		1.06 (0.21 to 5.28)	
P-value	-	0.8307		0.9386	
Improvement probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	78 (56.9)	70 (50.7)	7 (43.8)	6 (37.5)	0.7493
Number (%) of patients censored	59 (43.1)	68 (49.3)	9 (56.3)	10 (62.5)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	1.28 (1.051 to 1.938)	2.27 (1.511 to 2.957)	1.91 (0.986 to 9.922)	2.63 (0.986 to NC)	
Median (95% CI)	3.75 (2.825 to 7.458)	8.05 (4.830 to NC)	9.92 (1.873 to NC)	NC (1.906 to NC)	
75% quantile (95% CI)	NC (11.926 to NC)	NC (14.949 to NC)	NC (9.922 to NC)	NC (5.224 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0464		0.7804	
Hazard ratio (95% CI) vs Pd	-	0.72 (0.52 to 1.00)		0.86 (0.29 to 2.55)	
P-value	-	0.0474		0.7810	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (8.0)	7 (5.1)	2 (12.5)	3 (18.8)	0.3407
Number (%) of patients censored	126 (92.0)	131 (94.9)	14 (87.5)	13 (81.3)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (1.281 to NC)	11.99 (5.158 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.158 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.992 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2365		0.6360	
Hazard ratio (95% CI) vs Pd	-	0.57 (0.22 to 1.47)		1.54 (0.26 to 9.21)	
P-value	-	0.2427		0.6385	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (18.2)	22 (15.9)	6 (37.5)	3 (18.8)	0.4402
Number (%) of patients censored	112 (81.8)	116 (84.1)	10 (62.5)	13 (81.3)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	14.69 (5.585 to NC)	NC (12.123 to NC)	1.94 (0.986 to NC)	7.98 (1.314 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	9.92 (1.873 to NC)	NC (7.984 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.922 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3498		0.2339	
Hazard ratio (95% CI) vs Pd	-	0.76 (0.43 to 1.35)		0.44 (0.11 to 1.77)	
P-value	-	0.3513		0.2469	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (7.8)	7 (10.9)	7 (12.5)	8 (15.1)	7 (16.3)	5 (14.7)	0.7883
Number (%) of patients censored	47 (92.2)	57 (89.1)	49 (87.5)	45 (84.9)	36 (83.7)	29 (85.3)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.877 to NC)	NC (4.665 to NC)	NC (1.281 to NC)	NC (1.380 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5724		0.7450		0.7320	
Hazard ratio (95% CI) vs Pd	-	1.42 (0.42 to 4.86)		1.18 (0.43 to 3.26)		0.82 (0.26 to 2.58)	
P-value	-	0.5744		0.7455		0.7325	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (60.8)	27 (42.2)	32 (57.1)	30 (56.6)	20 (46.5)	17 (50.0)	0.5847
Number (%) of patients censored	20 (39.2)	37 (57.8)	24 (42.9)	23 (43.4)	23 (53.5)	17 (50.0)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	1.28 (1.051 to 2.103)	3.02 (1.248 to 4.731)	1.74 (1.018 to 2.168)	2.07 (1.084 to 2.793)	1.91 (1.018 to 2.464)	2.89 (1.051 to 5.224)	
Median (95% CI)	5.78 (2.037 to NC)	14.95 (4.731 to NC)	4.27 (2.136 to 11.926)	6.08 (2.793 to 12.320)	3.06 (2.037 to NC)	6.01 (3.713 to NC)	
75% quantile (95% CI)	NC (9.922 to NC)	NC (14.949 to NC)	NC (11.926 to NC)	NC (10.251 to NC)	NC (4.665 to NC)	NC (6.571 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0711		0.6373		0.2804	
Hazard ratio (95% CI) vs Pd	-	0.62 (0.37 to 1.05)		0.89 (0.54 to 1.46)		0.70 (0.36 to 1.34)	
P-value	-	0.0737		0.6373		0.2828	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (5.9)	4 (6.3)	3 (5.4)	3 (5.7)	7 (16.3)	3 (8.8)	0.5653
Number (%) of patients censored	48 (94.1)	60 (93.8)	53 (94.6)	50 (94.3)	36 (83.7)	31 (91.2)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.992 to NC)	12.06 (1.446 to NC)	NC (8.345 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	NC (12.057 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8588		0.8760		0.2194	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.26 to 5.12)		0.88 (0.18 to 4.38)		0.44 (0.11 to 1.70)	
P-value	-	0.8589		0.8757		0.2325	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (23.5)	12 (18.8)	13 (23.2)	10 (18.9)	4 (9.3)	3 (8.8)	0.9673
Number (%) of patients censored	39 (76.5)	52 (81.3)	43 (76.8)	43 (81.1)	39 (90.7)	31 (91.2)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	14.69 (1.971 to NC)	NC (7.425 to NC)	9.49 (1.938 to NC)	12.32 (6.078 to NC)	NC (5.585 to NC)	NC (5.322 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6001		0.3672		0.6676	
Hazard ratio (95% CI) vs Pd	-	0.81 (0.36 to 1.80)		0.68 (0.30 to 1.57)		0.72 (0.16 to 3.24)	
P-value	-	0.6008		0.3700		0.6689	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (9.7)	7 (17.9)	8 (8.2)	10 (10.1)	7 (29.2)	3 (18.8)	0.3827
Number (%) of patients censored	28 (90.3)	32 (82.1)	90 (91.8)	89 (89.9)	17 (70.8)	13 (81.3)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	NC (2.004 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	1.94 (0.953 to NC)	NC (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.938 to NC)	NC (1.971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3317		0.6875		0.3640	
Hazard ratio (95% CI) vs Pd	-	1.93 (0.50 to 7.47)		1.21 (0.48 to 3.07)		0.54 (0.14 to 2.09)	
P-value	-	0.3406		0.6880		0.3718	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (51.6)	14 (35.9)	60 (61.2)	57 (57.6)	9 (37.5)	5 (31.3)	0.4979
Number (%) of patients censored	15 (48.4)	25 (64.1)	38 (38.8)	42 (42.4)	15 (62.5)	11 (68.8)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	2.04 (1.018 to 6.144)	4.73 (1.150 to 14.949)	1.15 (1.051 to 1.906)	1.94 (1.084 to 2.431)	1.91 (0.986 to 3.055)	6.01 (1.314 to NC)	
Median (95% CI)	9.92 (2.891 to NC)	14.95 (6.571 to NC)	3.38 (2.136 to 6.669)	5.03 (2.891 to 10.251)	3.06 (1.906 to NC)	11.30 (2.037 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.949 to NC)	NC (7.918 to NC)	NC (12.320 to NC)	NC (3.055 to NC)	NC (11.302 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1761		0.3445		0.1656	
Hazard ratio (95% CI) vs Pd	-	0.61 (0.30 to 1.26)		0.84 (0.58 to 1.21)		0.46 (0.15 to 1.41)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (6.5)	4 (10.3)	4 (4.1)	4 (4.0)	7 (29.2)	2 (12.5)	0.3389
Number (%) of patients censored	29 (93.5)	35 (89.7)	94 (95.9)	95 (96.0)	17 (70.8)	14 (87.5)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	NC (10.546 to NC)	NC (6.998 to NC)	NC (NC to NC)	NC (14.554 to NC)	4.53 (0.953 to 12.057)	NC (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	12.06 (4.534 to NC)	NC (8.345 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.692 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5404		0.8842		0.1288	
Hazard ratio (95% CI) vs Pd	-	1.69 (0.31 to 9.22)		0.90 (0.23 to 3.61)		0.31 (0.06 to 1.52)	
P-value	-	0.5451		0.8841		0.1502	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (12.9)	6 (15.4)	25 (25.5)	18 (18.2)	2 (8.3)	1 (6.3)	0.6003
Number (%) of patients censored	27 (87.1)	33 (84.6)	73 (74.5)	81 (81.8)	22 (91.7)	15 (93.8)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	14.69 (9.922 to NC)	NC (9.331 to NC)	7.49 (1.938 to NC)	NC (7.984 to NC)	NC (0.986 to NC)	NC (1.314 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6846		0.1180		0.7077	
Hazard ratio (95% CI) vs Pd	-	1.30 (0.37 to 4.61)		0.62 (0.34 to 1.14)		0.63 (0.06 to 7.00)	
P-value	-	0.6855		0.1216		0.7102	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_detpl_seriss_de_i_t_x.rtf (08APR2021 14:53)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (26.1)	1 (7.1)	6 (6.3)	15 (12.7)	0.0744
Number (%) of patients censored	17 (73.9)	13 (92.9)	89 (93.7)	103 (87.3)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	2.83 (1.117 to NC)	NC (1.971 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (2.825 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1627		0.1355	
Hazard ratio (95% CI) vs Pd	-	0.25 (0.03 to 2.06)		2.03 (0.79 to 5.22)	
P-value	-	0.1973		0.1437	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (34.8)	3 (21.4)	54 (56.8)	64 (54.2)	0.5171
Number (%) of patients censored	15 (65.2)	11 (78.6)	41 (43.2)	54 (45.8)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	1.18 (0.953 to NC)	NC (0.953 to NC)	1.74 (1.051 to 1.906)	2.20 (1.281 to 2.891)	
Median (95% CI)	NC (1.183 to NC)	NC (1.938 to NC)	3.88 (2.168 to 9.922)	5.59 (3.877 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.926 to NC)	NC (14.949 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3467		0.2907	
Hazard ratio (95% CI) vs Pd	-	0.53 (0.14 to 2.02)		0.82 (0.57 to 1.18)	
P-value	-	0.3545		0.2914	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (17.4)	1 (7.1)	5 (5.3)	8 (6.8)	0.4125
Number (%) of patients censored	19 (82.6)	13 (92.9)	90 (94.7)	110 (93.2)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	12.06 (1.117 to NC)	NC (1.971 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (12.057 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4488		0.7673	
Hazard ratio (95% CI) vs Pd	-	0.44 (0.05 to 3.96)		1.18 (0.39 to 3.62)	
P-value	-	0.4613		0.7676	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (8.7)	1 (7.1)	20 (21.1)	20 (16.9)	0.9330
Number (%) of patients censored	21 (91.3)	13 (92.9)	75 (78.9)	98 (83.1)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (0.953 to NC)	NC (1.314 to NC)	NC (2.464 to NC)	NC (9.528 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8174		0.2556	
Hazard ratio (95% CI) vs Pd	-	0.75 (0.07 to 8.33)		0.70 (0.38 to 1.30)	
P-value	-	0.8180		0.2581	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (22.2)	2 (8.3)	4 (5.1)	14 (13.6)	0.0396
Number (%) of patients censored	28 (77.8)	22 (91.7)	74 (94.9)	89 (86.4)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (1.446 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1813		0.0743	
Hazard ratio (95% CI) vs Pd	-	0.36 (0.08 to 1.71)		2.65 (0.87 to 8.04)	
P-value	-	0.2001		0.0861	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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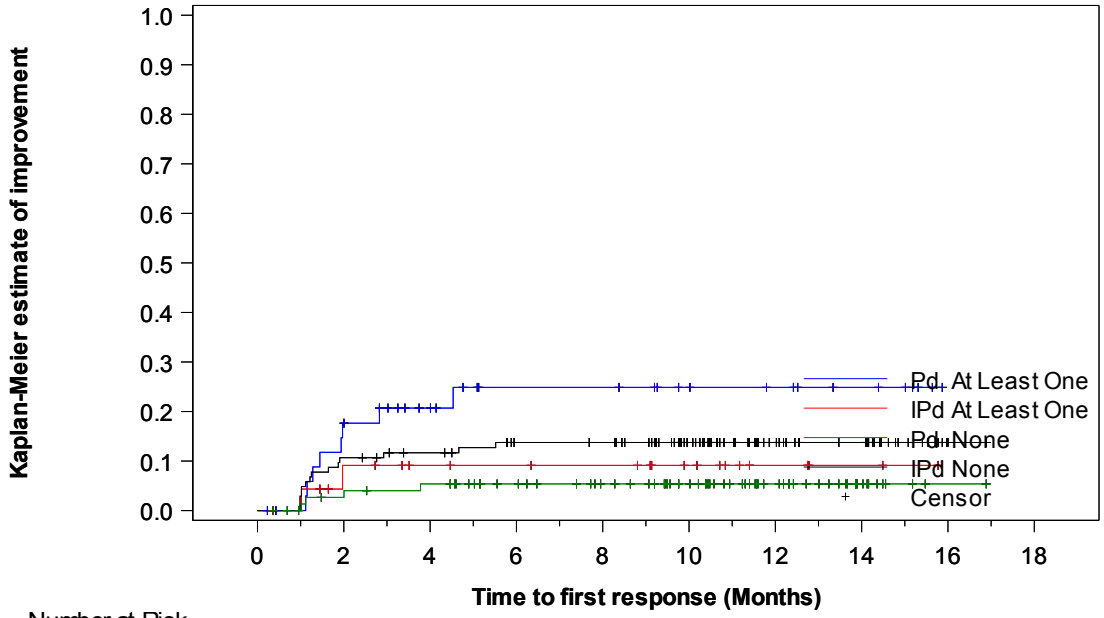
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-C30 - Time to first improvement by 10 pt in constipation according to cytogenetic abnormality (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd At Least One	36	25	15	14	9	5	0
IPd At Least One	24	18	15	13	4	1	0
Pd None	78	70	60	51	24	3	0
IPd None	103	89	79	74	32	9	0

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (47.2)	10 (41.7)	42 (53.8)	54 (52.4)	0.9770
Number (%) of patients censored	19 (52.8)	14 (58.3)	36 (46.2)	49 (47.6)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	1.15 (1.018 to 3.088)	1.31 (0.953 to 2.957)	1.91 (1.018 to 2.037)	2.43 (1.478 to 3.023)	
Median (95% CI)	3.75 (1.873 to NC)	NC (1.938 to NC)	5.45 (2.825 to NC)	6.08 (4.271 to NC)	
75% quantile (95% CI)	NC (5.782 to NC)	NC (NC to NC)	NC (11.926 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6300		0.4043	
Hazard ratio (95% CI) vs Pd	-	0.83 (0.38 to 1.80)		0.84 (0.56 to 1.26)	
P-value	-	0.6305		0.4049	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (16.7)	1 (4.2)	3 (3.8)	8 (7.8)	0.1073
Number (%) of patients censored	30 (83.3)	23 (95.8)	75 (96.2)	95 (92.2)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (1.446 to NC)	NC (1.971 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1714		0.3467	
Hazard ratio (95% CI) vs Pd	-	0.25 (0.03 to 2.12)		1.87 (0.50 to 7.06)	
P-value	-	0.2051		0.3545	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.7 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (22.2)	4 (16.7)	12 (15.4)	16 (15.5)	0.6856
Number (%) of patients censored	28 (77.8)	20 (83.3)	66 (84.6)	87 (84.5)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	4.14 (1.873 to NC)	10.02 (1.314 to NC)	NC (9.495 to NC)	NC (9.528 to NC)	
Median (95% CI)	NC (NC to NC)	NC (10.021 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4851		0.7732	
Hazard ratio (95% CI) vs Pd	-	0.65 (0.20 to 2.18)		0.90 (0.42 to 1.89)	
P-value	-	0.4883		0.7733	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (10.0)	9 (10.8)	9 (14.3)	11 (15.5)	0.8833
Number (%) of patients censored	81 (90.0)	74 (89.2)	54 (85.7)	60 (84.5)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.778 to NC)	NC (4.665 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8456		0.9698	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.44 to 2.76)		0.98 (0.41 to 2.37)	
P-value	-	0.8454		0.9698	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	53 (58.9)	33 (39.8)	32 (50.8)	43 (60.6)	0.1512
Number (%) of patients censored	37 (41.1)	50 (60.2)	31 (49.2)	28 (39.4)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	1.87 (1.051 to 2.136)	2.83 (1.248 to 5.027)	1.35 (1.018 to 1.938)	2.07 (1.478 to 2.957)	
Median (95% CI)	4.67 (2.858 to 9.396)	NC (5.585 to NC)	3.88 (1.938 to NC)	5.22 (3.187 to 11.302)	
75% quantile (95% CI)	NC (9.922 to NC)	NC (NC to NC)	NC (11.926 to NC)	14.95 (11.302 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0156		0.6376	
Hazard ratio (95% CI) vs Pd	-	0.59 (0.38 to 0.91)		0.90 (0.57 to 1.42)	
P-value	-	0.0169		0.6378	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (7.8)	6 (7.2)	6 (9.5)	4 (5.6)	0.4439
Number (%) of patients censored	83 (92.2)	77 (92.8)	57 (90.5)	67 (94.4)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (9.692 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8652		0.2479	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.31 to 2.71)		0.48 (0.14 to 1.71)	
P-value	-	0.8655		0.2582	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_imppl_auto_de_i_t_x.rtf (08APR2021 14:53)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (23.3)	11 (13.3)	10 (15.9)	14 (19.7)	0.2084
Number (%) of patients censored	69 (76.7)	72 (86.7)	53 (84.1)	57 (80.3)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	14.69 (2.136 to NC)	NC (10.021 to NC)	NC (5.585 to NC)	12.32 (7.425 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0671		0.9787	
Hazard ratio (95% CI) vs Pd	-	0.51 (0.25 to 1.06)		1.01 (0.45 to 2.28)	
P-value	-	0.0723		0.9787	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	18 (11.9)	20 (13.2)	1.0000
Number (%) of patients censored	2 (100.0)	2 (100.0)	133 (88.1)	132 (86.8)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.8422	
Hazard ratio (95% CI) vs Pd	-			1.07 (0.56 to 2.02)	
P-value	-			0.8424	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	1 (50.0)	83 (55.0)	75 (49.3)	0.6677
Number (%) of patients censored	0 (0.0)	1 (50.0)	68 (45.0)	77 (50.7)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	2.86 (2.858 to 9.626)	5.03 (5.027 to NC)	1.74 (1.084 to 1.906)	2.27 (1.544 to 2.957)	
Median (95% CI)	6.24 (2.858 to 9.626)	NC (5.027 to NC)	4.27 (2.891 to 7.918)	8.05 (4.830 to NC)	
75% quantile (95% CI)	9.63 (2.858 to 9.626)	NC (5.027 to NC)	NC (NC to NC)	NC (14.949 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.0630	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		0.74 (0.54 to 1.02)	
P-value	-	0.8092		0.0639	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	13 (8.6)	10 (6.6)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	138 (91.4)	142 (93.4)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.3804	
Hazard ratio (95% CI) vs Pd	-			0.69 (0.30 to 1.58)	
P-value	-			0.3830	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	31 (20.5)	25 (16.4)	0.9998
Number (%) of patients censored	2 (100.0)	2 (100.0)	120 (79.5)	127 (83.6)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	14.69 (4.632 to NC)	NC (10.021 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.1739	
Hazard ratio (95% CI) vs Pd	-			0.70 (0.41 to 1.18)	
P-value	-			0.1763	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (12.9)	14 (13.5)	3 (7.3)	4 (12.1)	0.6944
Number (%) of patients censored	88 (87.1)	90 (86.5)	38 (92.7)	29 (87.9)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.975 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9528		0.5443	
Hazard ratio (95% CI) vs Pd	-	1.02 (0.48 to 2.18)		1.58 (0.35 to 7.07)	
P-value	-	0.9528		0.5478	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	62 (61.4)	46 (44.2)	17 (41.5)	21 (63.6)	0.0126
Number (%) of patients censored	39 (38.6)	58 (55.8)	24 (58.5)	12 (36.4)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	1.12 (1.018 to 1.906)	2.89 (1.938 to 4.107)	2.89 (1.051 to 4.665)	2.04 (1.216 to 2.793)	
Median (95% CI)	3.02 (2.037 to 6.669)	14.95 (5.585 to NC)	NC (3.745 to NC)	3.19 (2.136 to 12.320)	
75% quantile (95% CI)	NC (9.396 to NC)	NC (14.949 to NC)	NC (NC to NC)	NC (4.830 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0011		0.1405	
Hazard ratio (95% CI) vs Pd	-	0.53 (0.36 to 0.78)		1.61 (0.85 to 3.06)	
P-value	-	0.0013		0.1443	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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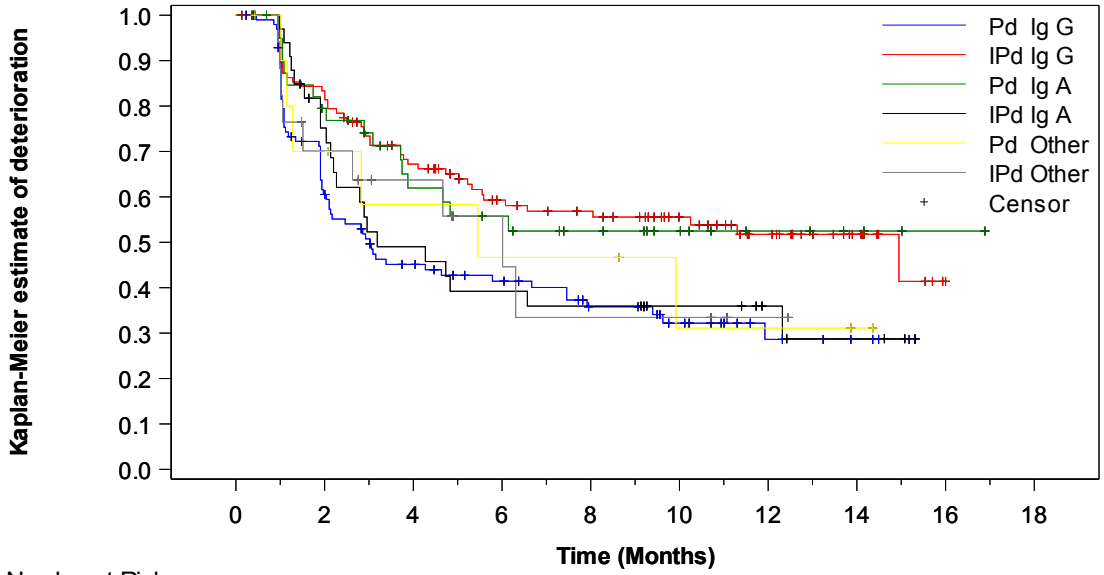
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to MM type at SE (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd Ig G	101	46	32	23	8	2	0
IPd Ig G	104	72	49	40	22	4	0
Pd Ig A	41	26	17	12	5	2	0
IPd Ig A	33	16	12	11	5	2	0
Pd Other	11	5	4	3	2	0	0
IPd Other	17	9	5	3	1	0	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (7.9)	7 (6.7)	3 (7.3)	1 (3.0)	0.8476
Number (%) of patients censored	93 (92.1)	97 (93.3)	38 (92.7)	32 (97.0)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (12.057 to NC)	NC (14.554 to NC)	NC (10.546 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5781		0.3630	
Hazard ratio (95% CI) vs Pd	-	0.75 (0.27 to 2.07)		0.36 (0.04 to 3.51)	
P-value	-	0.5794		0.3830	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.7 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (19.8)	13 (12.5)	8 (19.5)	8 (24.2)	0.4909
Number (%) of patients censored	81 (80.2)	91 (87.5)	33 (80.5)	25 (75.8)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	14.69 (4.271 to NC)	NC (12.123 to NC)	NC (1.741 to NC)	12.32 (1.314 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.320 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0756		0.7943	
Hazard ratio (95% CI) vs Pd	-	0.54 (0.27 to 1.08)		1.14 (0.43 to 3.04)	
P-value	-	0.0804		0.7939	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (13.0)	13 (12.7)	5 (9.6)	6 (11.8)	0.8000
Number (%) of patients censored	87 (87.0)	89 (87.3)	47 (90.4)	45 (88.2)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.665 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9027		0.8195	
Hazard ratio (95% CI) vs Pd	-	0.95 (0.44 to 2.06)		1.15 (0.35 to 3.76)	
P-value	-	0.9027		0.8196	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_impl_dghc_de_i_t_x.rtf (08APR2021 14:52)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	61 (61.0)	46 (45.1)	23 (44.2)	30 (58.8)	0.0066
Number (%) of patients censored	39 (39.0)	56 (54.9)	29 (55.8)	21 (41.2)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	1.12 (1.018 to 1.906)	2.83 (1.938 to 3.877)	2.83 (1.084 to 3.877)	1.91 (1.216 to 2.793)	
Median (95% CI)	3.02 (1.971 to 7.458)	14.95 (5.552 to NC)	9.92 (3.745 to NC)	4.73 (2.628 to 12.320)	
75% quantile (95% CI)	NC (9.396 to NC)	NC (14.949 to NC)	NC (NC to NC)	NC (6.571 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0021		0.2455	
Hazard ratio (95% CI) vs Pd	-	0.55 (0.38 to 0.81)		1.38 (0.80 to 2.37)	
P-value	-	0.0024		0.2475	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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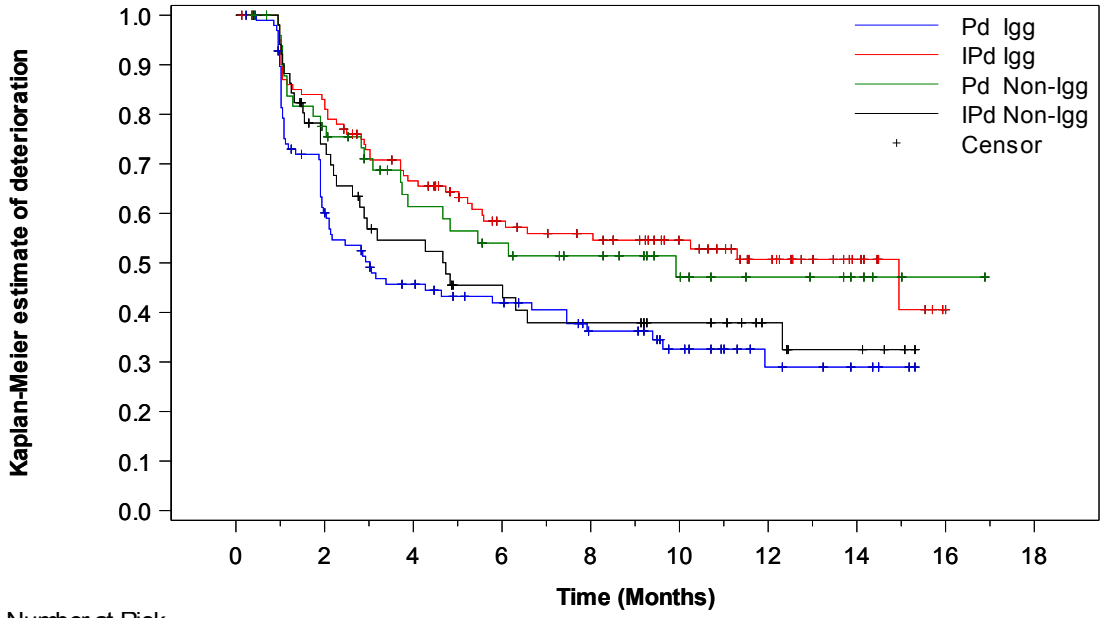
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to MM type at initial diagnosis (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd Igg	100	45	32	23	8	2	0
IPd Igg	102	70	47	38	21	4	0
Pd Non-Igg	52	31	21	15	7	2	0
IPd Non-Igg	51	26	18	15	7	2	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (8.0)	6 (5.9)	5 (9.6)	3 (5.9)	0.8594
Number (%) of patients censored	92 (92.0)	96 (94.1)	47 (90.4)	48 (94.1)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (12.057 to NC)	NC (14.554 to NC)	NC (10.546 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4027		0.4292	
Hazard ratio (95% CI) vs Pd	-	0.64 (0.22 to 1.84)		0.57 (0.14 to 2.37)	
P-value	-	0.4066		0.4354	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_imppl_dghc_de_i_t_x.rtf (08APR2021 14:53)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.7 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (20.0)	13 (12.7)	11 (21.2)	12 (23.5)	0.2684
Number (%) of patients censored	80 (80.0)	89 (87.3)	41 (78.8)	39 (76.5)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	14.69 (4.271 to NC)	NC (12.123 to NC)	9.92 (1.741 to NC)	12.32 (2.628 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0794		0.9878	
Hazard ratio (95% CI) vs Pd	-	0.54 (0.27 to 1.09)		1.01 (0.44 to 2.28)	
P-value	-	0.0842		0.9878	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	2 (14.3)	17 (11.9)	18 (12.9)	0.9126
Number (%) of patients censored	9 (90.0)	12 (85.7)	126 (88.1)	122 (87.1)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (0.953 to NC)	NC (0.986 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (0.953 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8715		0.8752	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.11 to 13.45)		1.05 (0.54 to 2.05)	
P-value	-	0.8717		0.8752	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (20.0)	7 (50.0)	83 (58.0)	69 (49.3)	0.2708
Number (%) of patients censored	8 (80.0)	7 (50.0)	60 (42.0)	71 (50.7)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	2.83 (1.741 to NC)	5.59 (1.314 to 14.949)	1.28 (1.051 to 1.906)	2.20 (1.511 to 2.891)	
Median (95% CI)	NC (1.741 to NC)	14.95 (5.027 to NC)	3.88 (2.825 to 7.458)	6.57 (4.665 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.251 to NC)	NC (11.926 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6630		0.0421	
Hazard ratio (95% CI) vs Pd	-	1.43 (0.28 to 7.26)		0.72 (0.52 to 0.99)	
P-value	-	0.6647		0.0430	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	1 (7.1)	12 (8.4)	9 (6.4)	0.7182
Number (%) of patients censored	9 (90.0)	13 (92.9)	131 (91.6)	131 (93.6)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (0.953 to NC)	NC (6.538 to NC)	NC (NC to NC)	NC (14.554 to NC)	
Median (95% CI)	NC (0.953 to NC)	NC (6.538 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6272		0.4463	
Hazard ratio (95% CI) vs Pd	-	0.51 (0.03 to 8.27)		0.72 (0.30 to 1.70)	
P-value	-	0.6335		0.4484	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	2 (14.3)	30 (21.0)	23 (16.4)	0.8366
Number (%) of patients censored	9 (90.0)	12 (85.7)	113 (79.0)	117 (83.6)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (1.741 to NC)	NC (1.314 to NC)	14.69 (4.632 to NC)	NC (10.021 to NC)	
Median (95% CI)	NC (1.741 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7880		0.1854	
Hazard ratio (95% CI) vs Pd	-	1.39 (0.13 to 15.33)		0.69 (0.40 to 1.20)	
P-value	-	0.7889		0.1878	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (12.5)	8 (9.2)	5 (10.2)	12 (21.8)	0.1155
Number (%) of patients censored	84 (87.5)	79 (90.8)	44 (89.8)	43 (78.2)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.534 to NC)	NC (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4436		0.1415	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.29 to 1.73)		2.15 (0.76 to 6.09)	
P-value	-	0.4459		0.1513	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	53 (55.2)	41 (47.1)	28 (57.1)	31 (56.4)	0.9629
Number (%) of patients censored	43 (44.8)	46 (52.9)	21 (42.9)	24 (43.6)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	1.91 (1.051 to 2.825)	2.27 (1.511 to 3.713)	1.08 (1.018 to 1.906)	2.50 (1.281 to 3.713)	
Median (95% CI)	4.67 (3.088 to 9.922)	14.95 (4.830 to NC)	3.02 (1.906 to 7.458)	6.01 (3.713 to 12.320)	
75% quantile (95% CI)	NC (11.926 to NC)	NC (14.949 to NC)	NC (7.458 to NC)	NC (11.302 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1261		0.2716	
Hazard ratio (95% CI) vs Pd	-	0.73 (0.48 to 1.10)		0.75 (0.45 to 1.25)	
P-value	-	0.1277		0.2732	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (8.3)	5 (5.7)	4 (8.2)	5 (9.1)	0.6452
Number (%) of patients censored	88 (91.7)	82 (94.3)	45 (91.8)	50 (90.9)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4156		0.9887	
Hazard ratio (95% CI) vs Pd	-	0.63 (0.21 to 1.93)		0.99 (0.27 to 3.69)	
P-value	-	0.4197		0.9887	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (15.6)	14 (16.1)	13 (26.5)	8 (14.5)	0.1464
Number (%) of patients censored	81 (84.4)	73 (83.9)	36 (73.5)	47 (85.5)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	14.69 (9.922 to NC)	NC (9.331 to NC)	7.49 (1.150 to NC)	NC (10.021 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8617		0.0443	
Hazard ratio (95% CI) vs Pd	-	0.94 (0.45 to 1.94)		0.42 (0.17 to 1.00)	
P-value	-	0.8618		0.0513	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	17 (11.3)	19 (12.5)	0.8082
Number (%) of patients censored	1 (50.0)	1 (50.0)	134 (88.7)	133 (87.5)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	3.98 (3.975 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (3.975 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (3.975 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.8242	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		1.08 (0.56 to 2.07)	
P-value	-	0.8092		0.8244	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	84 (55.6)	75 (49.3)	0.7977
Number (%) of patients censored	1 (50.0)	1 (50.0)	67 (44.4)	77 (50.7)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	2.10 (2.103 to NC)	12.32 (NC to NC)	1.74 (1.084 to 1.906)	2.27 (1.544 to 2.957)	
Median (95% CI)	NC (2.103 to NC)	12.32 (NC to NC)	4.27 (2.891 to 7.918)	6.57 (4.830 to NC)	
75% quantile (95% CI)	NC (2.103 to NC)	12.32 (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.0590	
Hazard ratio (95% CI) vs Pd	-			0.74 (0.54 to 1.01)	
P-value	-	0.9990		0.0599	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	12 (7.9)	10 (6.6)	0.9917
Number (%) of patients censored	1 (50.0)	2 (100.0)	139 (92.1)	142 (93.4)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.5125	
Hazard ratio (95% CI) vs Pd	-			0.76 (0.33 to 1.75)	
P-value	-	0.9990		0.5138	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	31 (20.5)	24 (15.8)	0.9863
Number (%) of patients censored	2 (100.0)	1 (50.0)	120 (79.5)	128 (84.2)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	12.32 (NC to NC)	14.69 (4.632 to NC)	NC (10.021 to NC)	
Median (95% CI)	NC (NC to NC)	12.32 (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	12.32 (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.1402	
Hazard ratio (95% CI) vs Pd	-			0.67 (0.39 to 1.14)	
P-value	-			0.1425	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (12.2)	14 (11.9)	4 (10.5)	6 (16.7)	0.4613
Number (%) of patients censored	101 (87.8)	104 (88.1)	34 (89.5)	30 (83.3)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.464 to NC)	NC (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8381		0.4500	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.44 to 1.94)		1.62 (0.46 to 5.75)	
P-value	-	0.8380		0.4544	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	64 (55.7)	57 (48.3)	21 (55.3)	19 (52.8)	0.5199
Number (%) of patients censored	51 (44.3)	61 (51.7)	17 (44.7)	17 (47.2)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	1.87 (1.084 to 1.971)	2.63 (1.511 to 3.713)	1.15 (0.986 to 2.103)	2.04 (1.051 to 2.891)	
Median (95% CI)	4.67 (2.858 to 7.918)	11.30 (5.224 to NC)	3.09 (1.906 to NC)	4.27 (2.267 to NC)	
75% quantile (95% CI)	NC (11.926 to NC)	NC (14.949 to NC)	NC (9.396 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0410		0.6662	
Hazard ratio (95% CI) vs Pd	-	0.69 (0.48 to 0.99)		0.87 (0.47 to 1.62)	
P-value	-	0.0422		0.6665	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (7.8)	8 (6.8)	4 (10.5)	2 (5.6)	0.7943
Number (%) of patients censored	106 (92.2)	110 (93.2)	34 (89.5)	34 (94.4)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (10.546 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5308		0.5124	
Hazard ratio (95% CI) vs Pd	-	0.74 (0.28 to 1.92)		0.57 (0.10 to 3.13)	
P-value	-	0.5324		0.5179	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (19.1)	19 (16.1)	9 (23.7)	6 (16.7)	0.9008
Number (%) of patients censored	93 (80.9)	99 (83.9)	29 (76.3)	30 (83.3)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (4.830 to NC)	NC (9.331 to NC)	14.69 (1.150 to NC)	12.12 (9.528 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (12.123 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2929		0.4651	
Hazard ratio (95% CI) vs Pd	-	0.72 (0.39 to 1.33)		0.68 (0.24 to 1.92)	
P-value	-	0.2951		0.4678	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (12.5)	19 (12.9)	0 (0.0)	1 (14.3)	0.9885
Number (%) of patients censored	126 (87.5)	128 (87.1)	9 (100.0)	6 (85.7)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9755		0.2568	
Hazard ratio (95% CI) vs Pd	-	0.99 (0.52 to 1.89)			
P-value	-	0.9755		0.9984	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	78 (54.2)	72 (49.0)	7 (77.8)	4 (57.1)	0.8698
Number (%) of patients censored	66 (45.8)	75 (51.0)	2 (22.2)	3 (42.9)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	1.35 (1.084 to 1.938)	2.27 (1.544 to 3.023)	1.91 (1.018 to 3.055)	1.94 (1.018 to 5.322)	
Median (95% CI)	4.67 (2.891 to 9.626)	8.05 (4.830 to NC)	3.06 (1.018 to NC)	5.32 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.949 to NC)	9.40 (1.906 to NC)	NC (2.037 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0706		0.5507	
Hazard ratio (95% CI) vs Pd	-	0.74 (0.54 to 1.03)		0.69 (0.20 to 2.38)	
P-value	-	0.0716		0.5530	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (9.0)	10 (6.8)	0 (0.0)	0 (0.0)	0.9998
Number (%) of patients censored	131 (91.0)	137 (93.2)	9 (100.0)	7 (100.0)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3327			
Hazard ratio (95% CI) vs Pd	-	0.67 (0.29 to 1.52)			
P-value	-	0.3357			
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (20.1)	23 (15.6)	2 (22.2)	2 (28.6)	0.4459
Number (%) of patients censored	115 (79.9)	124 (84.4)	7 (77.8)	5 (71.4)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (4.632 to NC)	NC (12.123 to NC)	14.69 (1.906 to NC)	9.53 (5.322 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	14.69 (1.906 to NC)	NC (5.322 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (9.528 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1486		0.3679	
Hazard ratio (95% CI) vs Pd	-	0.67 (0.39 to 1.16)		2.89 (0.26 to 32.40)	
P-value	-	0.1513		0.3892	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (17.0)	13 (14.0)	3 (4.6)	7 (11.5)	0.1689
Number (%) of patients censored	73 (83.0)	80 (86.0)	62 (95.4)	54 (88.5)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (3.778 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5623		0.2073	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.38 to 1.69)		2.33 (0.60 to 9.00)	
P-value	-	0.5630		0.2210	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (55.7)	47 (50.5)	36 (55.4)	29 (47.5)	0.8582
Number (%) of patients censored	39 (44.3)	46 (49.5)	29 (44.6)	32 (52.5)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	1.18 (1.018 to 1.938)	2.79 (1.544 to 3.713)	1.91 (1.084 to 2.858)	2.04 (1.051 to 2.957)	
Median (95% CI)	4.27 (2.103 to 9.922)	6.57 (4.107 to NC)	3.88 (2.858 to 9.626)	14.95 (4.830 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.626 to NC)	NC (14.949 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1513		0.1664	
Hazard ratio (95% CI) vs Pd	-	0.75 (0.50 to 1.11)		0.71 (0.43 to 1.16)	
P-value	-	0.1527		0.1682	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (13.6)	6 (6.5)	1 (1.5)	4 (6.6)	0.0919
Number (%) of patients censored	76 (86.4)	87 (93.5)	64 (98.5)	57 (93.4)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (12.057 to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1096		0.2825	
Hazard ratio (95% CI) vs Pd	-	0.46 (0.17 to 1.22)		3.13 (0.35 to 28.20)	
P-value	-	0.1188		0.3080	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Constipation
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (18.2)	14 (15.1)	15 (23.1)	11 (18.0)	0.6567
Number (%) of patients censored	72 (81.8)	79 (84.9)	50 (76.9)	50 (82.0)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (4.271 to NC)	NC (10.021 to NC)	14.69 (1.938 to NC)	NC (6.899 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4961		0.1899	
Hazard ratio (95% CI) vs Pd	-	0.78 (0.38 to 1.60)		0.60 (0.27 to 1.30)	
P-value	-	0.4972		0.1948	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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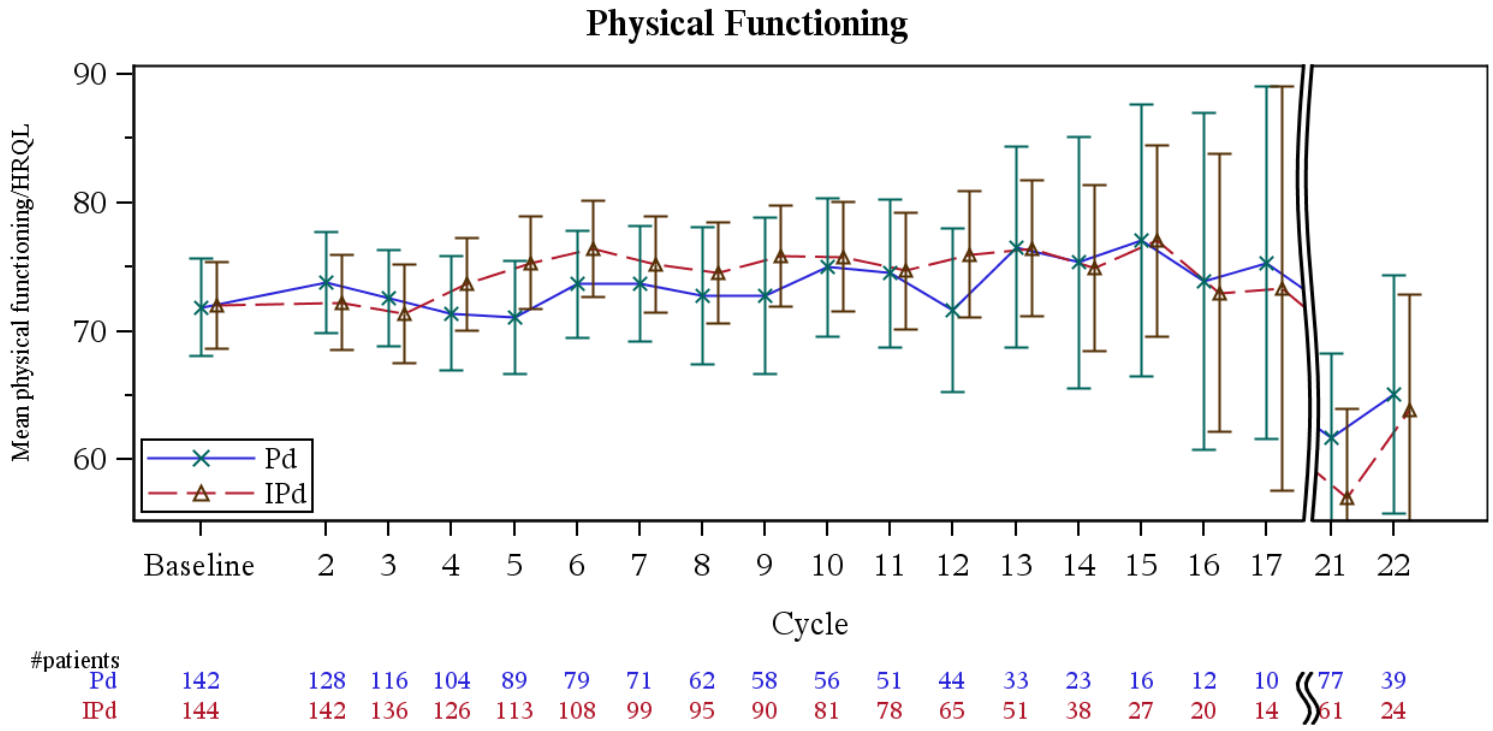
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Physical functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-C30 - Mean and 95% CI for physical functioning score over time (LOCF) - ITT population



A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Physical functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-C30 - Time to first improvement by 15 pt in physical functioning (LOCF) - ITT population

First improvement 15 points Physical functioning (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	30 (19.6)	37 (24.0)
Number (%) of patients censored	123 (80.4)	117 (76.0)
Kaplan-Meier estimates of physical functioning in months		
25% quantile (95% CI)	NC (3.910 to NC)	11.40 (3.220 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4813
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.19 (0.73 to 1.93)
P-value	-	0.4818
Probability (95% CI)[c]		
2 Months	0.12 (0.076 to 0.182)	0.16 (0.111 to 0.228)
4 Months	0.18 (0.123 to 0.249)	0.21 (0.152 to 0.282)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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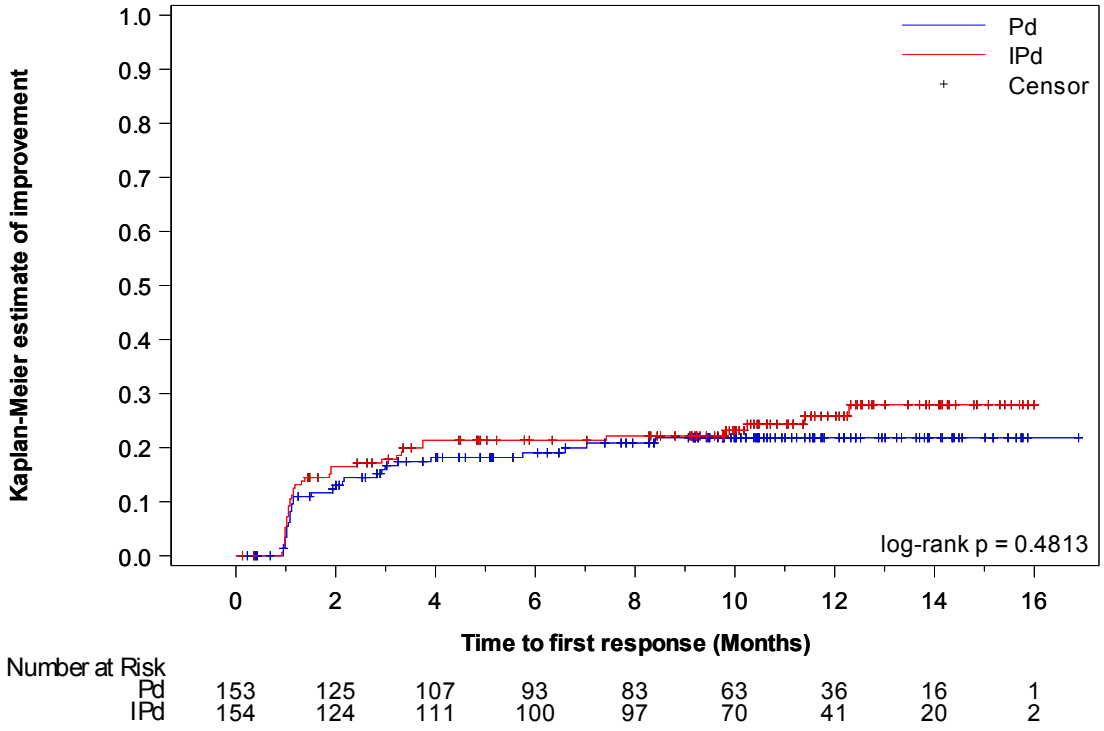
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Physical functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-C30 - Time to first improvement by 15 pt in physical functioning - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_imp15l_de_i_f_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Physical functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-C30 - Time to first deterioration by 15 pt in physical functioning (LOCF) - ITT population

First deterioration 15 points Physical functioning (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	67 (43.8)	74 (48.1)
Number (%) of patients censored	86 (56.2)	80 (51.9)
Kaplan-Meier estimates of physical functioning in months		
25% quantile (95% CI)	2.83 (1.938 to 3.778)	2.89 (1.938 to 4.435)
Median (95% CI)	11.99 (5.618 to NC)	10.12 (6.702 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (15.244 to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.7695
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.95 (0.68 to 1.33)
P-value	-	0.7693
Probability (95% CI)[c]		
2 Months	0.81 (0.733 to 0.863)	0.79 (0.721 to 0.851)
4 Months	0.66 (0.577 to 0.733)	0.70 (0.616 to 0.765)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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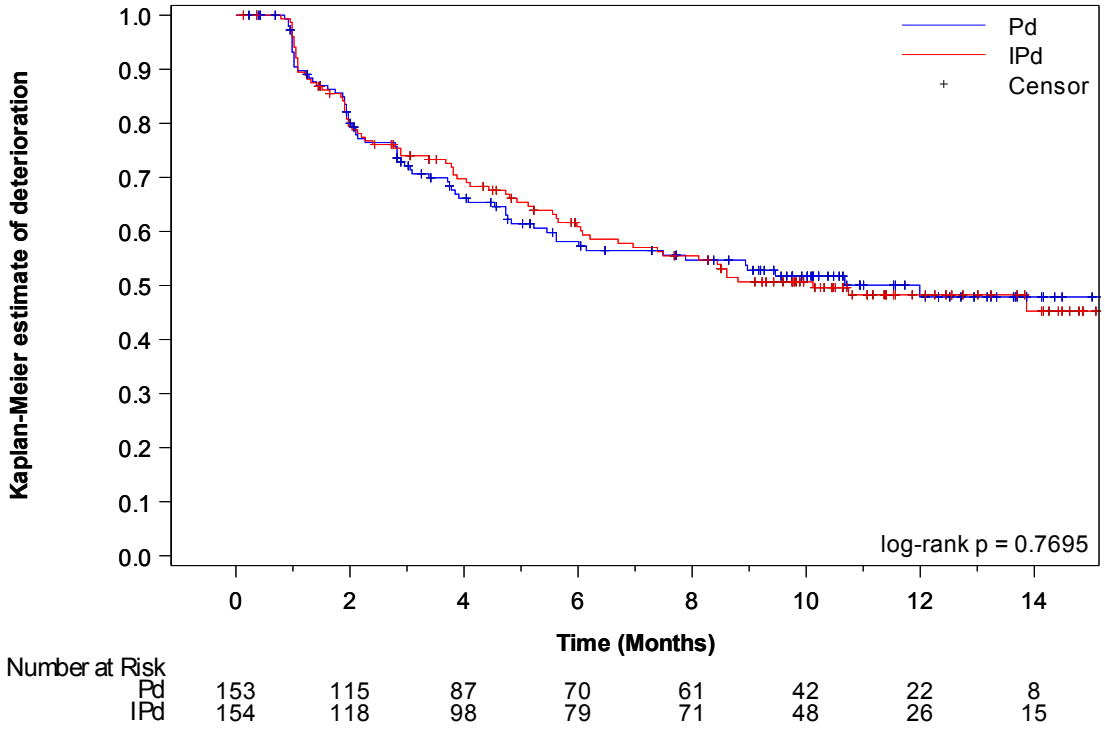
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Physical functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-C30 - Time to first deterioration by 15 pt in physical functioning - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_det15l_de_i_f_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Physical functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in physical functioning (LOCF) - ITT population

First permanent improvement 15 points Physical functioning (%)	Pd (N=153)	IPd (N=154)
Number (%) of events	9 (5.9)	14 (9.1)
Number (%) of patients censored	144 (94.1)	140 (90.9)
Kaplan-Meier estimates of physical functioning in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3992
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.43 (0.62 to 3.31)
P-value	-	0.4017
Probability (95% CI)[c]		
2 Months	0.01 (0.003 to 0.044)	0.03 (0.009 to 0.062)
4 Months	0.02 (0.006 to 0.055)	0.04 (0.016 to 0.080)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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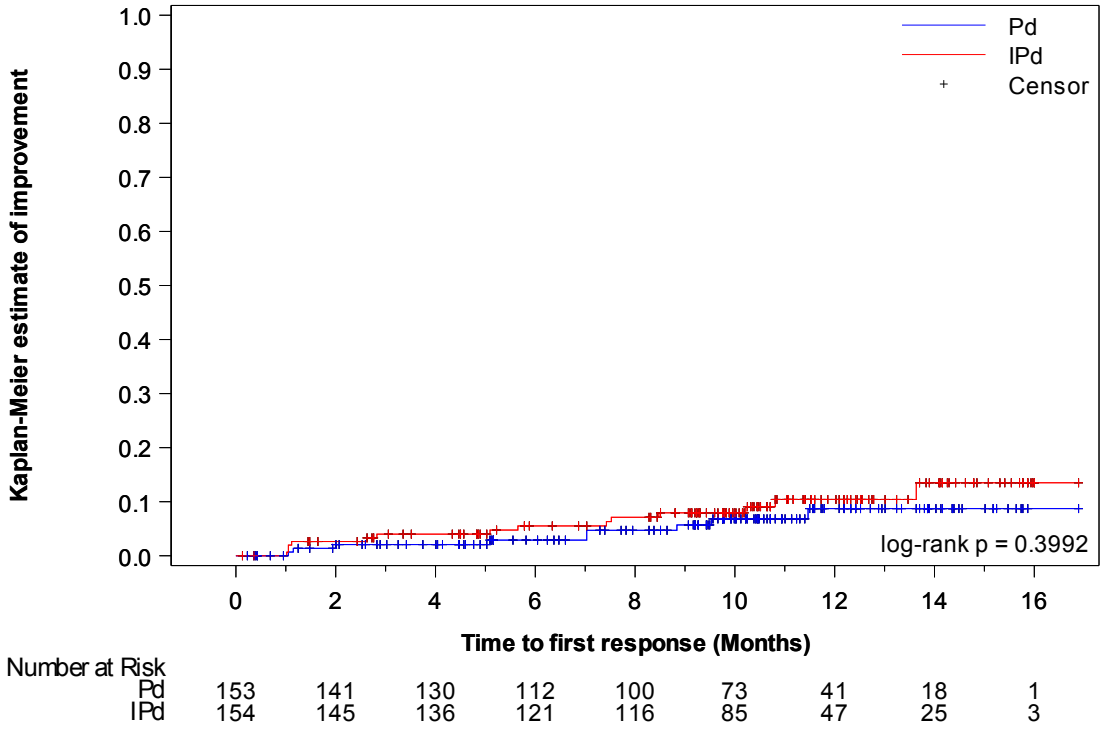
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Physical functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-C30 - Time until permanent improvement by 15 pt in physical functioning - Kaplan-Meier curve (LOCF) - ITT population



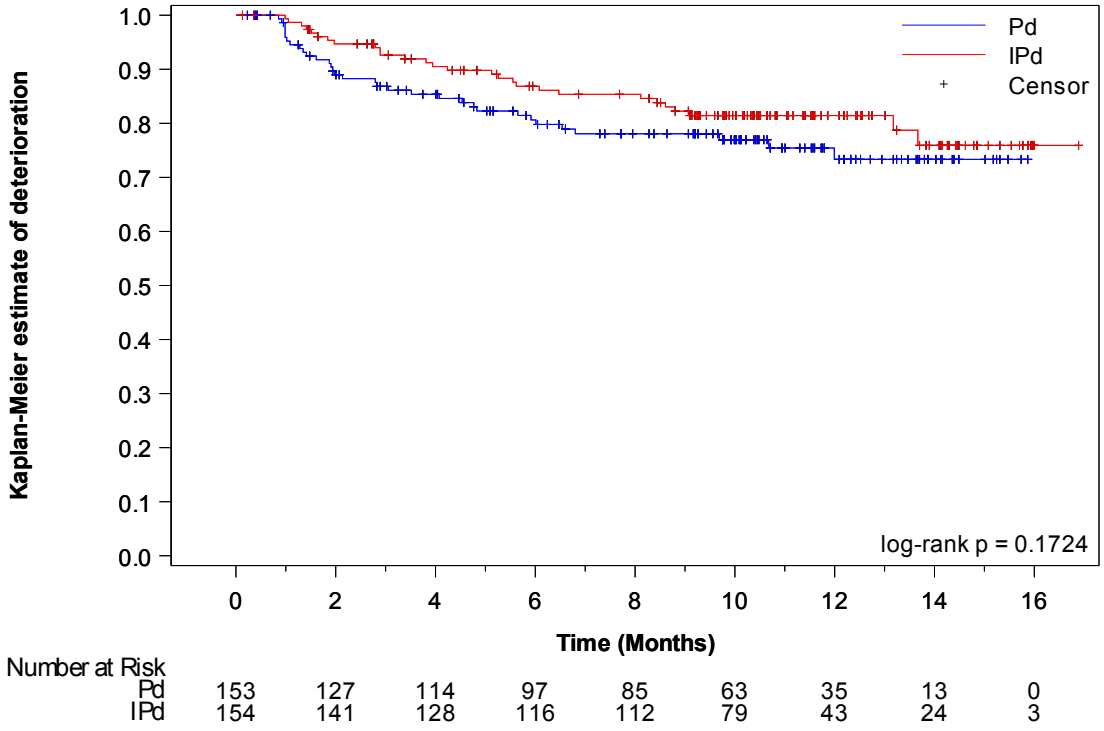
A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_imp15pl_de_i_f_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Physical functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in physical functioning (LOCF) - ITT population

First permanent deterioration 15 points Physical functioning (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	33 (21.6)	28 (18.2)
Number (%) of patients censored	120 (78.4)	126 (81.8)
Kaplan-Meier estimates of physical functioning in months		
25% quantile (95% CI)	11.99 (4.830 to NC)	NC (8.805 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1724
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.70 (0.42 to 1.17)
P-value	-	0.1746
Probability (95% CI)[c]		
2 Months	0.89 (0.826 to 0.931)	0.95 (0.897 to 0.973)
4 Months	0.85 (0.784 to 0.902)	0.91 (0.845 to 0.943)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_det15pl_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Physical functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-C30 - Time until permanent deterioration by 15 pt in physical functioning - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_det15pl_de_i_f_x.rtf (08APR2021 15:30)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (30.0)	21 (38.9)	12 (22.2)	29 (42.6)	6 (20.7)	14 (43.8)	0.4796
Number (%) of patients censored	49 (70.0)	33 (61.1)	42 (77.8)	39 (57.4)	23 (79.3)	18 (56.3)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	1.94 (1.051 to NC)	2.23 (1.051 to 8.706)	NC (1.084 to NC)	1.91 (1.084 to 4.304)	NC (1.018 to NC)	1.82 (0.986 to 3.515)	
Median (95% CI)	NC (NC to NC)	NC (7.425 to NC)	NC (NC to NC)	NC (7.392 to NC)	NC (NC to NC)	NC (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4939		0.0453		0.1086	
Hazard ratio (95% CI) vs Pd	-	1.23 (0.67 to 2.26)		1.96 (1.00 to 3.85)		2.15 (0.82 to 5.60)	
P-value	-	0.4947		0.0496		0.1175	
Hazard ratio inverted (95% CI) vs IPd		-		0.51 (0.26 to 1.00)		0.47 (0.18 to 1.21)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_impl_age_de_i_t_x.rtf (08APR2021 14:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (47.1)	29 (53.7)	28 (51.9)	39 (57.4)	21 (72.4)	23 (71.9)	0.1424
Number (%) of patients censored	37 (52.9)	25 (46.3)	26 (48.1)	29 (42.6)	8 (27.6)	9 (28.1)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	2.14 (1.413 to 4.107)	2.04 (1.018 to 3.778)	2.04 (1.610 to 2.957)	1.91 (1.084 to 2.793)	1.02 (0.953 to 1.183)	1.92 (1.084 to 3.285)	
Median (95% CI)	9.10 (4.435 to NC)	7.49 (3.581 to NC)	5.22 (2.957 to NC)	5.55 (2.891 to 10.119)	2.04 (1.018 to 4.698)	4.73 (1.971 to 8.969)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.010 to NC)	NC (NC to NC)	NC (10.119 to NC)	5.78 (3.384 to NC)	9.72 (5.224 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6096		0.6699		0.0311	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.69 to 1.88)		1.11 (0.68 to 1.81)		0.51 (0.27 to 0.95)	
P-value	-	0.6099		0.6700		0.0341	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detl_age_de_i_t_x.rtf (08APR2021 14:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (12.9)	10 (18.5)	3 (5.6)	10 (14.7)	0 (0.0)	4 (12.5)	0.7792
Number (%) of patients censored	61 (87.1)	44 (81.5)	51 (94.4)	58 (85.3)	29 (100.0)	28 (87.5)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	NC (11.466 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (9.232 to NC)	NC (NC to NC)	NC (9.823 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4368		0.1520		0.0862	
Hazard ratio (95% CI) vs Pd	-	1.43 (0.58 to 3.51)		2.49 (0.68 to 9.05)			
P-value	-	0.4392		0.1663		0.9969	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (27.1)	20 (37.0)	16 (29.6)	14 (20.6)	13 (44.8)	12 (37.5)	0.1326
Number (%) of patients censored	51 (72.9)	34 (63.0)	38 (70.4)	54 (79.4)	16 (55.2)	20 (62.5)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	6.80 (2.825 to NC)	3.81 (2.201 to 9.331)	4.83 (1.873 to NC)	13.17 (6.439 to NC)	1.35 (0.986 to 9.331)	5.13 (1.084 to 13.667)	
Median (95% CI)	NC (14.686 to NC)	NC (9.298 to NC)	NC (11.992 to NC)	NC (NC to NC)	9.59 (1.971 to NC)	13.67 (8.476 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.593 to NC)	NC (13.667 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3650		0.1341		0.1746	
Hazard ratio (95% CI) vs Pd	-	1.34 (0.71 to 2.50)		0.58 (0.28 to 1.19)		0.58 (0.26 to 1.28)	
P-value	-	0.3667		0.1389		0.1796	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detpl_age_de_i_t_x.rtf (08APR2021 14:33)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	27 (26.7)	39 (38.2)	12 (23.1)	25 (48.1)	0.4052
Number (%) of patients censored	74 (73.3)	63 (61.8)	40 (76.9)	27 (51.9)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.99 (1.117 to NC)	1.94 (1.150 to 3.811)	6.24 (0.986 to NC)	2.17 (1.051 to 3.844)	
Median (95% CI)	NC (NC to NC)	NC (10.283 to NC)	NC (NC to NC)	10.25 (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1500		0.0319	
Hazard ratio (95% CI) vs Pd	-	1.43 (0.88 to 2.34)		2.09 (1.05 to 4.16)	
P-value	-	0.1522		0.0360	
Hazard ratio inverted (95% CI) vs IPd		-		0.48 (0.24 to 0.95)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_impl_plne_de_i_t_x.rtf (08APR2021 14:33)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	51 (50.5)	57 (55.9)	31 (59.6)	34 (65.4)	0.6635
Number (%) of patients censored	50 (49.5)	45 (44.1)	21 (40.4)	18 (34.6)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.04 (1.051 to 2.825)	1.91 (1.216 to 2.793)	1.97 (1.018 to 2.825)	1.97 (1.084 to 3.778)	
Median (95% CI)	5.78 (4.107 to NC)	5.29 (3.581 to 10.119)	4.73 (2.136 to 7.885)	6.70 (3.384 to 9.725)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.979 to NC)	13.01 (8.706 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7143		0.7100	
Hazard ratio (95% CI) vs Pd	-	1.07 (0.74 to 1.57)		0.91 (0.56 to 1.49)	
P-value	-	0.7146		0.7092	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detl_plne_de_i_t_x.rtf (08APR2021 14:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (7.9)	16 (15.7)	4 (7.7)	8 (15.4)	0.9557
Number (%) of patients censored	93 (92.1)	86 (84.3)	48 (92.3)	44 (84.6)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (9.823 to NC)	NC (11.466 to NC)	NC (7.491 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1232		0.3271	
Hazard ratio (95% CI) vs Pd	-	1.93 (0.82 to 4.50)		1.81 (0.54 to 6.01)	
P-value	-	0.1300		0.3342	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (27.7)	31 (30.4)	20 (38.5)	15 (28.8)	0.2306
Number (%) of patients censored	73 (72.3)	71 (69.6)	32 (61.5)	37 (71.2)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	5.59 (2.793 to NC)	7.03 (4.238 to 13.175)	4.44 (1.708 to 9.593)	9.30 (3.384 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	11.99 (5.914 to NC)	NC (13.667 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9932		0.1149	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.60 to 1.66)		0.59 (0.30 to 1.15)	
P-value	-	0.9932		0.1191	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (21.4)	37 (41.6)	24 (28.9)	27 (41.5)	0.2978
Number (%) of patients censored	55 (78.6)	52 (58.4)	59 (71.1)	38 (58.5)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (1.511 to NC)	1.94 (1.150 to 3.745)	1.45 (1.018 to NC)	2.46 (1.084 to 7.425)	
Median (95% CI)	NC (NC to NC)	NC (4.008 to NC)	NC (NC to NC)	NC (7.425 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0152		0.2883	
Hazard ratio (95% CI) vs Pd	-	2.07 (1.14 to 3.77)		1.35 (0.78 to 2.33)	
P-value	-	0.0175		0.2901	
Hazard ratio inverted (95% CI) vs IPd		-		0.74 (0.43 to 1.29)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_impl_sex_de_i_t_x.rtf (08APR2021 14:33)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (50.0)	52 (58.4)	47 (56.6)	39 (60.0)	0.6907
Number (%) of patients censored	35 (50.0)	37 (41.6)	36 (43.4)	26 (40.0)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.00 (1.281 to 2.858)	1.97 (1.117 to 2.891)	1.91 (1.018 to 2.825)	1.84 (1.084 to 2.333)	
Median (95% CI)	5.55 (3.844 to NC)	5.55 (3.811 to 9.988)	4.83 (2.957 to 9.101)	5.29 (2.891 to 8.969)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.010 to NC)	NC (9.429 to NC)	NC (8.969 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6225		0.9413	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.73 to 1.71)		0.98 (0.64 to 1.50)	
P-value	-	0.6227		0.9414	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detl_sex_de_i_t_x.rtf (08APR2021 14:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (7.1)	15 (16.9)	7 (8.4)	9 (13.8)	0.5325
Number (%) of patients censored	65 (92.9)	74 (83.1)	76 (91.6)	56 (86.2)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (8.542 to NC)	NC (NC to NC)	NC (9.232 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0876		0.4042	
Hazard ratio (95% CI) vs Pd	-	2.35 (0.86 to 6.48)		1.52 (0.56 to 4.08)	
P-value	-	0.0975		0.4076	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (28.6)	24 (27.0)	28 (33.7)	22 (33.8)	0.9878
Number (%) of patients censored	50 (71.4)	65 (73.0)	55 (66.3)	43 (66.2)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	5.91 (2.136 to NC)	9.30 (4.238 to NC)	4.73 (1.413 to 9.692)	6.97 (2.333 to 10.875)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	14.69 (10.678 to NC)	NC (10.875 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5931		0.5445	
Hazard ratio (95% CI) vs Pd	-	0.85 (0.47 to 1.54)		0.84 (0.48 to 1.47)	
P-value	-	0.5935		0.5450	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detpl_sex_de_i_t_x.rtf (08APR2021 14:33)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (26.2)	48 (40.7)	5 (26.3)	13 (54.2)	0.5913
Number (%) of patients censored	93 (73.8)	70 (59.3)	14 (73.7)	11 (45.8)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	3.78 (1.117 to NC)	1.91 (1.117 to 3.844)	1.15 (0.986 to NC)	2.23 (1.018 to 3.515)	
Median (95% CI)	NC (NC to NC)	NC (10.251 to NC)	NC (1.150 to NC)	4.30 (2.793 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.396 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0553		0.1291	
Hazard ratio (95% CI) vs Pd	-	1.54 (0.99 to 2.40)		2.19 (0.78 to 6.15)	
P-value	-	0.0572		0.1388	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_impl_race_de_i_t_x.rtf (08APR2021 14:33)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	71 (56.3)	72 (61.0)	7 (36.8)	16 (66.7)	0.2134
Number (%) of patients censored	55 (43.7)	46 (39.0)	12 (63.2)	8 (33.3)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.97 (1.281 to 2.793)	1.87 (1.117 to 1.971)	2.00 (0.953 to NC)	3.88 (1.084 to 5.552)	
Median (95% CI)	5.16 (4.074 to 5.979)	5.13 (2.891 to 8.608)	NC (2.004 to NC)	7.49 (4.107 to 9.988)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.010 to NC)	NC (NC to NC)	NC (8.246 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9413		0.1393	
Hazard ratio (95% CI) vs Pd	-	1.01 (0.73 to 1.41)		1.94 (0.79 to 4.73)	
P-value	-	0.9413		0.1465	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detl_race_de_i_t_x.rtf (08APR2021 14:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (7.9)	17 (14.4)	1 (5.3)	4 (16.7)	0.6121
Number (%) of patients censored	116 (92.1)	101 (85.6)	18 (94.7)	20 (83.3)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (1.150 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.809 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1783		0.3283	
Hazard ratio (95% CI) vs Pd	-	1.70 (0.78 to 3.71)		2.87 (0.32 to 26.08)	
P-value	-	0.1834		0.3496	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_imppl_race_de_i_t_x.rtf (08APR2021 14:33)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (31.0)	34 (28.8)	6 (31.6)	10 (41.7)	0.4787
Number (%) of patients censored	87 (69.0)	84 (71.2)	13 (68.4)	14 (58.3)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	5.22 (2.793 to 10.678)	8.71 (3.811 to NC)	4.83 (0.953 to NC)	5.55 (1.314 to 13.667)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (4.830 to NC)	13.67 (6.702 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.667 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3326		0.8968	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.50 to 1.26)		1.07 (0.38 to 3.04)	
P-value	-	0.3333		0.8974	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (50.0)	36 (26.9)	58 (44.6)	0.9862
Number (%) of patients censored	3 (100.0)	2 (50.0)	98 (73.1)	72 (55.4)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	5.01 (1.314 to NC)	3.78 (1.150 to NC)	1.94 (1.150 to 3.055)	
Median (95% CI)	NC (NC to NC)	NC (1.314 to NC)	NC (NC to NC)	NC (4.304 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.314 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3621		0.0117	
Hazard ratio (95% CI) vs Pd	-			1.70 (1.12 to 2.57)	
P-value	-	0.9981		0.0127	
Hazard ratio inverted (95% CI) vs IPd		-		0.59 (0.39 to 0.89)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	2 (50.0)	70 (52.2)	81 (62.3)	0.6162
Number (%) of patients censored	2 (66.7)	2 (50.0)	64 (47.8)	49 (37.7)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.27 (2.267 to NC)	3.29 (2.136 to NC)	2.00 (1.708 to 2.825)	1.91 (1.248 to 2.793)	
Median (95% CI)	NC (2.267 to NC)	NC (2.136 to NC)	5.59 (4.534 to NC)	5.55 (3.778 to 8.608)	
75% quantile (95% CI)	NC (2.267 to NC)	NC (2.136 to NC)	NC (NC to NC)	NC (10.119 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6949		0.3836	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.04 to 9.30)		1.15 (0.84 to 1.59)	
P-value	-	0.6985		0.3849	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detl_ethn_de_i_t_x.rtf (08APR2021 14:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	11 (8.2)	21 (16.2)	0.9998
Number (%) of patients censored	3 (100.0)	4 (100.0)	123 (91.8)	109 (83.8)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.823 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0782	
Hazard ratio (95% CI) vs Pd	-			1.90 (0.92 to 3.95)	
P-value	-			0.0834	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	41 (30.6)	41 (31.5)	1.0000
Number (%) of patients censored	3 (100.0)	4 (100.0)	93 (69.4)	89 (68.5)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	5.22 (2.793 to 10.678)	7.03 (4.665 to 10.875)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	14.69 (14.686 to NC)	NC (13.667 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.6340	
Hazard ratio (95% CI) vs Pd	-			0.90 (0.58 to 1.39)	
P-value	-			0.6335	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	12 (15.8)	17 (30.9)	7 (35.0)	16 (57.1)	1 (20.0)	4 (57.1)	4 (26.7)	10 (47.6)	15 (40.5)	17 (39.5)	0.3948
Number (%) of patients censored	64 (84.2)	38 (69.1)	13 (65.0)	12 (42.9)	4 (80.0)	3 (42.9)	11 (73.3)	11 (52.4)	22 (59.5)	26 (60.5)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (3.910 to NC)	1.31 (1.018 to NC)	1.08 (0.953 to NC)	1.48 (0.953 to 7.392)	NC (0.953 to NC)	1.15 (0.953 to 3.515)	1.15 (0.986 to NC)	2.79 (1.084 to 4.304)	1.18 (1.018 to 2.990)	2.83 (1.117 to 7.425)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.084 to NC)	8.71 (1.906 to NC)	NC (0.953 to NC)	3.52 (0.953 to NC)	NC (1.150 to NC)	9.40 (2.793 to NC)	NC (1.511 to NC)	NC (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.251 to NC)	NC (0.953 to NC)	NC (1.938 to NC)	NC (NC to NC)	NC (9.396 to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_impl_greg_de_i_t_x.rtf (08APR2021 14:33)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.0546		0.2528		0.2869		0.3086		0.6055	
Hazard ratio (95% CI) vs Pd	-	2.03 (0.97 to 4.26)		1.67 (0.69 to 4.07)		3.10 (0.35 to 27.86)		1.81 (0.57 to 5.80)		0.83 (0.42 to 1.67)	
P-value	-	0.0597		0.2580		0.3121		0.3159		0.6060	
Improvement probability (95% CI)[b]											
2 Months	0.112 (0.052 to 0.198)	0.278 (0.166 to 0.400)	0.263 (0.096 to 0.468)	0.321 (0.161 to 0.493)	0.200 (0.008 to 0.582)	0.429 (0.098 to 0.734)	0.267 (0.083 to 0.496)	0.098 (0.017 to 0.267)	0.363 (0.211 to 0.517)	0.191 (0.090 to 0.321)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Number (%) of events	41 (53.9)	29 (52.7)	14 (70.0)	16 (57.1)	2 (40.0)	5 (71.4)	5 (33.3)	14 (66.7)	20 (54.1)	27 (62.8)	0.4045
Number (%) of patients censored	35 (46.1)	26 (47.3)	6 (30.0)	12 (42.9)	3 (60.0)	2 (28.6)	10 (66.7)	7 (33.3)	17 (45.9)	16 (37.2)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	1.97 (1.018 to 2.858)	1.64 (1.051 to 2.267)	1.22 (0.986 to 3.384)	1.94 (1.018 to 4.238)	2.27 (0.986 to NC)	2.14 (1.084 to 4.731)	2.83 (1.018 to NC)	3.88 (1.084 to 6.965)	1.91 (1.051 to 2.136)	1.91 (1.051 to 2.891)	
Median (95% CI)	5.22 (4.074 to 9.101)	6.70 (2.267 to NC)	4.44 (1.216 to 9.429)	4.93 (2.793 to NC)	NC (0.986 to NC)	4.73 (1.084 to NC)	NC (2.004 to NC)	8.25 (3.877 to 9.988)	4.73 (2.037 to NC)	3.81 (1.938 to 13.010)	
75% quantile (95% CI)	NC (9.101 to NC)	NC (NC to NC)	NC (4.435 to NC)	NC (8.148 to NC)	NC (0.986 to NC)	NC (2.793 to NC)	NC (NC to NC)	9.99 (8.246 to NC)	NC (7.885 to NC)	NC (8.706 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.7066		0.3611		0.4753		0.0965		0.8386	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.57 to 1.47)		0.72 (0.35 to 1.47)		1.81 (0.35 to 9.35)		2.33 (0.83 to 6.50)		1.06 (0.59 to 1.90)	
P-value	-	0.7067		0.3633		0.4815		0.1063		0.8392	
Deterioration probability (95% CI)[b]											
2 Months	0.746 (0.628 to 0.832)	0.684 (0.541 to 0.790)	0.684 (0.428 to 0.844)	0.714 (0.509 to 0.846)	0.800 (0.204 to 0.969)	0.857 (0.334 to 0.979)	0.867 (0.564 to 0.965)	0.905 (0.670 to 0.975)	0.689 (0.509 to 0.814)	0.638 (0.473 to 0.764)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	4 (5.3)	7 (12.7)	1 (5.0)	4 (14.3)	0 (0.0)	1 (14.3)	1 (6.7)	3 (14.3)	6 (16.2)	9 (20.9)	0.8586
Number (%) of patients censored	72 (94.7)	48 (87.3)	19 (95.0)	24 (85.7)	5 (100.0)	6 (85.7)	14 (93.3)	18 (85.7)	31 (83.8)	34 (79.1)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (NC to NC)	NC (9.823 to NC)	NC (0.953 to NC)	NC (1.051 to NC)	NC (NC to NC)	NC (2.628 to NC)	NC (1.150 to NC)	NC (1.084 to NC)	NC (6.735 to NC)	13.63 (7.425 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.628 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.634 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.1422		0.3428		0.3980		0.4708		0.9816	
Hazard ratio (95% CI) vs Pd	-	2.44 (0.71 to 8.33)		2.76 (0.31 to 24.75)				2.25 (0.23 to 21.64)		1.01 (0.36 to 2.86)	
P-value	-	0.1555		0.3633		0.9984		0.4827		0.9816	
Improvement probability (95% CI)[b]											
2 Months	0.014 (0.001 to 0.067)	0.074 (0.024 to 0.163)	0.053 (0.004 to 0.214)	0.071 (0.013 to 0.204)			0.067 (0.004 to 0.260)	0.048 (0.003 to 0.197)	0.056 (0.010 to 0.163)	0.048 (0.009 to 0.142)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	23 (30.3)	16 (29.1)	10 (50.0)	7 (25.0)	0 (0.0)	1 (14.3)	4 (26.7)	8 (38.1)	11 (29.7)	14 (32.6)	0.5159
Number (%) of patients censored	53 (69.7)	39 (70.9)	10 (50.0)	21 (75.0)	5 (100.0)	6 (85.7)	11 (73.3)	13 (61.9)	26 (70.3)	29 (67.4)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	5.55 (2.858 to 10.678)	8.48 (1.840 to NC)	1.22 (0.986 to 9.593)	7.46 (1.018 to NC)	NC (NC to NC)	NC (4.731 to NC)	5.91 (1.971 to NC)	6.97 (1.314 to 13.667)	2.14 (1.347 to NC)	8.61 (3.778 to NC)	
Median (95% CI)	NC (10.678 to NC)	NC (13.175 to NC)	11.99 (1.216 to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.731 to NC)	NC (4.830 to NC)	NC (6.965 to NC)	14.69 (14.686 to NC)	NC (9.298 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.667 to NC)	NC (14.686 to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.7801		0.0549		0.3980		0.8325		0.6242	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.48 to 1.73)		0.40 (0.15 to 1.05)				1.14 (0.33 to 4.00)		0.82 (0.37 to 1.81)	
P-value	-	0.7802		0.0637		0.9984		0.8326		0.6247	
Deterioration probability (95% CI)[b]											

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detpl_greg_de_i_t_x.rtf (08APR2021 14:33)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (17.5)	25 (32.5)	22 (39.3)	39 (50.6)	0.2523
Number (%) of patients censored	80 (82.5)	52 (67.5)	34 (60.7)	38 (49.4)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (3.778 to NC)	1.94 (1.084 to NC)	1.12 (0.986 to 2.136)	2.17 (1.117 to 3.055)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.136 to NC)	9.40 (3.844 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0382		0.4752	
Hazard ratio (95% CI) vs Pd	-	1.90 (1.02 to 3.51)		1.21 (0.72 to 2.04)	
P-value	-	0.0416		0.4759	
Hazard ratio inverted (95% CI) vs IPd		-		0.83 (0.49 to 1.39)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_impl_rreg_de_i_t_x.rtf (08APR2021 14:33)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	52 (53.6)	42 (54.5)	30 (53.6)	49 (63.6)	0.4428
Number (%) of patients censored	45 (46.4)	35 (45.5)	26 (46.4)	28 (36.4)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.97 (1.084 to 2.825)	1.94 (1.117 to 2.891)	1.97 (1.051 to 2.825)	1.91 (1.084 to 2.891)	
Median (95% CI)	5.22 (3.844 to 7.885)	6.70 (3.285 to NC)	5.09 (2.825 to NC)	5.55 (3.581 to 8.608)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.969 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6776		0.5155	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.61 to 1.38)		1.16 (0.74 to 1.83)	
P-value	-	0.6787		0.5159	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (7.2)	10 (13.0)	5 (8.9)	14 (18.2)	0.8171
Number (%) of patients censored	90 (92.8)	67 (87.0)	51 (91.1)	63 (81.8)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (10.809 to NC)	NC (NC to NC)	NC (8.936 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2875		0.1724	
Hazard ratio (95% CI) vs Pd	-	1.68 (0.64 to 4.41)		2.01 (0.72 to 5.57)	
P-value	-	0.2929		0.1811	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (27.8)	23 (29.9)	21 (37.5)	23 (29.9)	0.3406
Number (%) of patients censored	70 (72.2)	54 (70.1)	35 (62.5)	54 (70.1)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	5.59 (2.858 to NC)	8.48 (3.285 to NC)	4.44 (1.347 to 9.593)	8.61 (4.665 to NC)	
Median (95% CI)	NC (NC to NC)	NC (13.175 to NC)	14.69 (9.593 to NC)	NC (13.667 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9523		0.1523	
Hazard ratio (95% CI) vs Pd	-	0.98 (0.56 to 1.71)		0.65 (0.36 to 1.18)	
P-value	-	0.9523		0.1554	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (23.4)	56 (40.6)	7 (43.8)	8 (50.0)	0.5441
Number (%) of patients censored	105 (76.6)	82 (59.4)	9 (56.3)	8 (50.0)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	6.24 (1.446 to NC)	2.76 (1.478 to 3.811)	0.99 (0.953 to 2.004)	0.99 (0.296 to 1.084)	
Median (95% CI)	NC (NC to NC)	NC (10.251 to NC)	NC (0.986 to NC)	11.14 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.138 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0124		0.7887	
Hazard ratio (95% CI) vs Pd	-	1.73 (1.12 to 2.67)		1.15 (0.41 to 3.21)	
P-value	-	0.0135		0.7889	
Hazard ratio inverted (95% CI) vs IPd		-		0.87 (0.31 to 2.43)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	74 (54.0)	85 (61.6)	8 (50.0)	6 (37.5)	0.4975
Number (%) of patients censored	63 (46.0)	53 (38.4)	8 (50.0)	10 (62.5)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.00 (1.281 to 2.825)	1.94 (1.281 to 2.333)	1.35 (0.986 to 2.793)	1.31 (0.986 to NC)	
Median (95% CI)	5.22 (4.435 to 7.885)	5.55 (3.811 to 8.608)	4.83 (1.018 to NC)	NC (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.010 to NC)	NC (4.830 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7234		0.5296	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.77 to 1.44)		0.71 (0.25 to 2.06)	
P-value	-	0.7238		0.5315	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (7.3)	18 (13.0)	2 (12.5)	6 (37.5)	0.4227
Number (%) of patients censored	127 (92.7)	120 (87.0)	14 (87.5)	10 (62.5)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (2.004 to NC)	2.63 (0.296 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.092 to NC)	NC (2.628 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.823 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1872		0.1208	
Hazard ratio (95% CI) vs Pd	-	1.67 (0.77 to 3.62)		3.35 (0.67 to 16.89)	
P-value	-	0.1921		0.1426	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (29.9)	43 (31.2)	7 (43.8)	3 (18.8)	0.1671
Number (%) of patients censored	96 (70.1)	95 (68.8)	9 (56.3)	13 (81.3)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	5.59 (2.858 to 10.678)	7.03 (4.665 to 10.875)	1.41 (0.986 to 4.830)	13.17 (1.051 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (1.347 to NC)	NC (13.175 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.830 to NC)	NC (13.175 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6682		0.1617	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.59 to 1.40)		0.39 (0.10 to 1.52)	
P-value	-	0.6675		0.1769	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (21.6)	20 (31.3)	11 (19.6)	26 (49.1)	16 (37.2)	18 (52.9)	0.3341
Number (%) of patients censored	40 (78.4)	44 (68.8)	45 (80.4)	27 (50.9)	27 (62.8)	16 (47.1)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	NC (1.084 to NC)	7.39 (1.906 to NC)	NC (1.051 to NC)	1.31 (1.051 to 3.515)	1.25 (0.986 to 3.910)	1.08 (0.986 to 2.168)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	10.28 (3.220 to NC)	NC (2.136 to NC)	3.98 (1.380 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.251 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3027		0.0037		0.3358	
Hazard ratio (95% CI) vs Pd	-	1.47 (0.70 to 3.07)		2.73 (1.35 to 5.53)		1.39 (0.71 to 2.73)	
P-value	-	0.3057		0.0053		0.3380	
Hazard ratio inverted (95% CI) vs IPd		-		0.37 (0.18 to 0.74)		0.72 (0.37 to 1.41)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (56.9)	37 (57.8)	31 (55.4)	31 (58.5)	20 (46.5)	21 (61.8)	0.8620
Number (%) of patients censored	22 (43.1)	27 (42.2)	25 (44.6)	22 (41.5)	23 (53.5)	13 (38.2)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	2.86 (1.610 to 4.435)	1.87 (1.084 to 3.187)	1.94 (1.018 to 2.825)	1.91 (1.084 to 2.793)	1.74 (0.986 to 2.103)	1.97 (1.051 to 4.928)	
Median (95% CI)	5.78 (4.107 to NC)	6.83 (3.384 to NC)	5.16 (2.267 to NC)	5.55 (2.793 to 13.010)	5.09 (2.004 to NC)	7.03 (3.581 to 9.725)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.119 to NC)	NC (NC to NC)	NC (8.969 to NC)	NC (5.191 to NC)	NC (8.608 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5909		0.9840		0.7383	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.70 to 1.86)		0.99 (0.60 to 1.64)		0.90 (0.48 to 1.67)	
P-value	-	0.5911		0.9840		0.7377	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detl_seiss_de_i_t_x.rtf (08APR2021 14:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (9.8)	9 (14.1)	4 (7.1)	10 (18.9)	3 (7.0)	5 (14.7)	0.8215
Number (%) of patients censored	46 (90.2)	55 (85.9)	52 (92.9)	43 (81.1)	40 (93.0)	29 (85.3)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	NC (11.466 to NC)	NC (9.396 to NC)	NC (NC to NC)	NC (7.491 to NC)	NC (6.735 to NC)	NC (1.117 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4366		0.1156		0.4006	
Hazard ratio (95% CI) vs Pd	-	1.54 (0.52 to 4.60)		2.46 (0.77 to 7.86)		1.83 (0.44 to 7.70)	
P-value	-	0.4402		0.1281		0.4077	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (33.3)	14 (21.9)	17 (30.4)	18 (34.0)	12 (27.9)	12 (35.3)	0.6182
Number (%) of patients censored	34 (66.7)	50 (78.1)	39 (69.6)	35 (66.0)	31 (72.1)	22 (64.7)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	5.55 (2.793 to NC)	NC (4.731 to NC)	4.76 (1.183 to NC)	8.48 (3.055 to 13.175)	5.59 (1.347 to 11.992)	3.78 (1.051 to 13.667)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (10.678 to NC)	NC (10.875 to NC)	NC (5.914 to NC)	13.67 (7.031 to NC)	
75% quantile (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.667 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2006		0.9102		0.9162	
Hazard ratio (95% CI) vs Pd	-	0.63 (0.31 to 1.28)		0.96 (0.50 to 1.87)		1.04 (0.47 to 2.33)	
P-value	-	0.2045		0.9101		0.9162	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (22.6)	8 (20.5)	24 (24.5)	49 (49.5)	8 (33.3)	7 (43.8)	0.2430
Number (%) of patients censored	24 (77.4)	31 (79.5)	74 (75.5)	50 (50.5)	16 (66.7)	9 (56.3)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	NC (1.018 to NC)	NC (1.906 to NC)	6.24 (1.117 to NC)	1.87 (1.084 to 2.825)	1.45 (0.953 to NC)	1.02 (0.723 to 2.825)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	10.25 (3.844 to NC)	NC (1.446 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.825 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7798		0.0017		0.6776	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.31 to 2.39)		2.15 (1.32 to 3.50)		1.24 (0.45 to 3.42)	
P-value	-	0.7800		0.0022		0.6781	
Hazard ratio inverted (95% CI) vs IPd		-		0.47 (0.29 to 0.76)		0.81 (0.29 to 2.23)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (51.6)	22 (56.4)	57 (58.2)	61 (61.6)	9 (37.5)	8 (50.0)	0.8766
Number (%) of patients censored	15 (48.4)	17 (43.6)	41 (41.8)	38 (38.4)	15 (62.5)	8 (50.0)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	2.86 (1.216 to 5.585)	1.97 (1.018 to 3.877)	1.87 (1.018 to 2.136)	1.91 (1.084 to 2.333)	2.00 (0.953 to 4.534)	1.84 (1.051 to 6.702)	
Median (95% CI)	9.10 (4.074 to NC)	8.25 (2.891 to NC)	4.73 (2.825 to 6.867)	5.29 (3.581 to 8.608)	4.53 (1.906 to NC)	6.70 (1.314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.119 to NC)	NC (NC to NC)	NC (9.725 to NC)	5.19 (4.435 to NC)	NC (6.702 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5862		0.9944		0.7739	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.63 to 2.28)		1.00 (0.70 to 1.44)		0.86 (0.32 to 2.33)	
P-value	-	0.5867		0.9944		0.7740	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (12.9)	6 (15.4)	6 (6.1)	16 (16.2)	2 (8.3)	2 (12.5)	0.6272
Number (%) of patients censored	27 (87.1)	33 (84.6)	92 (93.9)	83 (83.8)	22 (91.7)	14 (87.5)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	NC (8.838 to NC)	NC (6.965 to NC)	NC (NC to NC)	NC (9.396 to NC)	NC (0.953 to NC)	NC (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7450		0.0450		0.7326	
Hazard ratio (95% CI) vs Pd	-	1.23 (0.35 to 4.38)		2.53 (0.99 to 6.46)		1.41 (0.20 to 9.98)	
P-value	-	0.7454		0.0530		0.7338	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (25.8)	7 (17.9)	33 (33.7)	34 (34.3)	7 (29.2)	5 (31.3)	0.8842
Number (%) of patients censored	23 (74.2)	32 (82.1)	65 (66.3)	65 (65.7)	17 (70.8)	11 (68.8)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	14.69 (2.858 to NC)	NC (4.731 to NC)	4.73 (1.708 to 9.593)	6.97 (3.581 to 9.331)	4.44 (1.347 to 9.692)	3.78 (1.051 to NC)	
Median (95% CI)	14.69 (14.686 to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (13.175 to NC)	9.69 (4.435 to NC)	NC (1.840 to NC)	
75% quantile (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.914 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4158		0.6796		0.6917	
Hazard ratio (95% CI) vs Pd	-	0.66 (0.24 to 1.82)		0.90 (0.56 to 1.46)		0.79 (0.25 to 2.53)	
P-value	-	0.4191		0.6790		0.6923	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (17.4)	6 (42.9)	24 (25.3)	48 (40.7)	0.3395
Number (%) of patients censored	19 (82.6)	8 (57.1)	71 (74.7)	70 (59.3)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (0.953 to NC)	1.15 (0.296 to NC)	3.91 (1.117 to NC)	2.79 (1.183 to 3.844)	
Median (95% CI)	NC (NC to NC)	NC (1.084 to NC)	NC (NC to NC)	NC (10.251 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1180		0.0530	
Hazard ratio (95% CI) vs Pd	-	2.64 (0.74 to 9.36)		1.61 (0.99 to 2.64)	
P-value	-	0.1328		0.0553	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (39.1)	6 (42.9)	52 (54.7)	74 (62.7)	0.9141
Number (%) of patients censored	14 (60.9)	8 (57.1)	43 (45.3)	44 (37.3)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.83 (1.018 to 4.435)	1.84 (1.018 to 6.834)	1.71 (1.018 to 2.004)	1.91 (1.117 to 2.267)	
Median (95% CI)	4.44 (2.825 to NC)	6.83 (1.314 to NC)	5.45 (2.825 to NC)	5.55 (3.778 to 8.608)	
75% quantile (95% CI)	NC (4.435 to NC)	NC (3.778 to NC)	NC (NC to NC)	NC (10.119 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9739		0.6326	
Hazard ratio (95% CI) vs Pd	-	1.02 (0.36 to 2.91)		1.09 (0.76 to 1.55)	
P-value	-	0.9738		0.6327	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (13.0)	2 (14.3)	6 (6.3)	19 (16.1)	0.4552
Number (%) of patients censored	20 (87.0)	12 (85.7)	89 (93.7)	99 (83.9)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (0.953 to NC)	NC (0.296 to NC)	NC (NC to NC)	NC (9.823 to NC)	
Median (95% CI)	NC (NC to NC)	NC (8.476 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9469		0.0472	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.18 to 6.36)		2.46 (0.98 to 6.15)	
P-value	-	0.9469		0.0549	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (13.0)	5 (35.7)	31 (32.6)	35 (29.7)	0.0704
Number (%) of patients censored	20 (87.0)	9 (64.3)	64 (67.4)	83 (70.3)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (1.906 to NC)	1.84 (1.018 to NC)	2.83 (1.281 to 10.678)	8.61 (4.731 to 13.667)	
Median (95% CI)	NC (8.936 to NC)	NC (1.314 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (7.458 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0950		0.2743	
Hazard ratio (95% CI) vs Pd	-	3.19 (0.76 to 13.39)		0.76 (0.47 to 1.24)	
P-value	-	0.1138		0.2758	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (19.4)	8 (33.3)	21 (26.9)	44 (42.7)	0.7012
Number (%) of patients censored	29 (80.6)	16 (66.7)	57 (73.1)	59 (57.3)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (1.051 to NC)	1.28 (0.296 to NC)	3.78 (1.084 to NC)	2.76 (1.117 to 3.811)	
Median (95% CI)	NC (NC to NC)	NC (1.906 to NC)	NC (NC to NC)	NC (7.425 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2414		0.0891	
Hazard ratio (95% CI) vs Pd	-	1.82 (0.66 to 5.02)		1.56 (0.93 to 2.63)	
P-value	-	0.2484		0.0918	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_impl_care_de_i_t_x.rtf (20APR2021 10:48)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (50.0)	14 (58.3)	40 (51.3)	63 (61.2)	0.8757
Number (%) of patients censored	18 (50.0)	10 (41.7)	38 (48.7)	40 (38.8)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.17 (1.183 to 2.825)	1.31 (1.018 to 2.333)	1.74 (1.018 to 2.037)	1.91 (1.117 to 2.793)	
Median (95% CI)	4.44 (2.793 to NC)	3.78 (1.840 to NC)	6.14 (2.957 to NC)	6.70 (4.041 to 9.002)	
75% quantile (95% CI)	NC (4.534 to NC)	NC (3.778 to NC)	NC (NC to NC)	NC (13.010 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5779		0.5166	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.60 to 2.46)		1.14 (0.77 to 1.69)	
P-value	-	0.5786		0.5169	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (11.1)	3 (12.5)	5 (6.4)	17 (16.5)	0.3872
Number (%) of patients censored	32 (88.9)	21 (87.5)	73 (93.6)	86 (83.5)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (1.446 to NC)	NC (0.296 to NC)	NC (NC to NC)	NC (9.823 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9394		0.0653	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.24 to 4.74)		2.48 (0.91 to 6.71)	
P-value	-	0.9391		0.0748	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (25.0)	10 (41.7)	23 (29.5)	30 (29.1)	0.1720
Number (%) of patients censored	27 (75.0)	14 (58.3)	55 (70.5)	73 (70.9)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	4.76 (1.906 to NC)	3.78 (1.018 to 7.458)	2.86 (1.281 to NC)	9.10 (4.731 to 13.667)	
Median (95% CI)	NC (4.764 to NC)	8.48 (3.778 to NC)	NC (NC to NC)	NC (13.667 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2355		0.5289	
Hazard ratio (95% CI) vs Pd	-	1.71 (0.70 to 4.22)		0.84 (0.49 to 1.45)	
P-value	-	0.2411		0.5294	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (26.7)	31 (37.3)	15 (23.8)	33 (46.5)	0.4766
Number (%) of patients censored	66 (73.3)	52 (62.7)	48 (76.2)	38 (53.5)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.99 (1.084 to NC)	2.23 (1.281 to 8.706)	6.24 (1.051 to NC)	1.91 (1.084 to 3.220)	
Median (95% CI)	NC (NC to NC)	NC (10.251 to NC)	NC (NC to NC)	NC (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1911		0.0326	
Hazard ratio (95% CI) vs Pd	-	1.42 (0.84 to 2.43)		1.92 (1.04 to 3.54)	
P-value	-	0.1934		0.0358	
Hazard ratio inverted (95% CI) vs IPd		-		0.52 (0.28 to 0.96)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (54.4)	45 (54.2)	33 (52.4)	46 (64.8)	0.8426
Number (%) of patients censored	41 (45.6)	38 (45.8)	30 (47.6)	25 (35.2)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.97 (1.610 to 2.825)	1.97 (1.216 to 2.793)	1.35 (1.018 to 2.825)	1.91 (1.084 to 2.891)	
Median (95% CI)	5.45 (4.074 to NC)	5.55 (3.581 to NC)	4.83 (2.825 to NC)	5.55 (3.285 to 8.608)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.969 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9836		0.8527	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.66 to 1.49)		1.04 (0.67 to 1.63)	
P-value	-	0.9836		0.8531	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (12.2)	13 (15.7)	1 (1.6)	11 (15.5)	0.0962
Number (%) of patients censored	79 (87.8)	70 (84.3)	62 (98.4)	60 (84.5)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (11.466 to NC)	NC (8.542 to NC)	NC (NC to NC)	NC (9.823 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5114		0.0158	
Hazard ratio (95% CI) vs Pd	-	1.31 (0.59 to 2.92)		8.26 (1.06 to 64.04)	
P-value	-	0.5123		0.0434	
Hazard ratio inverted (95% CI) vs IPd		-		0.12 (0.02 to 0.94)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (32.2)	26 (31.3)	19 (30.2)	20 (28.2)	0.6299
Number (%) of patients censored	61 (67.8)	57 (68.7)	44 (69.8)	51 (71.8)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	5.55 (1.971 to 10.678)	5.55 (3.055 to 10.448)	4.83 (1.281 to 11.992)	9.33 (4.731 to 13.667)	
Median (95% CI)	14.69 (14.686 to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (13.175 to NC)	
75% quantile (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6914		0.3302	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.53 to 1.53)		0.73 (0.39 to 1.37)	
P-value	-	0.6919		0.3321	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	0 (0.0)	37 (24.5)	64 (42.1)	0.9757
Number (%) of patients censored	0 (0.0)	2 (100.0)	114 (75.5)	88 (57.9)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.08 (1.084 to 3.778)	NC (NC to NC)	5.59 (1.150 to NC)	2.00 (1.183 to 3.515)	
Median (95% CI)	2.43 (1.084 to 3.778)	NC (NC to NC)	NC (NC to NC)	NC (8.706 to NC)	
75% quantile (95% CI)	3.78 (1.084 to 3.778)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.0073	
Hazard ratio (95% CI) vs Pd	-			1.73 (1.15 to 2.59)	
P-value	-	0.9991		0.0081	
Hazard ratio inverted (95% CI) vs IPd		-		0.58 (0.39 to 0.87)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (100.0)	82 (54.3)	89 (58.6)	0.9786
Number (%) of patients censored	2 (100.0)	0 (0.0)	69 (45.7)	63 (41.4)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	4.11 (4.107 to 8.706)	1.97 (1.281 to 2.168)	1.91 (1.248 to 2.267)	
Median (95% CI)	NC (NC to NC)	6.41 (4.107 to 8.706)	5.16 (4.107 to 6.867)	5.55 (3.877 to 8.608)	
75% quantile (95% CI)	NC (NC to NC)	8.71 (4.107 to 8.706)	NC (NC to NC)	NC (13.010 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.9962	
Hazard ratio (95% CI) vs Pd	-			1.00 (0.74 to 1.35)	
P-value	-	0.9991		0.9962	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	0 (0.0)	10 (6.6)	24 (15.8)	0.9842
Number (%) of patients censored	0 (0.0)	2 (100.0)	141 (93.4)	128 (84.2)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	7.03 (7.031 to 11.466)	NC (NC to NC)	NC (NC to NC)	NC (10.809 to NC)	
Median (95% CI)	9.25 (7.031 to 11.466)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	11.47 (7.031 to 11.466)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.0244	
Hazard ratio (95% CI) vs Pd	-			2.28 (1.09 to 4.77)	
P-value	-	0.9990		0.0286	
Hazard ratio inverted (95% CI) vs IPd		-		0.44 (0.21 to 0.92)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	48 (31.8)	45 (29.6)	0.9789
Number (%) of patients censored	2 (100.0)	1 (50.0)	103 (68.2)	107 (70.4)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	8.71 (8.706 to NC)	4.83 (2.793 to 9.593)	7.46 (4.665 to 13.175)	
Median (95% CI)	NC (NC to NC)	NC (8.706 to NC)	NC (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (8.706 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.3016	
Hazard ratio (95% CI) vs Pd	-			0.81 (0.54 to 1.21)	
P-value	-	0.9991		0.3025	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (23.8)	47 (45.2)	10 (24.4)	12 (36.4)	0.1403
Number (%) of patients censored	77 (76.2)	57 (54.8)	31 (75.6)	21 (63.6)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	6.24 (1.150 to NC)	2.00 (1.183 to 3.515)	1.45 (0.986 to NC)	1.91 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (4.304 to NC)	NC (NC to NC)	NC (3.975 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0053		0.4232	
Hazard ratio (95% CI) vs Pd	-	1.99 (1.21 to 3.25)		1.41 (0.61 to 3.26)	
P-value	-	0.0063		0.4254	
Hazard ratio inverted (95% CI) vs IPd		-		0.71 (0.31 to 1.65)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	63 (62.4)	60 (57.7)	16 (39.0)	22 (66.7)	0.0336
Number (%) of patients censored	38 (37.6)	44 (42.3)	25 (61.0)	11 (33.3)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.94 (1.018 to 2.103)	1.91 (1.117 to 2.333)	2.04 (1.051 to 5.224)	1.97 (1.084 to 2.891)	
Median (95% CI)	4.67 (2.825 to 5.782)	5.55 (3.778 to 9.002)	NC (4.107 to NC)	4.11 (1.971 to 7.491)	
75% quantile (95% CI)	NC (6.867 to NC)	NC (13.010 to NC)	NC (NC to NC)	NC (5.290 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1933		0.0597	
Hazard ratio (95% CI) vs Pd	-	0.79 (0.55 to 1.13)		1.84 (0.97 to 3.51)	
P-value	-	0.1943		0.0637	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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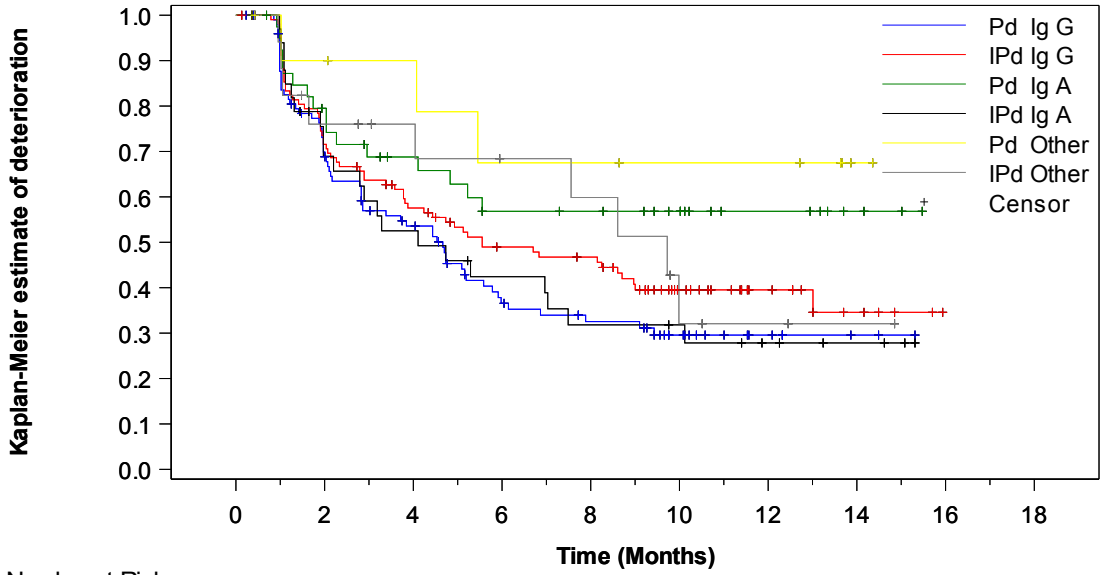
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to MM type at SE (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd Ig G	101	52	29	23	6	1	0
IPd Ig G	104	64	44	33	12	2	0
Pd Ig A	41	25	18	16	7	2	0
IPd Ig A	33	18	12	9	5	2	0
Pd Other	11	8	6	5	5	0	0
IPd Other	17	11	8	6	2	0	0

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (7.9)	17 (16.3)	2 (4.9)	5 (15.2)	0.4626
Number (%) of patients censored	93 (92.1)	87 (83.7)	39 (95.1)	28 (84.8)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (9.396 to NC)	NC (NC to NC)	NC (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1207		0.1448	
Hazard ratio (95% CI) vs Pd	-	1.92 (0.83 to 4.46)		3.17 (0.62 to 16.35)	
P-value	-	0.1275		0.1676	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.7 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (35.6)	33 (31.7)	11 (26.8)	8 (24.2)	0.3352
Number (%) of patients censored	65 (64.4)	71 (68.3)	30 (73.2)	25 (75.8)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.86 (1.873 to 9.593)	7.46 (4.665 to 13.175)	6.80 (1.610 to NC)	9.10 (1.314 to NC)	
Median (95% CI)	14.69 (10.678 to NC)	NC (13.667 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1762		0.6211	
Hazard ratio (95% CI) vs Pd	-	0.72 (0.45 to 1.16)		0.79 (0.32 to 1.98)	
P-value	-	0.1781		0.6218	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (24.0)	47 (46.1)	15 (28.8)	17 (33.3)	0.1447
Number (%) of patients censored	76 (76.0)	55 (53.9)	37 (71.2)	34 (66.7)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	6.24 (1.150 to NC)	1.97 (1.183 to 3.515)	1.45 (0.986 to NC)	2.76 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	11.14 (4.304 to NC)	NC (NC to NC)	NC (10.251 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0045		0.8767	
Hazard ratio (95% CI) vs Pd	-	2.01 (1.23 to 3.29)		1.06 (0.53 to 2.12)	
P-value	-	0.0053		0.8769	
Hazard ratio inverted (95% CI) vs IPd		-		0.95 (0.47 to 1.90)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	62 (62.0)	58 (56.9)	19 (36.5)	32 (62.7)	0.0101
Number (%) of patients censored	38 (38.0)	44 (43.1)	33 (63.5)	19 (37.3)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.91 (1.018 to 2.070)	1.92 (1.117 to 2.793)	2.96 (1.051 to 5.454)	1.97 (1.084 to 3.285)	
Median (95% CI)	4.67 (2.825 to 5.782)	5.55 (3.778 to 13.010)	NC (5.224 to NC)	5.29 (3.187 to 9.725)	
75% quantile (95% CI)	NC (6.867 to NC)	NC (13.010 to NC)	NC (NC to NC)	NC (8.608 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1735		0.0286	
Hazard ratio (95% CI) vs Pd	-	0.78 (0.54 to 1.12)		1.87 (1.06 to 3.30)	
P-value	-	0.1746		0.0312	
Hazard ratio inverted (95% CI) vs IPd		-		0.54 (0.30 to 0.95)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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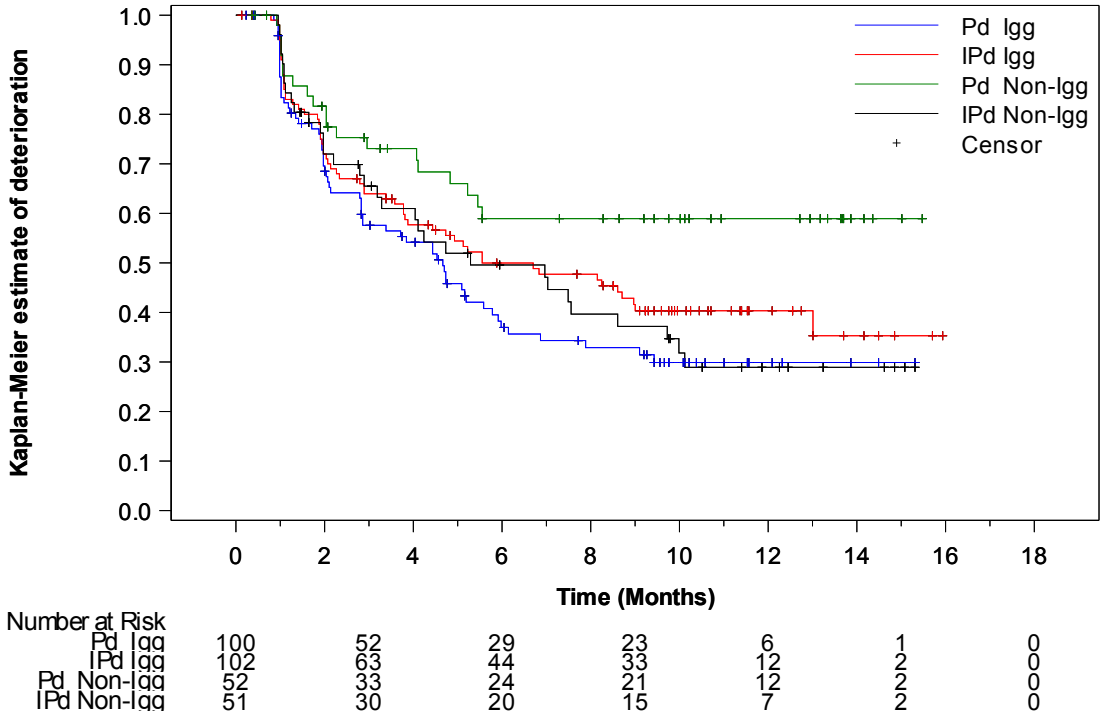
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to MM type at initial diagnosis (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd Igg	100	52	29	23	6	1	0
IPd Igg	102	63	44	33	12	2	0
Pd Non-Igg	52	33	24	21	12	2	0
IPd Non-Igg	51	30	20	15	7	2	0

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (8.0)	17 (16.7)	4 (7.7)	7 (13.7)	0.8787
Number (%) of patients censored	92 (92.0)	85 (83.3)	48 (92.3)	44 (86.3)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (9.396 to NC)	NC (NC to NC)	NC (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1159		0.3496	
Hazard ratio (95% CI) vs Pd	-	1.94 (0.84 to 4.49)		1.78 (0.52 to 6.09)	
P-value	-	0.1227		0.3563	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.7 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (36.0)	32 (31.4)	12 (23.1)	13 (25.5)	0.3941
Number (%) of patients censored	64 (64.0)	70 (68.6)	40 (76.9)	38 (74.5)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.86 (1.873 to 5.914)	8.48 (4.665 to 13.175)	9.33 (4.074 to NC)	8.61 (2.201 to NC)	
Median (95% CI)	14.69 (10.678 to NC)	NC (13.667 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1425		0.9074	
Hazard ratio (95% CI) vs Pd	-	0.70 (0.43 to 1.13)		1.05 (0.48 to 2.30)	
P-value	-	0.1446		0.9075	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	8 (57.1)	38 (26.6)	56 (40.0)	0.2443
Number (%) of patients censored	9 (90.0)	6 (42.9)	105 (73.4)	84 (60.0)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (0.953 to NC)	1.91 (1.084 to 3.844)	3.78 (1.150 to NC)	2.17 (1.150 to 3.745)	
Median (95% CI)	NC (0.953 to NC)	3.84 (1.906 to NC)	NC (NC to NC)	NC (10.251 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (3.844 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0700		0.0486	
Hazard ratio (95% CI) vs Pd	-	5.52 (0.69 to 44.20)		1.51 (1.00 to 2.28)	
P-value	-	0.1075		0.0502	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_impl_mri_de_i_t_x.rtf (08APR2021 14:33)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (60.0)	10 (71.4)	76 (53.1)	81 (57.9)	0.1550
Number (%) of patients censored	4 (40.0)	4 (28.6)	67 (46.9)	59 (42.1)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.02 (0.920 to 1.741)	1.84 (0.986 to 6.834)	2.04 (1.610 to 2.825)	1.94 (1.248 to 2.267)	
Median (95% CI)	1.74 (0.920 to NC)	6.83 (1.314 to 13.010)	5.45 (4.435 to 9.429)	5.55 (3.877 to 8.969)	
75% quantile (95% CI)	NC (1.281 to NC)	13.01 (6.834 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1558		0.7326	
Hazard ratio (95% CI) vs Pd	-	0.45 (0.15 to 1.39)		1.06 (0.77 to 1.44)	
P-value	-	0.1655		0.7327	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detl_mri_de_i_t_x.rtf (08APR2021 14:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	2 (14.3)	11 (7.7)	22 (15.7)	0.5551
Number (%) of patients censored	9 (90.0)	12 (85.7)	132 (92.3)	118 (84.3)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (0.953 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (10.809 to NC)	
Median (95% CI)	NC (0.953 to NC)	NC (8.542 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8830		0.0565	
Hazard ratio (95% CI) vs Pd	-	0.83 (0.07 to 9.55)		1.99 (0.97 to 4.11)	
P-value	-	0.8831		0.0615	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (50.0)	6 (42.9)	43 (30.1)	40 (28.6)	0.1456
Number (%) of patients censored	5 (50.0)	8 (57.1)	100 (69.9)	100 (71.4)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.28 (0.920 to 2.858)	8.61 (1.314 to NC)	5.59 (2.858 to 10.678)	7.46 (4.731 to 13.667)	
Median (95% CI)	2.86 (0.920 to NC)	NC (3.581 to NC)	NC (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.938 to NC)	NC (9.331 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0454		0.4783	
Hazard ratio (95% CI) vs Pd	-	0.25 (0.06 to 1.08)		0.86 (0.56 to 1.32)	
P-value	-	0.0627		0.4782	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (24.0)	34 (39.1)	15 (30.6)	27 (49.1)	0.9320
Number (%) of patients censored	73 (76.0)	53 (60.9)	34 (69.4)	28 (50.9)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (1.084 to NC)	3.06 (1.873 to 7.392)	2.14 (1.018 to NC)	1.31 (1.018 to 2.825)	
Median (95% CI)	NC (NC to NC)	NC (9.396 to NC)	NC (6.242 to NC)	10.28 (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0822		0.1209	
Hazard ratio (95% CI) vs Pd	-	1.59 (0.94 to 2.70)		1.64 (0.87 to 3.09)	
P-value	-	0.0850		0.1247	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (50.0)	52 (59.8)	30 (61.2)	36 (65.5)	0.3527
Number (%) of patients censored	48 (50.0)	35 (40.2)	19 (38.8)	19 (34.5)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.04 (1.281 to 2.957)	1.91 (1.117 to 2.793)	1.94 (0.986 to 2.793)	1.91 (1.117 to 3.187)	
Median (95% CI)	5.98 (4.107 to NC)	6.97 (3.384 to 9.988)	4.70 (2.103 to 5.454)	4.44 (3.187 to 8.608)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.010 to NC)	NC (5.224 to NC)	NC (8.608 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3915		0.6127	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.80 to 1.76)		0.88 (0.54 to 1.43)	
P-value	-	0.3914		0.6130	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detl_crcl_de_i_t_x.rtf (08APR2021 14:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (9.4)	13 (14.9)	2 (4.1)	8 (14.5)	0.3760
Number (%) of patients censored	87 (90.6)	74 (85.1)	47 (95.9)	47 (85.5)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (9.823 to NC)	NC (NC to NC)	NC (7.491 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3396		0.0982	
Hazard ratio (95% CI) vs Pd	-	1.51 (0.64 to 3.53)		3.42 (0.73 to 16.11)	
P-value	-	0.3430		0.1201	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_imppl_crcl_de_i_t_x.rtf (08APR2021 14:33)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (28.1)	25 (28.7)	18 (36.7)	19 (34.5)	0.6774
Number (%) of patients censored	69 (71.9)	62 (71.3)	31 (63.3)	36 (65.5)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	6.80 (2.136 to NC)	8.71 (3.811 to NC)	4.53 (1.873 to 5.914)	7.03 (1.971 to 13.667)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	11.99 (5.585 to NC)	NC (9.331 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7053		0.3851	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.52 to 1.55)		0.75 (0.39 to 1.44)	
P-value	-	0.7055		0.3867	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detpl_crcl_de_i_t_x.rtf (08APR2021 14:33)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (100.0)	39 (25.8)	62 (40.8)	0.9786
Number (%) of patients censored	2 (100.0)	0 (0.0)	112 (74.2)	90 (59.2)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	1.91 (1.906 to 3.975)	3.78 (1.150 to NC)	2.17 (1.183 to 3.745)	
Median (95% CI)	NC (NC to NC)	2.94 (1.906 to 3.975)	NC (NC to NC)	NC (10.251 to NC)	
75% quantile (95% CI)	NC (NC to NC)	3.98 (1.906 to 3.975)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.0255	
Hazard ratio (95% CI) vs Pd	-			1.57 (1.05 to 2.35)	
P-value	-	0.9991		0.0268	
Hazard ratio inverted (95% CI) vs IPd		-		0.64 (0.43 to 0.95)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_impl_prmab_de_i_t_x.rtf (08APR2021 14:33)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	81 (53.6)	90 (59.2)	0.8811
Number (%) of patients censored	1 (50.0)	1 (50.0)	70 (46.4)	62 (40.8)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.10 (2.103 to NC)	0.99 (0.986 to NC)	1.97 (1.281 to 2.267)	1.94 (1.281 to 2.333)	
Median (95% CI)	NC (2.103 to NC)	NC (0.986 to NC)	5.19 (4.435 to 7.885)	5.55 (4.041 to 8.608)	
75% quantile (95% CI)	NC (2.103 to NC)	NC (0.986 to NC)	NC (NC to NC)	NC (13.010 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.8455	
Hazard ratio (95% CI) vs Pd	-	1.41 (0.08 to 23.57)		1.03 (0.76 to 1.39)	
P-value	-	0.8092		0.8456	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detl_prmab_de_i_t_x.rtf (08APR2021 14:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	12 (7.9)	23 (15.1)	0.9889
Number (%) of patients censored	2 (100.0)	1 (50.0)	139 (92.1)	129 (84.9)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	5.09 (5.092 to NC)	NC (NC to NC)	NC (10.809 to NC)	
Median (95% CI)	NC (NC to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.0860	
Hazard ratio (95% CI) vs Pd	-			1.83 (0.91 to 3.67)	
P-value	-	0.9991		0.0908	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	48 (31.8)	46 (30.3)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	103 (68.2)	106 (69.7)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	4.83 (2.793 to 9.593)	7.46 (4.665 to 10.875)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.3724	
Hazard ratio (95% CI) vs Pd	-			0.83 (0.55 to 1.25)	
P-value	-			0.3731	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (24.3)	48 (40.7)	11 (28.9)	16 (44.4)	0.9774
Number (%) of patients censored	87 (75.7)	70 (59.3)	27 (71.1)	20 (55.6)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	5.59 (1.150 to NC)	2.79 (1.873 to 3.844)	2.99 (0.986 to NC)	1.23 (0.986 to 1.938)	
Median (95% CI)	NC (NC to NC)	NC (7.425 to NC)	NC (NC to NC)	NC (1.380 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0360		0.2213	
Hazard ratio (95% CI) vs Pd	-	1.64 (1.03 to 2.61)		1.61 (0.75 to 3.47)	
P-value	-	0.0379		0.2256	
Hazard ratio inverted (95% CI) vs IPd		-		0.62 (0.29 to 1.34)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	61 (53.0)	73 (61.9)	21 (55.3)	18 (50.0)	0.3930
Number (%) of patients censored	54 (47.0)	45 (38.1)	17 (44.7)	18 (50.0)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.04 (1.413 to 2.858)	1.91 (1.117 to 2.793)	1.61 (0.986 to 2.070)	2.04 (1.117 to 3.581)	
Median (95% CI)	5.45 (4.435 to 9.101)	5.55 (3.811 to 8.608)	4.44 (1.971 to NC)	7.03 (2.267 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.119 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5957		0.5332	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.78 to 1.54)		0.82 (0.44 to 1.54)	
P-value	-	0.5968		0.5343	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (7.8)	16 (13.6)	3 (7.9)	8 (22.2)	0.3835
Number (%) of patients censored	106 (92.2)	102 (86.4)	35 (92.1)	28 (77.8)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (10.809 to NC)	NC (6.735 to NC)	NC (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2857		0.0919	
Hazard ratio (95% CI) vs Pd	-	1.56 (0.69 to 3.52)		2.97 (0.79 to 11.19)	
P-value	-	0.2896		0.1084	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (31.3)	37 (31.4)	12 (31.6)	9 (25.0)	0.8202
Number (%) of patients censored	79 (68.7)	81 (68.6)	26 (68.4)	27 (75.0)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	4.83 (1.906 to 9.692)	6.97 (3.778 to 13.175)	6.80 (1.938 to NC)	9.10 (3.581 to NC)	
Median (95% CI)	NC (11.992 to NC)	NC (NC to NC)	14.69 (9.331 to NC)	NC (10.448 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5112		0.4903	
Hazard ratio (95% CI) vs Pd	-	0.86 (0.54 to 1.36)		0.74 (0.31 to 1.75)	
P-value	-	0.5116		0.4920	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (24.3)	60 (40.8)	4 (44.4)	4 (57.1)	0.9928
Number (%) of patients censored	109 (75.7)	87 (59.2)	5 (55.6)	3 (42.9)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	5.59 (1.150 to NC)	2.43 (1.314 to 3.745)	1.25 (0.986 to NC)	1.02 (0.986 to 1.117)	
Median (95% CI)	NC (NC to NC)	NC (10.251 to NC)	NC (0.986 to NC)	1.12 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.990 to NC)	NC (1.051 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0155		0.4717	
Hazard ratio (95% CI) vs Pd	-	1.66 (1.10 to 2.53)		1.66 (0.41 to 6.69)	
P-value	-	0.0166		0.4762	
Hazard ratio inverted (95% CI) vs IPd		-		0.60 (0.15 to 2.43)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	75 (52.1)	89 (60.5)	7 (77.8)	2 (28.6)	0.0864
Number (%) of patients censored	69 (47.9)	58 (39.5)	2 (22.2)	5 (71.4)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.97 (1.347 to 2.267)	1.91 (1.248 to 2.201)	2.07 (0.986 to 5.158)	4.93 (1.018 to NC)	
Median (95% CI)	5.45 (4.074 to 9.429)	5.55 (3.778 to 8.608)	5.16 (0.986 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.010 to NC)	6.14 (4.731 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5491		0.0855	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.81 to 1.49)		0.27 (0.06 to 1.33)	
P-value	-	0.5502		0.1076	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (7.6)	22 (15.0)	1 (11.1)	2 (28.6)	0.5732
Number (%) of patients censored	133 (92.4)	125 (85.0)	8 (88.9)	5 (71.4)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (10.809 to NC)	NC (6.735 to NC)	1.12 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.735 to NC)	NC (1.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0988		0.3411	
Hazard ratio (95% CI) vs Pd	-	1.82 (0.88 to 3.76)		3.04 (0.27 to 33.67)	
P-value	-	0.1039		0.3653	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (31.3)	44 (29.9)	3 (33.3)	2 (28.6)	0.9024
Number (%) of patients censored	99 (68.8)	103 (70.1)	6 (66.7)	5 (71.4)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	4.83 (2.136 to 9.331)	7.46 (4.238 to 13.175)	10.68 (0.986 to NC)	10.45 (4.928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	14.69 (0.986 to NC)	NC (4.928 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (10.448 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3734		0.6822	
Hazard ratio (95% CI) vs Pd	-	0.83 (0.55 to 1.26)		1.51 (0.21 to 10.82)	
P-value	-	0.3741		0.6842	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (25.0)	33 (35.5)	17 (26.2)	31 (50.8)	0.5048
Number (%) of patients censored	66 (75.0)	60 (64.5)	48 (73.8)	30 (49.2)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	3.91 (1.084 to NC)	2.76 (1.183 to 7.392)	3.78 (1.084 to NC)	1.91 (1.051 to 3.055)	
Median (95% CI)	NC (NC to NC)	NC (11.138 to NC)	NC (NC to NC)	8.71 (3.515 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1879		0.0301	
Hazard ratio (95% CI) vs Pd	-	1.43 (0.84 to 2.46)		1.90 (1.05 to 3.44)	
P-value	-	0.1903		0.0330	
Hazard ratio inverted (95% CI) vs IPd		-		0.53 (0.29 to 0.95)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (55.7)	56 (60.2)	33 (50.8)	35 (57.4)	0.6152
Number (%) of patients censored	39 (44.3)	37 (39.8)	32 (49.2)	26 (42.6)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.94 (1.051 to 2.136)	1.91 (1.216 to 1.971)	2.04 (1.216 to 3.384)	3.29 (1.084 to 4.731)	
Median (95% CI)	5.22 (2.825 to 9.101)	4.11 (2.267 to 8.246)	5.19 (3.844 to NC)	8.61 (4.731 to 13.010)	
75% quantile (95% CI)	NC (NC to NC)	NC (9.988 to NC)	NC (NC to NC)	NC (13.010 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6271		0.7505	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.75 to 1.61)		0.93 (0.57 to 1.49)	
P-value	-	0.6278		0.7500	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (9.1)	15 (16.1)	4 (6.2)	9 (14.8)	0.7846
Number (%) of patients censored	80 (90.9)	78 (83.9)	61 (93.8)	52 (85.2)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (9.823 to NC)	NC (11.466 to NC)	NC (8.476 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1893		0.1957	
Hazard ratio (95% CI) vs Pd	-	1.76 (0.75 to 4.16)		2.14 (0.66 to 6.94)	
P-value	-	0.1952		0.2066	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Physical functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (34.1)	26 (28.0)	18 (27.7)	20 (32.8)	0.5378
Number (%) of patients censored	58 (65.9)	67 (72.0)	47 (72.3)	41 (67.2)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	4.73 (1.938 to 8.936)	8.48 (3.055 to NC)	9.59 (1.971 to 14.686)	7.46 (4.731 to 13.667)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	14.69 (11.992 to NC)	NC (13.175 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2935		0.8572	
Hazard ratio (95% CI) vs Pd	-	0.76 (0.45 to 1.28)		0.94 (0.50 to 1.78)	
P-value	-	0.2951		0.8570	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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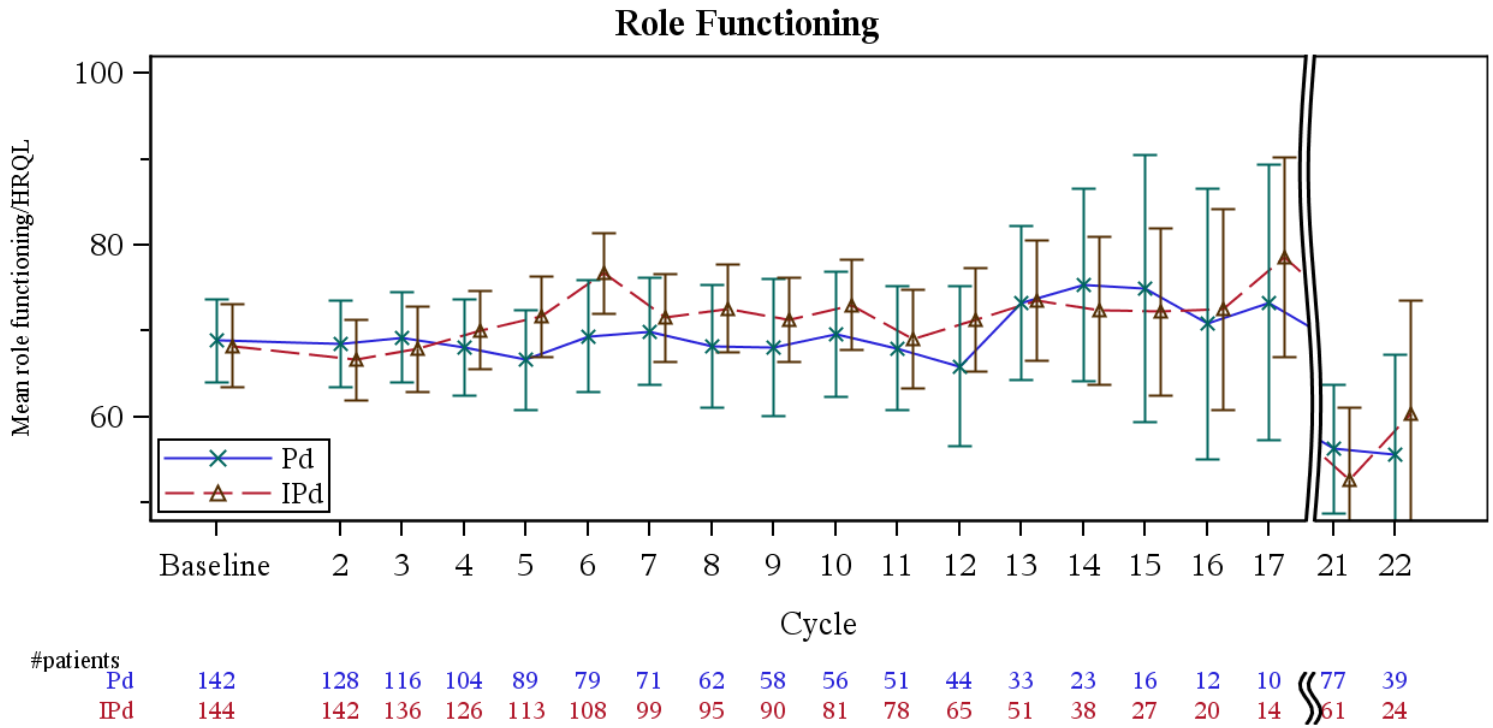
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Role functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-C30 - Mean and 95% CI for role functioning score over time (LOCF) - ITT population



A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Role functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-C30 - Time to first improvement by 15 pt in role functioning (LOCF) - ITT population

First improvement 15 points Role functioning (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	51 (33.3)	71 (46.1)
Number (%) of patients censored	102 (66.7)	83 (53.9)
Kaplan-Meier estimates of role functioning in months		
25% quantile (95% CI)	1.91 (1.117 to 5.618)	1.97 (1.380 to 2.530)
Median (95% CI)	NC (NC to NC)	13.83 (4.304 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1004
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.35 (0.94 to 1.94)
P-value	-	0.1016
Probability (95% CI)[c]		
2 Months	0.27 (0.205 to 0.349)	0.25 (0.185 to 0.323)
4 Months	0.31 (0.237 to 0.387)	0.41 (0.330 to 0.488)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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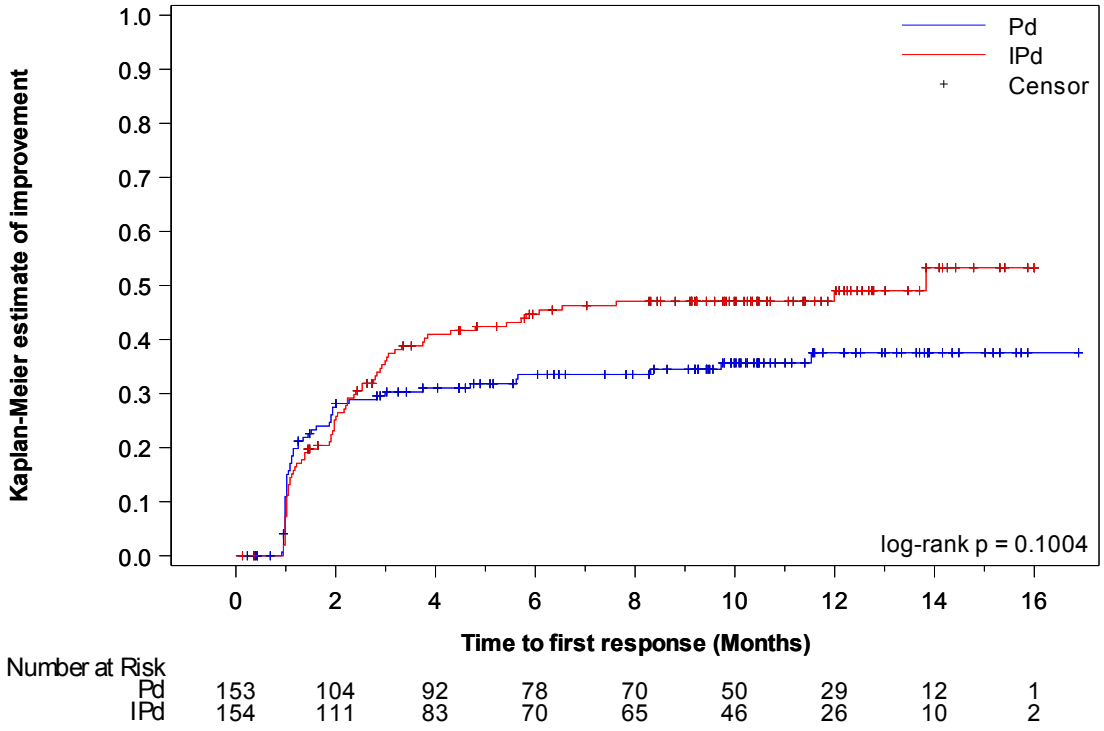
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Role functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-C30 - Time to first improvement by 15 pt in role functioning - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Role functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-C30 - Time to first deterioration by 15 pt in role functioning (LOCF) - ITT population

First deterioration 15 points Role functioning (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	96 (62.7)	94 (61.0)
Number (%) of patients censored	57 (37.3)	60 (39.0)
Kaplan-Meier estimates of role functioning in months		
25% quantile (95% CI)	1.12 (1.018 to 1.873)	1.51 (1.084 to 1.938)
Median (95% CI)	3.75 (2.793 to 4.830)	4.44 (2.891 to 6.965)
75% quantile (95% CI)	NC (9.232 to NC)	NC (12.485 to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2529
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.84 (0.63 to 1.13)
P-value	-	0.2524
Probability (95% CI)[c]		
2 Months	0.63 (0.545 to 0.702)	0.66 (0.582 to 0.732)
4 Months	0.46 (0.380 to 0.545)	0.52 (0.441 to 0.602)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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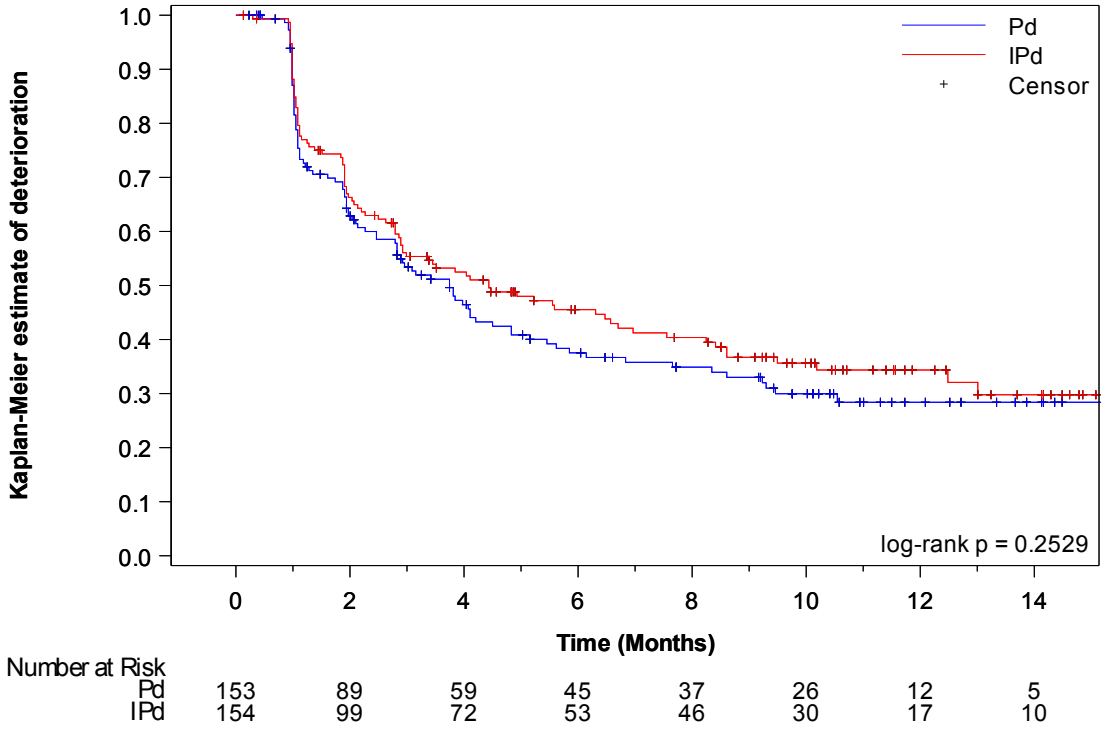
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Role functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-C30 - Time to first deterioration by 15 pt in role functioning - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Role functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in role functioning (LOCF) - ITT population

First permanent improvement 15 points Role functioning (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	19 (12.4)	23 (14.9)
Number (%) of patients censored	134 (87.6)	131 (85.1)
Kaplan-Meier estimates of role functioning in months		
25% quantile (95% CI)	NC (NC to NC)	NC (11.762 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6522
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.15 (0.63 to 2.11)
P-value	-	0.6525
Probability (95% CI)[c]		
2 Months	0.08 (0.045 to 0.134)	0.05 (0.021 to 0.088)
4 Months	0.10 (0.055 to 0.151)	0.07 (0.034 to 0.115)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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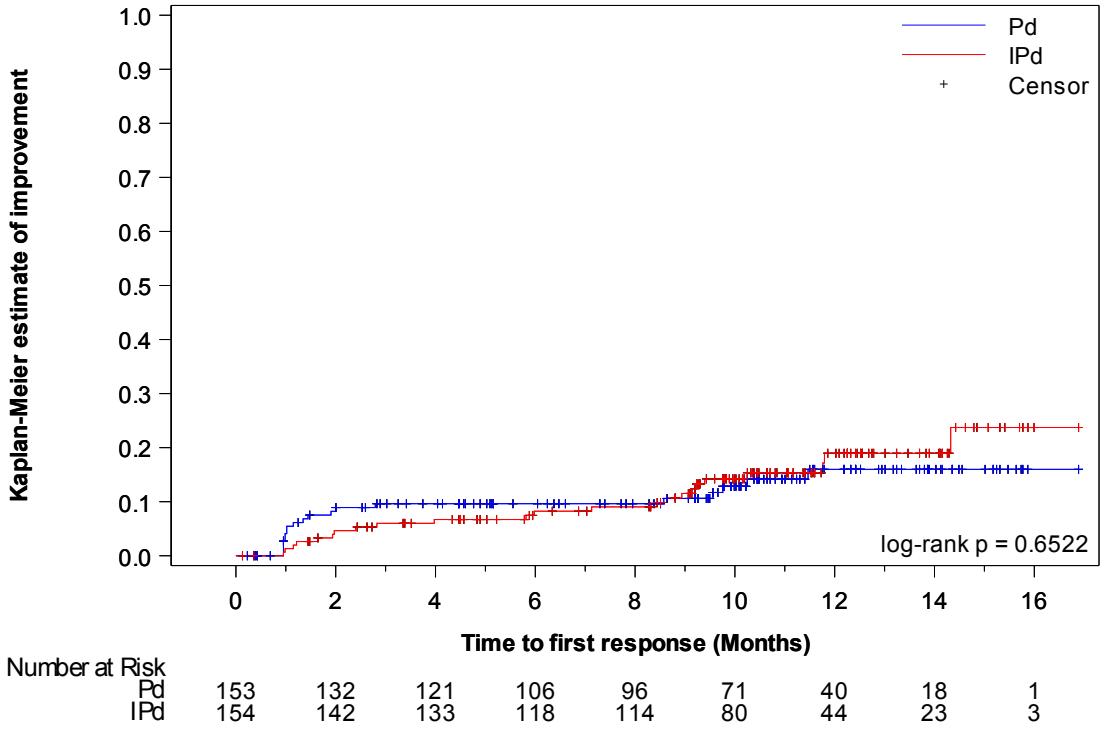
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Role functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-C30 - Time until permanent improvement by 15 pt in role functioning - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_imp15pl_de_i_f_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Role functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in role functioning (LOCF) - ITT population

First permanent deterioration 15 points Role functioning (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	60 (39.2)	37 (24.0)
Number (%) of patients censored	93 (60.8)	117 (76.0)
Kaplan-Meier estimates of role functioning in months		
25% quantile (95% CI)	2.86 (1.610 to 4.862)	9.00 (6.012 to NC)
Median (95% CI)	NC (9.462 to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0009
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.50 (0.33 to 0.76)
P-value	-	0.0011
Probability (95% CI)[c]		
2 Months	0.81 (0.734 to 0.863)	0.89 (0.833 to 0.934)
4 Months	0.70 (0.616 to 0.767)	0.86 (0.793 to 0.906)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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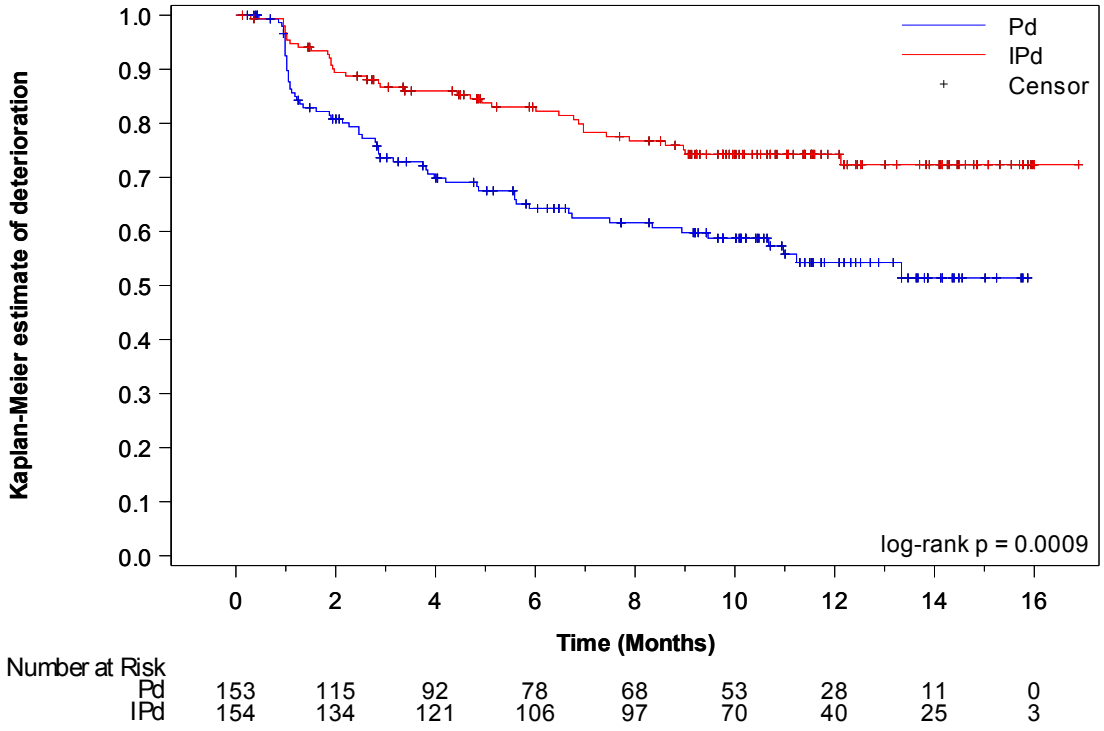
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Role functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-C30 - Time until permanent deterioration by 15 pt in role functioning - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_det15pl_de_i_f_x.rtf (08APR2021 15:30)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (34.3)	24 (44.4)	17 (31.5)	33 (48.5)	10 (34.5)	14 (43.8)	0.8578
Number (%) of patients censored	46 (65.7)	30 (55.6)	37 (68.5)	35 (51.5)	19 (65.5)	18 (56.3)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	1.66 (1.018 to 9.725)	1.91 (1.018 to 2.990)	1.51 (1.051 to NC)	2.17 (1.314 to 2.793)	1.94 (1.018 to 11.532)	2.17 (0.986 to 5.717)	
Median (95% CI)	NC (NC to NC)	NC (2.990 to NC)	NC (NC to NC)	11.99 (2.825 to NC)	11.53 (2.267 to NC)	NC (2.891 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.832 to NC)	NC (11.532 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4434		0.1395		0.6530	
Hazard ratio (95% CI) vs Pd	-	1.25 (0.71 to 2.20)		1.55 (0.86 to 2.79)		1.20 (0.53 to 2.71)	
P-value	-	0.4443		0.1427		0.6534	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (55.7)	32 (59.3)	35 (64.8)	43 (63.2)	22 (75.9)	19 (59.4)	0.0474
Number (%) of patients censored	31 (44.3)	22 (40.7)	19 (35.2)	25 (36.8)	7 (24.1)	13 (40.6)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	2.14 (1.051 to 2.924)	1.15 (0.986 to 2.070)	1.08 (0.986 to 1.741)	1.25 (0.986 to 2.136)	1.02 (0.953 to 1.084)	1.91 (1.084 to 3.515)	
Median (95% CI)	5.16 (3.745 to 10.546)	3.84 (2.070 to 13.010)	2.96 (1.741 to 4.830)	4.93 (2.267 to 8.246)	1.94 (1.018 to 3.417)	5.22 (1.971 to 12.485)	
75% quantile (95% CI)	NC (10.546 to NC)	NC (13.010 to NC)	NC (4.830 to NC)	NC (8.411 to NC)	4.11 (2.037 to NC)	12.48 (6.702 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5480		0.4905		0.0042	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.72 to 1.84)		0.85 (0.55 to 1.34)		0.41 (0.22 to 0.77)	
P-value	-	0.5484		0.4909		0.0056	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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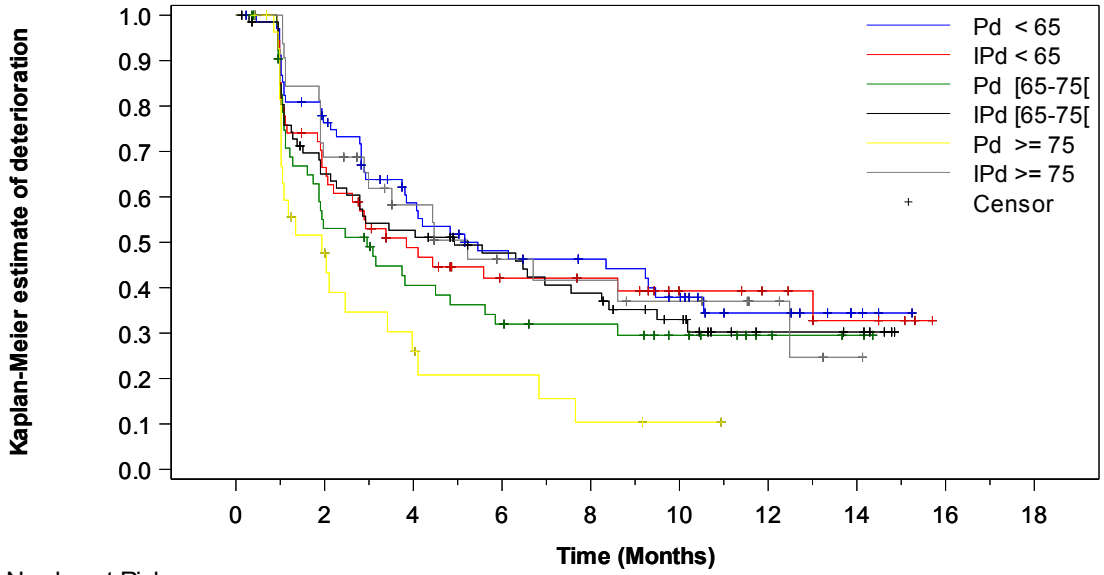
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to age (IRT) (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd < 65	70	40	26	21	8	1	0
IPd < 65	54	27	16	14	7	3	0
Pd [65-75[	54	24	15	12	4	0	0
IPd [65-75[	68	35	27	17	6	0	0
Pd >= 75	29	8	4	2	0	0	0
IPd >= 75	32	18	10	7	4	0	0

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (17.1)	8 (14.8)	6 (11.1)	11 (16.2)	1 (3.4)	4 (12.5)	0.4805
Number (%) of patients censored	58 (82.9)	46 (85.2)	48 (88.9)	57 (83.8)	28 (96.6)	28 (87.5)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	NC (8.575 to NC)	NC (9.396 to NC)	NC (9.561 to NC)	NC (9.199 to NC)	NC (NC to NC)	14.32 (7.129 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.324 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.324 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6573		0.5414		0.2843	
Hazard ratio (95% CI) vs Pd	-	0.82 (0.33 to 2.00)		1.36 (0.50 to 3.68)		3.12 (0.35 to 28.06)	
P-value	-	0.6579		0.5431		0.3097	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_imppl_age_de_i_t_x.rtf (08APR2021 14:35)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.7 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (32.9)	15 (27.8)	22 (40.7)	17 (25.0)	15 (51.7)	5 (15.6)	0.0804
Number (%) of patients censored	47 (67.1)	39 (72.2)	32 (59.3)	51 (75.0)	14 (48.3)	27 (84.4)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	5.59 (2.793 to 10.678)	6.87 (2.628 to NC)	1.87 (1.051 to 5.618)	8.97 (4.928 to NC)	1.18 (0.986 to 2.858)	NC (4.435 to NC)	
Median (95% CI)	NC (10.678 to NC)	NC (NC to NC)	NC (5.585 to NC)	NC (NC to NC)	3.98 (1.347 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.462 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4243		0.0337		0.0005	
Hazard ratio (95% CI) vs Pd	-	0.77 (0.40 to 1.47)		0.51 (0.27 to 0.96)		0.20 (0.07 to 0.55)	
P-value	-	0.4257		0.0372		0.0018	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_detpl_age_de_i_t_x.rtf (08APR2021 14:34)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	34 (33.7)	46 (45.1)	17 (32.7)	25 (48.1)	0.8276
Number (%) of patients censored	67 (66.3)	56 (54.9)	35 (67.3)	27 (51.9)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.87 (1.084 to 9.725)	1.97 (1.183 to 2.891)	2.27 (1.018 to NC)	1.97 (1.051 to 2.924)	
Median (95% CI)	NC (NC to NC)	13.83 (3.778 to NC)	NC (8.312 to NC)	7.62 (2.366 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2339		0.2618	
Hazard ratio (95% CI) vs Pd	-	1.31 (0.84 to 2.04)		1.42 (0.77 to 2.63)	
P-value	-	0.2353		0.2642	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	61 (60.4)	57 (55.9)	35 (67.3)	37 (71.2)	0.6838
Number (%) of patients censored	40 (39.6)	45 (44.1)	17 (32.7)	15 (28.8)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.18 (1.018 to 1.938)	1.91 (1.084 to 2.201)	1.05 (0.986 to 1.906)	1.10 (0.986 to 1.938)	
Median (95% CI)	3.81 (2.464 to 6.144)	5.59 (2.858 to 10.185)	3.42 (1.906 to 4.830)	2.99 (1.938 to 6.571)	
75% quantile (95% CI)	NC (9.298 to NC)	NC (NC to NC)	10.55 (4.830 to NC)	12.48 (5.552 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3444		0.7513	
Hazard ratio (95% CI) vs Pd	-	0.84 (0.59 to 1.21)		0.93 (0.58 to 1.48)	
P-value	-	0.3440		0.7509	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	13 (12.9)	17 (16.7)	6 (11.5)	6 (11.5)	0.6062
Number (%) of patients censored	88 (87.1)	85 (83.3)	46 (88.5)	46 (88.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (10.251 to NC)	NC (9.232 to NC)	NC (9.758 to NC)	14.32 (14.324 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.324 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5750		0.8470	
Hazard ratio (95% CI) vs Pd	-	1.23 (0.60 to 2.53)		0.89 (0.29 to 2.78)	
P-value	-	0.5757		0.8468	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	38 (37.6)	26 (25.5)	22 (42.3)	11 (21.2)	0.3694
Number (%) of patients censored	63 (62.4)	76 (74.5)	30 (57.7)	41 (78.8)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.89 (1.610 to 5.881)	8.97 (4.928 to NC)	2.86 (1.051 to 5.585)	NC (4.435 to NC)	
Median (95% CI)	NC (8.936 to NC)	NC (NC to NC)	11.24 (4.862 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0300		0.0085	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.35 to 0.95)		0.39 (0.19 to 0.81)	
P-value	-	0.0321		0.0112	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (25.7)	41 (46.1)	33 (39.8)	30 (46.2)	0.1048
Number (%) of patients censored	52 (74.3)	48 (53.9)	50 (60.2)	35 (53.8)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	8.31 (1.347 to NC)	1.97 (1.183 to 2.891)	1.15 (0.986 to 2.267)	2.04 (1.051 to 2.924)	
Median (95% CI)	NC (NC to NC)	11.99 (3.745 to NC)	NC (3.745 to NC)	13.83 (3.055 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.832 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0183		0.8499	
Hazard ratio (95% CI) vs Pd	-	1.93 (1.11 to 3.36)		1.05 (0.64 to 1.72)	
P-value	-	0.0205		0.8497	
Hazard ratio inverted (95% CI) vs IPd		-		0.95 (0.58 to 1.56)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (65.7)	51 (57.3)	50 (60.2)	43 (66.2)	0.2491
Number (%) of patients censored	24 (34.3)	38 (42.7)	33 (39.8)	22 (33.8)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.08 (1.018 to 1.938)	1.87 (1.018 to 2.628)	1.18 (1.018 to 1.971)	1.33 (1.018 to 1.906)	
Median (95% CI)	2.92 (1.938 to 5.454)	5.55 (2.891 to 12.485)	4.11 (2.464 to 5.848)	3.45 (1.938 to 6.472)	
75% quantile (95% CI)	NC (5.454 to NC)	NC (12.485 to NC)	NC (7.655 to NC)	NC (6.472 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1602		0.8191	
Hazard ratio (95% CI) vs Pd	-	0.75 (0.50 to 1.12)		1.05 (0.70 to 1.58)	
P-value	-	0.1616		0.8187	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (15.7)	12 (13.5)	8 (9.6)	11 (16.9)	0.2835
Number (%) of patients censored	59 (84.3)	77 (86.5)	75 (90.4)	54 (83.1)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (9.561 to NC)	NC (11.762 to NC)	NC (11.466 to NC)	NC (9.199 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6022		0.3234	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.36 to 1.82)		1.58 (0.63 to 3.92)	
P-value	-	0.6029		0.3276	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (37.1)	18 (20.2)	34 (41.0)	19 (29.2)	0.5025
Number (%) of patients censored	44 (62.9)	71 (79.8)	49 (59.0)	46 (70.8)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.46 (1.051 to 5.881)	NC (4.928 to NC)	3.15 (1.610 to 5.585)	7.89 (1.971 to NC)	
Median (95% CI)	NC (5.881 to NC)	NC (NC to NC)	11.24 (7.491 to NC)	NC (12.123 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0082		0.0519	
Hazard ratio (95% CI) vs Pd	-	0.45 (0.25 to 0.83)		0.58 (0.33 to 1.01)	
P-value	-	0.0100		0.0549	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (34.9)	56 (47.5)	6 (31.6)	12 (50.0)	0.6122
Number (%) of patients censored	82 (65.1)	62 (52.5)	13 (68.4)	12 (50.0)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.87 (1.084 to 3.745)	2.04 (1.380 to 2.891)	1.15 (0.986 to NC)	1.25 (0.986 to 2.234)	
Median (95% CI)	NC (NC to NC)	11.99 (3.844 to NC)	NC (1.150 to NC)	4.80 (1.380 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2060		0.3018	
Hazard ratio (95% CI) vs Pd	-	1.29 (0.87 to 1.91)		1.67 (0.62 to 4.45)	
P-value	-	0.2072		0.3071	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_impl_race_de_i_t_x.rtf (08APR2021 14:34)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	80 (63.5)	76 (64.4)	10 (52.6)	15 (62.5)	0.3813
Number (%) of patients censored	46 (36.5)	42 (35.6)	9 (47.4)	9 (37.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.28 (1.018 to 1.938)	1.28 (1.051 to 1.906)	1.12 (1.018 to 4.830)	1.91 (0.953 to 3.384)	
Median (95% CI)	3.75 (2.793 to 4.830)	4.04 (2.793 to 6.571)	9.46 (1.117 to NC)	4.11 (2.037 to NC)	
75% quantile (95% CI)	NC (7.655 to NC)	NC (9.495 to NC)	NC (9.462 to NC)	NC (4.928 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5803		0.4010	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.67 to 1.25)		1.41 (0.63 to 3.15)	
P-value	-	0.5803		0.4032	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (11.9)	18 (15.3)	4 (21.1)	3 (12.5)	0.2784
Number (%) of patients censored	111 (88.1)	100 (84.7)	15 (78.9)	21 (87.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.762 to NC)	NC (0.986 to NC)	NC (7.129 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (8.575 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6600		0.4082	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.59 to 2.31)		0.54 (0.12 to 2.40)	
P-value	-	0.6603		0.4157	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (38.9)	31 (26.3)	6 (31.6)	5 (20.8)	0.9871
Number (%) of patients censored	77 (61.1)	87 (73.7)	13 (68.4)	19 (79.2)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.89 (1.906 to 5.618)	8.61 (4.435 to NC)	4.83 (1.018 to NC)	NC (3.384 to NC)	
Median (95% CI)	NC (9.462 to NC)	NC (NC to NC)	NC (4.830 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0112		0.3737	
Hazard ratio (95% CI) vs Pd	-	0.56 (0.36 to 0.88)		0.59 (0.18 to 1.92)	
P-value	-	0.0123		0.3794	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (50.0)	47 (35.1)	63 (48.5)	0.9847
Number (%) of patients censored	3 (100.0)	2 (50.0)	87 (64.9)	67 (51.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (NC to NC)	3.70 (1.314 to NC)	1.45 (1.051 to 2.990)	1.97 (1.380 to 2.530)	
Median (95% CI)	NC (NC to NC)	NC (1.314 to NC)	NC (NC to NC)	11.99 (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.314 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3621		0.1351	
Hazard ratio (95% CI) vs Pd	-			1.33 (0.91 to 1.95)	
P-value	-	0.9981		0.1364	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	3 (75.0)	84 (62.7)	84 (64.6)	0.7606
Number (%) of patients censored	2 (66.7)	1 (25.0)	50 (37.3)	46 (35.4)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.27 (2.267 to NC)	1.76 (1.018 to 4.435)	1.22 (1.051 to 1.938)	1.28 (1.084 to 1.906)	
Median (95% CI)	NC (2.267 to NC)	3.47 (1.018 to NC)	3.75 (2.825 to 4.830)	4.04 (2.793 to 6.472)	
75% quantile (95% CI)	NC (2.267 to NC)	NC (1.018 to NC)	NC (9.232 to NC)	NC (8.608 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9835		0.8513	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.09 to 10.98)		0.97 (0.72 to 1.31)	
P-value	-	0.9834		0.8513	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	18 (13.4)	20 (15.4)	1.0000
Number (%) of patients censored	3 (100.0)	4 (100.0)	116 (86.6)	110 (84.6)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.466 to NC)	14.32 (11.762 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.9304	
Hazard ratio (95% CI) vs Pd	-			1.03 (0.54 to 1.95)	
P-value	-			0.9305	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	0 (0.0)	51 (38.1)	34 (26.2)	0.9788
Number (%) of patients censored	2 (66.7)	4 (100.0)	83 (61.9)	96 (73.8)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.27 (2.267 to NC)	NC (NC to NC)	3.75 (2.136 to 5.618)	8.61 (5.125 to NC)	
Median (95% CI)	NC (2.267 to NC)	NC (NC to NC)	NC (10.678 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (2.267 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.0122	
Hazard ratio (95% CI) vs Pd	-			0.58 (0.37 to 0.89)	
P-value	-	0.9990		0.0134	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_detpl_ethn_de_i_t_x.rtf (08APR2021 14:34)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	22 (28.9)	22 (40.0)	7 (35.0)	15 (53.6)	2 (40.0)	3 (42.9)	4 (26.7)	10 (47.6)	16 (43.2)	21 (48.8)	0.7694
Number (%) of patients censored	54 (71.1)	33 (60.0)	13 (65.0)	13 (46.4)	3 (60.0)	4 (57.1)	11 (73.3)	11 (52.4)	21 (56.8)	22 (51.2)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	2.27 (1.084 to NC)	1.97 (1.051 to 7.622)	2.83 (0.953 to NC)	1.89 (0.986 to 2.924)	0.99 (0.953 to NC)	3.32 (2.530 to NC)	1.15 (0.986 to NC)	2.00 (0.986 to 3.778)	1.25 (0.986 to 1.906)	2.17 (1.084 to 2.990)	
Median (95% CI)	NC (NC to NC)	13.83 (5.717 to NC)	NC (2.825 to NC)	5.42 (1.971 to NC)	NC (0.953 to NC)	NC (2.530 to NC)	NC (1.150 to NC)	4.80 (2.004 to NC)	NC (1.511 to NC)	5.82 (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.832 to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (6.078 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_impl_greg_de_i_t_x.rtf (08APR2021 14:34)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.2914		0.2654		0.8831		0.2279		0.9340	
Hazard ratio (95% CI) vs Pd	-	1.37 (0.76 to 2.48)		1.66 (0.67 to 4.09)		0.87 (0.14 to 5.28)		2.01 (0.63 to 6.43)		1.03 (0.54 to 1.97)	
P-value	-	0.2934		0.2704		0.8832		0.2373		0.9341	
Improvement probability (95% CI)[b]											
2 Months	0.226 (0.137 to 0.329)	0.260 (0.152 to 0.382)	0.211 (0.066 to 0.410)	0.357 (0.189 to 0.530)	0.400 (0.052 to 0.753)		0.267 (0.083 to 0.496)	0.238 (0.087 to 0.431)	0.392 (0.235 to 0.547)	0.215 (0.106 to 0.348)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_impl_greg_de_i_t_x.rtf (08APR2021 14:34)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	40 (52.6)	27 (49.1)	17 (85.0)	19 (67.9)	3 (60.0)	6 (85.7)	9 (60.0)	13 (61.9)	27 (73.0)	29 (67.4)	0.4223
Number (%) of patients censored	36 (47.4)	28 (50.9)	3 (15.0)	9 (32.1)	2 (40.0)	1 (14.3)	6 (40.0)	8 (38.1)	10 (27.0)	14 (32.6)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	1.28 (1.018 to 2.103)	1.97 (1.051 to 2.891)	0.99 (0.953 to 1.216)	1.48 (0.953 to 4.041)	1.12 (0.986 to NC)	1.02 (0.920 to 2.793)	1.08 (1.018 to 4.205)	1.91 (0.953 to 2.924)	1.48 (0.986 to 2.037)	1.12 (0.986 to 1.906)	
Median (95% CI)	5.16 (2.793 to NC)	6.70 (2.891 to NC)	1.97 (0.986 to 3.975)	4.93 (1.906 to 8.411)	2.27 (0.986 to NC)	2.79 (0.920 to 3.515)	4.83 (1.084 to NC)	4.11 (1.906 to NC)	2.89 (1.906 to 4.501)	2.63 (1.873 to 10.185)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	4.83 (1.971 to NC)	9.49 (5.585 to NC)	NC (0.986 to NC)	3.52 (1.084 to NC)	NC (4.830 to NC)	NC (4.107 to NC)	5.85 (3.088 to NC)	13.01 (6.571 to NC)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.4270		0.0451		0.5527		0.6171		0.4026	
Hazard ratio (95% CI) vs Pd	-	0.82 (0.50 to 1.34)		0.51 (0.26 to 1.00)		1.52 (0.38 to 6.11)		1.24 (0.53 to 2.92)		0.80 (0.47 to 1.36)	
P-value	-	0.4278		0.0489		0.5556		0.6178		0.4036	
Deterioration probability (95% CI)[b]											
2 Months	0.661 (0.538 to 0.759)	0.741 (0.602 to 0.838)	0.474 (0.244 to 0.673)	0.679 (0.473 to 0.818)	0.600 (0.126 to 0.882)	0.571 (0.172 to 0.837)	0.667 (0.375 to 0.846)	0.711 (0.466 to 0.859)	0.635 (0.455 to 0.769)	0.543 (0.381 to 0.680)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	8 (10.5)	8 (14.5)	1 (5.0)	6 (21.4)	1 (20.0)	0 (0.0)	2 (13.3)	2 (9.5)	7 (18.9)	7 (16.3)	0.5181
Number (%) of patients censored	68 (89.5)	47 (85.5)	19 (95.0)	22 (78.6)	4 (80.0)	7 (100.0)	13 (86.7)	19 (90.5)	30 (81.1)	36 (83.7)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (11.466 to NC)	NC (5.979 to NC)	NC (0.953 to NC)	11.79 (1.971 to NC)	NC (0.953 to NC)	NC (NC to NC)	NC (1.150 to NC)	NC (8.444 to NC)	NC (1.018 to NC)	14.32 (8.936 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.795 to NC)	NC (0.953 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.324 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.5305		0.1107		0.2367		0.6822		0.3956	
Hazard ratio (95% CI) vs Pd	-	1.37 (0.51 to 3.64)		4.83 (0.57 to 40.62)				0.67 (0.09 to 4.73)		0.64 (0.22 to 1.82)	
P-value	-	0.5322		0.1476		0.9984		0.6843		0.3995	
Improvement probability (95% CI)[b]											
2 Months	0.057 (0.018 to 0.127)	0.093 (0.034 to 0.188)	0.053 (0.004 to 0.214)	0.071 (0.013 to 0.204)	0.200 (0.008 to 0.582)		0.067 (0.004 to 0.260)		0.139 (0.051 to 0.271)		

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	25 (32.9)	12 (21.8)	13 (65.0)	8 (28.6)	2 (40.0)	2 (28.6)	6 (40.0)	4 (19.0)	14 (37.8)	11 (25.6)	0.7967
Number (%) of patients censored	51 (67.1)	43 (78.2)	7 (35.0)	20 (71.4)	3 (60.0)	5 (71.4)	9 (60.0)	17 (81.0)	23 (62.2)	32 (74.4)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	3.84 (1.183 to 10.678)	NC (1.906 to NC)	1.12 (0.953 to 3.975)	7.89 (1.873 to NC)	5.88 (2.267 to NC)	8.97 (2.858 to NC)	4.21 (1.018 to NC)	NC (3.384 to NC)	2.53 (1.347 to 9.462)	6.87 (1.938 to NC)	
Median (95% CI)	NC (10.678 to NC)	NC (NC to NC)	6.67 (1.117 to 11.236)	NC (12.123 to NC)	NC (2.267 to NC)	NC (2.858 to NC)	NC (1.084 to NC)	NC (NC to NC)	NC (2.891 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.669 to NC)	NC (NC to NC)	NC (2.267 to NC)	NC (8.969 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.1308		0.0069		0.6897		0.1435		0.1531	
Hazard ratio (95% CI) vs Pd	-	0.59 (0.30 to 1.18)		0.31 (0.13 to 0.76)		0.67 (0.09 to 4.78)		0.40 (0.11 to 1.42)		0.57 (0.26 to 1.25)	
P-value	-	0.1353		0.0105		0.6916		0.1576		0.1586	
Deterioration probability (95% CI)[b]											
2 Months	0.817 (0.706 to 0.889)	0.852 (0.726 to 0.923)	0.684 (0.428 to 0.844)	0.893 (0.704 to 0.964)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.800 (0.500 to 0.931)	1.000 (1.000 to 1.000)	0.832 (0.663 to 0.921)	0.880 (0.736 to 0.948)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (32.0)	31 (40.3)	20 (35.7)	40 (51.9)	0.4695
Number (%) of patients censored	66 (68.0)	46 (59.7)	36 (64.3)	37 (48.1)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.94 (1.084 to 5.651)	2.40 (1.314 to 5.421)	1.15 (1.018 to 9.725)	1.91 (1.051 to 2.234)	
Median (95% CI)	NC (NC to NC)	13.83 (6.078 to NC)	NC (9.725 to NC)	4.80 (2.793 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.832 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5399		0.1185	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.71 to 1.92)		1.53 (0.89 to 2.62)	
P-value	-	0.5403		0.1213	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	54 (55.7)	42 (54.5)	42 (75.0)	52 (67.5)	0.7111
Number (%) of patients censored	43 (44.3)	35 (45.5)	14 (25.0)	25 (32.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.28 (1.018 to 1.971)	1.91 (1.084 to 2.497)	1.05 (1.018 to 1.347)	1.10 (0.986 to 1.906)	
Median (95% CI)	4.11 (2.464 to 7.655)	5.22 (2.793 to NC)	3.09 (1.347 to 4.205)	4.11 (2.136 to 6.965)	
75% quantile (95% CI)	NC (10.546 to NC)	NC (12.485 to NC)	8.61 (4.205 to NC)	13.01 (8.411 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5467		0.2434	
Hazard ratio (95% CI) vs Pd	-	0.88 (0.59 to 1.32)		0.78 (0.52 to 1.18)	
P-value	-	0.5469		0.2446	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_detl_rreg_de_i_t_x.rtf (08APR2021 14:34)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (12.4)	10 (13.0)	7 (12.5)	13 (16.9)	0.6500
Number (%) of patients censored	85 (87.6)	67 (87.0)	49 (87.5)	64 (83.1)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (11.466 to NC)	NC (14.324 to NC)	NC (9.561 to NC)	NC (9.232 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.324 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9214		0.6115	
Hazard ratio (95% CI) vs Pd	-	0.96 (0.41 to 2.22)		1.27 (0.51 to 3.18)	
P-value	-	0.9216		0.6123	
Improvement probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (33.0)	20 (26.0)	28 (50.0)	17 (22.1)	0.0868
Number (%) of patients censored	65 (67.0)	57 (74.0)	28 (50.0)	60 (77.9)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	3.15 (1.873 to 8.936)	8.97 (2.201 to NC)	2.83 (1.084 to 4.205)	12.12 (6.768 to NC)	
Median (95% CI)	NC (13.339 to NC)	NC (NC to NC)	9.46 (4.205 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.236 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2030		0.0001	
Hazard ratio (95% CI) vs Pd	-	0.70 (0.40 to 1.22)		0.32 (0.18 to 0.59)	
P-value	-	0.2055		0.0003	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (32.1)	65 (47.1)	7 (43.8)	6 (37.5)	0.2918
Number (%) of patients censored	93 (67.9)	73 (52.9)	9 (56.3)	10 (62.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.94 (1.117 to 8.312)	2.00 (1.380 to 2.530)	1.15 (0.953 to 2.004)	1.94 (0.986 to 11.992)	
Median (95% CI)	NC (NC to NC)	13.83 (3.778 to NC)	NC (0.986 to NC)	11.99 (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.078 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0594		0.6248	
Hazard ratio (95% CI) vs Pd	-	1.44 (0.98 to 2.12)		0.76 (0.25 to 2.28)	
P-value	-	0.0609		0.6259	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	86 (62.8)	89 (64.5)	10 (62.5)	5 (31.3)	0.1132
Number (%) of patients censored	51 (37.2)	49 (35.5)	6 (37.5)	11 (68.8)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.12 (1.018 to 1.906)	1.38 (1.084 to 1.906)	1.05 (0.986 to 2.793)	5.22 (0.296 to NC)	
Median (95% CI)	3.81 (2.464 to 5.158)	3.84 (2.793 to 6.472)	2.83 (1.018 to NC)	NC (5.224 to NC)	
75% quantile (95% CI)	NC (9.232 to NC)	NC (9.495 to NC)	NC (2.825 to NC)	NC (10.185 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6843		0.0818	
Hazard ratio (95% CI) vs Pd	-	0.94 (0.70 to 1.26)		0.39 (0.13 to 1.17)	
P-value	-	0.6840		0.0923	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (12.4)	22 (15.9)	2 (12.5)	1 (6.3)	0.4121
Number (%) of patients censored	120 (87.6)	116 (84.1)	14 (87.5)	15 (93.8)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (NC to NC)	14.32 (11.762 to NC)	NC (0.953 to NC)	NC (1.938 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6016		0.5781	
Hazard ratio (95% CI) vs Pd	-	1.18 (0.63 to 2.23)		0.51 (0.05 to 5.65)	
P-value	-	0.6020		0.5852	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (37.2)	36 (26.1)	9 (56.3)	1 (6.3)	0.0632
Number (%) of patients censored	86 (62.8)	102 (73.9)	7 (43.8)	15 (93.8)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	3.75 (1.873 to 5.881)	8.61 (5.125 to NC)	1.35 (0.986 to 2.825)	NC (0.296 to NC)	
Median (95% CI)	NC (10.973 to NC)	NC (NC to NC)	4.83 (1.051 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.830 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0120		0.0041	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.38 to 0.89)		0.09 (0.01 to 0.71)	
P-value	-	0.0131		0.0221	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (31.4)	25 (39.1)	17 (30.4)	28 (52.8)	16 (37.2)	18 (52.9)	0.8237
Number (%) of patients censored	35 (68.6)	39 (60.9)	39 (69.6)	25 (47.2)	27 (62.8)	16 (47.1)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	2.99 (1.084 to NC)	2.79 (1.117 to 4.304)	1.61 (1.018 to NC)	1.97 (1.183 to 2.366)	1.45 (0.986 to 5.618)	1.05 (0.986 to 2.168)	
Median (95% CI)	NC (NC to NC)	NC (6.078 to NC)	NC (NC to NC)	5.82 (2.366 to NC)	NC (1.938 to NC)	3.84 (1.906 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.832 to NC)	NC (NC to NC)	NC (7.622 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3831		0.0882		0.4016	
Hazard ratio (95% CI) vs Pd	-	1.32 (0.70 to 2.48)		1.68 (0.92 to 3.07)		1.33 (0.68 to 2.62)	
P-value	-	0.3846		0.0918		0.4032	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (66.7)	38 (59.4)	41 (73.2)	33 (62.3)	19 (44.2)	20 (58.8)	0.4912
Number (%) of patients censored	17 (33.3)	26 (40.6)	15 (26.8)	20 (37.7)	24 (55.8)	14 (41.2)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	1.22 (0.986 to 1.971)	1.12 (0.986 to 2.037)	1.05 (1.018 to 1.906)	1.91 (1.084 to 2.497)	1.28 (0.986 to 2.464)	1.94 (0.986 to 4.928)	
Median (95% CI)	3.84 (1.971 to 9.232)	4.04 (2.136 to NC)	2.92 (1.873 to 4.205)	3.52 (2.201 to 9.495)	5.85 (1.906 to NC)	6.57 (2.924 to 8.608)	
75% quantile (95% CI)	NC (8.608 to NC)	NC (NC to NC)	6.14 (4.107 to NC)	NC (6.965 to NC)	NC (8.345 to NC)	12.48 (6.702 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7296		0.1032		0.7946	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.58 to 1.46)		0.68 (0.43 to 1.08)		1.09 (0.58 to 2.04)	
P-value	-	0.7288		0.1051		0.7947	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (9.8)	9 (14.1)	9 (16.1)	9 (17.0)	4 (9.3)	5 (14.7)	0.7890
Number (%) of patients censored	46 (90.2)	55 (85.9)	47 (83.9)	44 (83.0)	39 (90.7)	29 (85.3)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	NC (11.466 to NC)	NC (9.396 to NC)	NC (2.793 to NC)	NC (7.129 to NC)	NC (8.575 to NC)	14.32 (3.975 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.324 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.324 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4132		0.8793		0.7844	
Hazard ratio (95% CI) vs Pd	-	1.57 (0.53 to 4.70)		0.93 (0.37 to 2.35)		1.20 (0.32 to 4.53)	
P-value	-	0.4172		0.8792		0.7847	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (39.2)	13 (20.3)	26 (46.4)	12 (22.6)	13 (30.2)	9 (26.5)	0.4141
Number (%) of patients censored	31 (60.8)	51 (79.7)	30 (53.6)	41 (77.4)	30 (69.8)	25 (73.5)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	3.81 (1.117 to 8.936)	NC (3.384 to NC)	2.27 (1.018 to 4.205)	12.12 (6.472 to NC)	3.84 (1.281 to 13.339)	8.61 (1.840 to NC)	
Median (95% CI)	NC (6.735 to NC)	NC (NC to NC)	10.68 (3.154 to NC)	NC (NC to NC)	13.34 (8.345 to NC)	NC (9.002 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.339 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0353		0.0014		0.4243	
Hazard ratio (95% CI) vs Pd	-	0.48 (0.24 to 0.97)		0.34 (0.17 to 0.68)		0.71 (0.30 to 1.66)	
P-value	-	0.0396		0.0022		0.4266	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (35.5)	14 (35.9)	32 (32.7)	50 (50.5)	8 (33.3)	7 (43.8)	0.4724
Number (%) of patients censored	20 (64.5)	25 (64.1)	66 (67.3)	49 (49.5)	16 (66.7)	9 (56.3)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	2.00 (1.018 to NC)	3.19 (1.643 to NC)	1.87 (1.018 to 11.532)	1.87 (1.084 to 2.201)	1.51 (0.953 to NC)	2.76 (0.953 to 7.622)	
Median (95% CI)	NC (4.698 to NC)	NC (6.078 to NC)	NC (NC to NC)	5.82 (2.793 to NC)	NC (1.511 to NC)	7.62 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.832 to NC)	NC (NC to NC)	NC (7.622 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9436		0.0386		0.9155	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.44 to 2.14)		1.59 (1.02 to 2.48)		1.06 (0.38 to 2.93)	
P-value	-	0.9435		0.0403		0.9153	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (61.3)	22 (56.4)	70 (71.4)	64 (64.6)	7 (29.2)	8 (50.0)	0.5072
Number (%) of patients censored	12 (38.7)	17 (43.6)	28 (28.6)	35 (35.4)	17 (70.8)	8 (50.0)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	1.87 (1.117 to 2.825)	1.08 (0.986 to 2.267)	1.02 (0.986 to 1.281)	1.51 (1.051 to 2.037)	1.91 (0.953 to NC)	1.94 (0.986 to 6.702)	
Median (95% CI)	4.07 (1.938 to NC)	5.59 (1.873 to NC)	3.15 (2.103 to 4.107)	4.44 (2.793 to 6.571)	NC (1.906 to NC)	6.70 (1.840 to NC)	
75% quantile (95% CI)	NC (9.462 to NC)	NC (NC to NC)	9.23 (5.454 to NC)	13.01 (8.608 to NC)	NC (NC to NC)	8.61 (6.702 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9746		0.1752		0.5086	
Hazard ratio (95% CI) vs Pd	-	0.99 (0.54 to 1.83)		0.79 (0.56 to 1.11)		1.41 (0.51 to 3.89)	
P-value	-	0.9746		0.1762		0.5107	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (12.9)	5 (12.8)	13 (13.3)	17 (17.2)	2 (8.3)	1 (6.3)	0.8476
Number (%) of patients censored	27 (87.1)	34 (87.2)	85 (86.7)	82 (82.8)	22 (91.7)	15 (93.8)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	NC (9.758 to NC)	NC (9.199 to NC)	NC (10.251 to NC)	14.32 (9.396 to NC)	NC (0.953 to NC)	NC (0.953 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9991		0.6190		0.7631	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.27 to 3.72)		1.20 (0.58 to 2.47)		0.69 (0.06 to 7.64)	
P-value	-	0.9991		0.6194		0.7644	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (32.3)	5 (12.8)	45 (45.9)	27 (27.3)	5 (20.8)	5 (31.3)	0.3183
Number (%) of patients censored	21 (67.7)	34 (87.2)	53 (54.1)	72 (72.7)	19 (79.2)	11 (68.8)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	5.62 (1.216 to NC)	NC (7.425 to NC)	2.53 (1.051 to 3.975)	6.97 (4.435 to NC)	3.84 (1.084 to NC)	4.70 (0.986 to NC)	
Median (95% CI)	NC (11.236 to NC)	NC (NC to NC)	10.97 (5.881 to NC)	NC (NC to NC)	NC (3.844 to NC)	NC (1.971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.608 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0660		0.0021		0.7911	
Hazard ratio (95% CI) vs Pd	-	0.38 (0.13 to 1.11)		0.48 (0.30 to 0.77)		1.18 (0.34 to 4.11)	
P-value	-	0.0770		0.0026		0.7913	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (34.8)	4 (28.6)	30 (31.6)	57 (48.3)	0.3193
Number (%) of patients censored	15 (65.2)	10 (71.4)	65 (68.4)	61 (51.7)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.94 (0.953 to 11.532)	3.84 (0.986 to NC)	1.91 (1.018 to NC)	2.00 (1.183 to 2.825)	
Median (95% CI)	NC (1.938 to NC)	NC (2.924 to NC)	NC (NC to NC)	11.99 (3.778 to NC)	
75% quantile (95% CI)	NC (11.532 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7634		0.0637	
Hazard ratio (95% CI) vs Pd	-	0.83 (0.25 to 2.79)		1.52 (0.97 to 2.36)	
P-value	-	0.7637		0.0657	
Improvement probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (52.2)	5 (35.7)	61 (64.2)	79 (66.9)	0.4520
Number (%) of patients censored	11 (47.8)	9 (64.3)	34 (35.8)	39 (33.1)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.10 (1.018 to 4.107)	1.84 (0.296 to NC)	1.08 (0.986 to 1.347)	1.15 (1.051 to 1.906)	
Median (95% CI)	4.11 (2.103 to 9.232)	NC (0.953 to NC)	2.96 (1.971 to 4.205)	2.92 (2.201 to 5.585)	
75% quantile (95% CI)	7.66 (4.107 to NC)	NC (NC to NC)	NC (6.144 to NC)	13.01 (8.608 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3365		0.9009	
Hazard ratio (95% CI) vs Pd	-	0.60 (0.21 to 1.72)		0.98 (0.70 to 1.37)	
P-value	-	0.3417		0.9008	
Deterioration probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (13.0)	2 (14.3)	14 (14.7)	18 (15.3)	0.7310
Number (%) of patients censored	20 (87.0)	12 (85.7)	81 (85.3)	100 (84.7)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (0.953 to NC)	10.25 (1.150 to NC)	NC (10.251 to NC)	NC (11.762 to NC)	
Median (95% CI)	NC (9.561 to NC)	NC (10.251 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.251 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7645		0.8072	
Hazard ratio (95% CI) vs Pd	-	1.32 (0.22 to 8.02)		0.92 (0.46 to 1.84)	
P-value	-	0.7652		0.8072	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (21.7)	4 (28.6)	44 (46.3)	29 (24.6)	0.0915
Number (%) of patients censored	18 (78.3)	10 (71.4)	51 (53.7)	89 (75.4)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	4.86 (1.051 to NC)	2.86 (0.296 to NC)	2.46 (1.084 to 3.811)	9.00 (6.472 to NC)	
Median (95% CI)	NC (4.862 to NC)	NC (1.840 to NC)	11.24 (5.585 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6363		0.0002	
Hazard ratio (95% CI) vs Pd	-	1.37 (0.37 to 5.11)		0.42 (0.26 to 0.68)	
P-value	-	0.6376		0.0003	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (33.3)	7 (29.2)	24 (30.8)	53 (51.5)	0.1772
Number (%) of patients censored	24 (66.7)	17 (70.8)	54 (69.2)	50 (48.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.87 (0.986 to NC)	3.84 (0.986 to NC)	1.51 (1.018 to NC)	1.91 (1.051 to 2.760)	
Median (95% CI)	NC (3.745 to NC)	NC (3.844 to NC)	NC (NC to NC)	7.62 (3.187 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6688		0.0330	
Hazard ratio (95% CI) vs Pd	-	0.82 (0.32 to 2.08)		1.68 (1.04 to 2.72)	
P-value	-	0.6693		0.0350	
Hazard ratio inverted (95% CI) vs IPd		-		0.59 (0.37 to 0.96)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (61.1)	12 (50.0)	48 (61.5)	68 (66.0)	0.7303
Number (%) of patients censored	14 (38.9)	12 (50.0)	30 (38.5)	35 (34.0)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.91 (1.051 to 2.793)	1.12 (0.296 to 1.971)	1.08 (0.986 to 1.610)	1.28 (1.051 to 1.906)	
Median (95% CI)	3.15 (2.103 to 6.144)	3.84 (1.248 to NC)	3.42 (1.938 to 5.618)	4.04 (2.628 to 6.472)	
75% quantile (95% CI)	7.66 (4.107 to NC)	NC (3.844 to NC)	NC (10.546 to NC)	NC (8.608 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6511		0.9512	
Hazard ratio (95% CI) vs Pd	-	0.85 (0.42 to 1.72)		0.99 (0.68 to 1.43)	
P-value	-	0.6514		0.9511	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (13.9)	3 (12.5)	12 (15.4)	16 (15.5)	0.8863
Number (%) of patients censored	31 (86.1)	21 (87.5)	66 (84.6)	87 (84.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (1.446 to NC)	NC (1.150 to NC)	NC (9.758 to NC)	NC (11.762 to NC)	
Median (95% CI)	NC (NC to NC)	NC (10.251 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9100		0.7293	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.22 to 3.86)		0.88 (0.41 to 1.85)	
P-value	-	0.9100		0.7294	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (36.1)	8 (33.3)	34 (43.6)	24 (23.3)	0.1776
Number (%) of patients censored	23 (63.9)	16 (66.7)	44 (56.4)	79 (76.7)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	3.15 (1.183 to 4.862)	2.86 (0.296 to NC)	2.83 (1.084 to 5.585)	NC (6.472 to NC)	
Median (95% CI)	NC (3.811 to NC)	NC (2.858 to NC)	13.34 (6.735 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7338		0.0013	
Hazard ratio (95% CI) vs Pd	-	0.86 (0.36 to 2.07)		0.43 (0.26 to 0.73)	
P-value	-	0.7340		0.0018	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (32.2)	34 (41.0)	22 (34.9)	37 (52.1)	0.9371
Number (%) of patients censored	61 (67.8)	49 (59.0)	41 (65.1)	34 (47.9)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.94 (1.018 to 11.532)	1.97 (1.150 to 2.924)	1.61 (1.018 to 8.312)	2.37 (1.084 to 2.891)	
Median (95% CI)	NC (NC to NC)	NC (3.745 to NC)	NC (8.312 to NC)	6.08 (3.055 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.832 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3153		0.2580	
Hazard ratio (95% CI) vs Pd	-	1.29 (0.78 to 2.12)		1.36 (0.80 to 2.30)	
P-value	-	0.3163		0.2598	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (56.7)	47 (56.6)	45 (71.4)	47 (66.2)	0.2848
Number (%) of patients censored	39 (43.3)	36 (43.4)	18 (28.6)	24 (33.8)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.74 (1.051 to 2.793)	1.94 (1.084 to 2.793)	1.02 (0.986 to 1.281)	1.08 (0.986 to 1.906)	
Median (95% CI)	5.16 (2.924 to 8.345)	6.31 (2.924 to 10.185)	2.04 (1.281 to 3.745)	2.99 (1.906 to 6.702)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.485 to NC)	8.61 (3.745 to NC)	NC (6.965 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8759		0.1368	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.65 to 1.44)		0.73 (0.49 to 1.11)	
P-value	-	0.8760		0.1384	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (15.6)	12 (14.5)	5 (7.9)	11 (15.5)	0.3868
Number (%) of patients censored	76 (84.4)	71 (85.5)	58 (92.1)	60 (84.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (10.251 to NC)	14.32 (11.762 to NC)	NC (9.758 to NC)	NC (8.641 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.324 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8633		0.3623	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.43 to 2.02)		1.63 (0.56 to 4.69)	
P-value	-	0.8636		0.3671	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (37.8)	20 (24.1)	26 (41.3)	17 (23.9)	0.5171
Number (%) of patients censored	56 (62.2)	63 (75.9)	37 (58.7)	54 (76.1)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.89 (1.216 to 6.735)	7.89 (2.858 to NC)	2.86 (1.018 to 4.862)	9.00 (6.768 to NC)	
Median (95% CI)	NC (10.678 to NC)	NC (NC to NC)	NC (4.862 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0434		0.0051	
Hazard ratio (95% CI) vs Pd	-	0.57 (0.33 to 0.99)		0.43 (0.23 to 0.79)	
P-value	-	0.0462		0.0066	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	0 (0.0)	49 (32.5)	71 (46.7)	0.9779
Number (%) of patients censored	0 (0.0)	2 (100.0)	102 (67.5)	81 (53.3)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.02 (1.018 to 1.084)	NC (NC to NC)	1.91 (1.150 to 5.651)	1.97 (1.314 to 2.530)	
Median (95% CI)	1.05 (1.018 to 1.084)	NC (NC to NC)	NC (NC to NC)	13.83 (4.304 to NC)	
75% quantile (95% CI)	1.08 (1.018 to 1.084)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.0567	
Hazard ratio (95% CI) vs Pd	-			1.42 (0.99 to 2.05)	
P-value	-	0.9991		0.0579	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	2 (100.0)	95 (62.9)	92 (60.5)	0.1924
Number (%) of patients censored	1 (50.0)	0 (0.0)	56 (37.1)	60 (39.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	10.55 (NC to NC)	1.12 (1.117 to 4.107)	1.12 (1.018 to 1.873)	1.51 (1.084 to 1.938)	
Median (95% CI)	10.55 (NC to NC)	2.61 (1.117 to 4.107)	3.75 (2.464 to 4.501)	4.47 (2.891 to 6.965)	
75% quantile (95% CI)	10.55 (NC to NC)	4.11 (1.117 to 4.107)	NC (8.345 to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.2888	
Hazard ratio (95% CI) vs Pd	-			0.86 (0.64 to 1.14)	
P-value	-	0.9991		0.2879	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	0 (0.0)	17 (11.3)	23 (15.1)	0.9837
Number (%) of patients censored	0 (0.0)	2 (100.0)	134 (88.7)	129 (84.9)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.02 (1.018 to 11.466)	NC (NC to NC)	NC (NC to NC)	NC (11.762 to NC)	
Median (95% CI)	6.24 (1.018 to 11.466)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	11.47 (1.018 to 11.466)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.5115	
Hazard ratio (95% CI) vs Pd	-			1.23 (0.66 to 2.31)	
P-value	-	0.9990		0.5123	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	60 (39.7)	36 (23.7)	0.9777
Number (%) of patients censored	2 (100.0)	1 (50.0)	91 (60.3)	116 (76.3)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (NC to NC)	6.87 (6.867 to NC)	2.86 (1.610 to 4.830)	9.00 (6.012 to NC)	
Median (95% CI)	NC (NC to NC)	NC (6.867 to NC)	NC (9.462 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (6.867 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.0005	
Hazard ratio (95% CI) vs Pd	-			0.49 (0.32 to 0.74)	
P-value	-	0.9990		0.0007	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (34.7)	47 (45.2)	12 (29.3)	15 (45.5)	0.9503
Number (%) of patients censored	66 (65.3)	57 (54.8)	29 (70.7)	18 (54.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.94 (1.117 to 5.651)	1.91 (1.150 to 2.793)	1.45 (0.986 to NC)	2.53 (0.986 to 3.318)	
Median (95% CI)	NC (11.532 to NC)	13.83 (5.717 to NC)	NC (NC to NC)	NC (2.891 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2770		0.3474	
Hazard ratio (95% CI) vs Pd	-	1.27 (0.82 to 1.97)		1.44 (0.67 to 3.07)	
P-value	-	0.2781		0.3500	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_impl_semm_de_i_t_x.rtf (08APR2021 14:34)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (34.0)	45 (44.1)	16 (30.8)	25 (49.0)	0.6017
Number (%) of patients censored	66 (66.0)	57 (55.9)	36 (69.2)	26 (51.0)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.94 (1.117 to 8.312)	1.95 (1.183 to 2.924)	1.25 (0.986 to NC)	2.37 (1.018 to 3.055)	
Median (95% CI)	NC (11.532 to NC)	13.83 (5.815 to NC)	NC (NC to NC)	5.42 (2.891 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3090		0.1984	
Hazard ratio (95% CI) vs Pd	-	1.26 (0.81 to 1.97)		1.51 (0.80 to 2.82)	
P-value	-	0.3101		0.2015	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_impl_dghc_de_i_t_x.rtf (08APR2021 14:34)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	64 (64.0)	64 (62.7)	31 (59.6)	30 (58.8)	0.6406
Number (%) of patients censored	36 (36.0)	38 (37.3)	21 (40.4)	21 (41.2)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.05 (0.986 to 1.216)	1.56 (1.051 to 1.938)	1.87 (1.018 to 2.825)	1.38 (1.018 to 2.201)	
Median (95% CI)	3.42 (1.938 to 4.501)	4.47 (2.793 to 6.702)	4.11 (2.464 to 9.232)	4.11 (2.136 to 12.485)	
75% quantile (95% CI)	NC (6.834 to NC)	NC (9.495 to NC)	NC (6.144 to NC)	NC (8.608 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3635		0.9538	
Hazard ratio (95% CI) vs Pd	-	0.85 (0.60 to 1.20)		0.99 (0.60 to 1.63)	
P-value	-	0.3640		0.9538	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (11.0)	14 (13.7)	7 (13.5)	8 (15.7)	0.8858
Number (%) of patients censored	89 (89.0)	88 (86.3)	45 (86.5)	43 (84.3)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (11.466 to NC)	NC (11.762 to NC)	NC (1.446 to NC)	14.32 (5.979 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.324 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7720		0.9336	
Hazard ratio (95% CI) vs Pd	-	1.12 (0.51 to 2.48)		1.04 (0.38 to 2.88)	
P-value	-	0.7721		0.9337	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (40.0)	24 (23.5)	20 (38.5)	13 (25.5)	0.7655
Number (%) of patients censored	60 (60.0)	78 (76.5)	32 (61.5)	38 (74.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.86 (1.084 to 5.585)	12.12 (4.698 to NC)	2.86 (1.281 to 8.936)	8.61 (4.435 to NC)	
Median (95% CI)	13.34 (6.735 to NC)	NC (NC to NC)	NC (8.345 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0043		0.0840	
Hazard ratio (95% CI) vs Pd	-	0.48 (0.29 to 0.81)		0.54 (0.27 to 1.10)	
P-value	-	0.0052		0.0888	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (30.0)	7 (50.0)	48 (33.6)	64 (45.7)	0.9463
Number (%) of patients censored	7 (70.0)	7 (50.0)	95 (66.4)	76 (54.3)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	0.99 (0.920 to NC)	1.91 (0.986 to 6.538)	1.91 (1.150 to 5.618)	2.00 (1.314 to 2.530)	
Median (95% CI)	NC (0.920 to NC)	6.54 (1.380 to NC)	NC (NC to NC)	13.83 (4.304 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (6.538 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7046		0.1162	
Hazard ratio (95% CI) vs Pd	-	1.30 (0.34 to 5.03)		1.35 (0.93 to 1.96)	
P-value	-	0.7054		0.1176	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (60.0)	9 (64.3)	90 (62.9)	85 (60.7)	0.4105
Number (%) of patients censored	4 (40.0)	5 (35.7)	53 (37.1)	55 (39.3)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.02 (0.920 to 1.741)	1.84 (0.986 to 5.585)	1.12 (1.051 to 1.906)	1.38 (1.084 to 1.938)	
Median (95% CI)	1.74 (0.920 to NC)	5.59 (1.117 to 13.010)	3.81 (2.793 to 5.158)	4.44 (2.793 to 6.965)	
75% quantile (95% CI)	3.75 (1.281 to NC)	13.01 (5.585 to NC)	NC (9.232 to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1927		0.4760	
Hazard ratio (95% CI) vs Pd	-	0.48 (0.16 to 1.48)		0.90 (0.67 to 1.21)	
P-value	-	0.2014		0.4761	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	1 (7.1)	18 (12.6)	22 (15.7)	0.4990
Number (%) of patients censored	9 (90.0)	13 (92.9)	125 (87.4)	118 (84.3)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (0.953 to NC)	NC (8.444 to NC)	NC (11.466 to NC)	14.32 (11.762 to NC)	
Median (95% CI)	NC (0.953 to NC)	NC (8.444 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4716		0.6140	
Hazard ratio (95% CI) vs Pd	-	0.36 (0.02 to 6.46)		1.17 (0.63 to 2.19)	
P-value	-	0.4868		0.6144	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (50.0)	4 (28.6)	55 (38.5)	33 (23.6)	0.3304
Number (%) of patients censored	5 (50.0)	10 (71.4)	88 (61.5)	107 (76.4)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.28 (0.920 to 3.745)	7.89 (1.840 to NC)	2.89 (1.873 to 5.585)	12.12 (5.125 to NC)	
Median (95% CI)	3.75 (0.920 to NC)	NC (6.867 to NC)	NC (10.678 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (2.858 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0087		0.0027	
Hazard ratio (95% CI) vs Pd	-	0.13 (0.02 to 0.75)		0.52 (0.34 to 0.80)	
P-value	-	0.0218		0.0032	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (34.4)	40 (46.0)	17 (34.7)	28 (50.9)	0.8158
Number (%) of patients censored	63 (65.6)	47 (54.0)	32 (65.3)	27 (49.1)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.94 (1.018 to 5.651)	2.04 (1.183 to 2.990)	1.61 (1.018 to 8.312)	1.94 (1.018 to 2.760)	
Median (95% CI)	NC (11.532 to NC)	13.83 (4.797 to NC)	NC (4.698 to NC)	3.84 (2.760 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2771		0.2860	
Hazard ratio (95% CI) vs Pd	-	1.29 (0.81 to 2.05)		1.39 (0.76 to 2.53)	
P-value	-	0.2790		0.2882	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	58 (60.4)	60 (69.0)	32 (65.3)	31 (56.4)	0.0310
Number (%) of patients censored	38 (39.6)	27 (31.0)	17 (34.7)	24 (43.6)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.61 (1.051 to 2.136)	1.25 (1.018 to 1.906)	1.05 (0.986 to 1.938)	1.91 (1.051 to 2.924)	
Median (95% CI)	4.21 (3.088 to 8.608)	2.92 (2.136 to 5.585)	2.79 (1.741 to 4.501)	6.57 (2.924 to NC)	
75% quantile (95% CI)	NC (9.462 to NC)	13.01 (7.556 to NC)	NC (3.844 to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3044		0.0665	
Hazard ratio (95% CI) vs Pd	-	1.21 (0.84 to 1.73)		0.63 (0.38 to 1.04)	
P-value	-	0.3051		0.0688	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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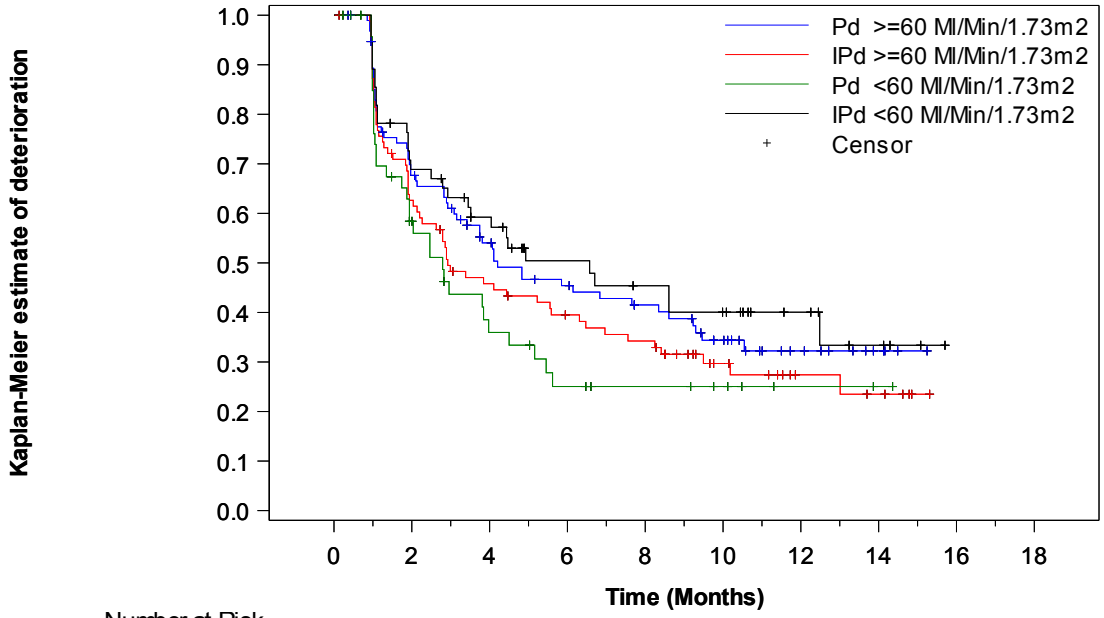
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to baseline creatinine clearance (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd >=60 Ml/Min/1.73m2	96	55	36	28	10	1	0
lPd >=60 Ml/Min/1.73m2	87	40	30	20	7	1	0
Pd <60 Ml/Min/1.73m2	49	17	9	7	2	0	0
lPd <60 Ml/Min/1.73m2	55	33	20	15	8	2	0

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_detl_crcl_de_i_f_x.rtf (08APR2021 14:38)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (14.6)	13 (14.9)	5 (10.2)	8 (14.5)	0.6527
Number (%) of patients censored	82 (85.4)	74 (85.1)	44 (89.8)	47 (85.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (10.251 to NC)	NC (10.251 to NC)	NC (8.575 to NC)	14.32 (8.641 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.324 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8384		0.7236	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.43 to 1.97)		1.22 (0.40 to 3.75)	
P-value	-	0.8385		0.7240	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_imppl_crcl_de_i_t_x.rtf (08APR2021 14:35)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.7 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (34.4)	23 (26.4)	22 (44.9)	13 (23.6)	0.2024
Number (%) of patients censored	63 (65.6)	64 (73.6)	27 (55.1)	42 (76.4)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	4.21 (1.906 to 8.936)	6.97 (2.891 to NC)	2.53 (1.051 to 5.585)	9.00 (4.928 to NC)	
Median (95% CI)	NC (11.236 to NC)	NC (NC to NC)	9.46 (3.844 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1500		0.0038	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.40 to 1.15)		0.37 (0.19 to 0.75)	
P-value	-	0.1525		0.0053	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (100.0)	51 (33.8)	69 (45.4)	0.9755
Number (%) of patients censored	2 (100.0)	0 (0.0)	100 (66.2)	83 (54.6)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (NC to NC)	1.91 (1.906 to 1.971)	1.87 (1.117 to 4.698)	2.04 (1.314 to 2.793)	
Median (95% CI)	NC (NC to NC)	1.94 (1.906 to 1.971)	NC (NC to NC)	13.83 (4.797 to NC)	
75% quantile (95% CI)	NC (NC to NC)	1.97 (1.906 to 1.971)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.1507	
Hazard ratio (95% CI) vs Pd	-			1.30 (0.91 to 1.87)	
P-value	-	0.9991		0.1519	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	96 (63.6)	93 (61.2)	0.9804
Number (%) of patients censored	2 (100.0)	1 (50.0)	55 (36.4)	59 (38.8)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (NC to NC)	0.99 (0.986 to NC)	1.12 (1.018 to 1.873)	1.51 (1.084 to 1.938)	
Median (95% CI)	NC (NC to NC)	NC (0.986 to NC)	3.75 (2.464 to 4.501)	4.44 (2.891 to 6.965)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.986 to NC)	NC (8.608 to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.3105	
Hazard ratio (95% CI) vs Pd	-			0.86 (0.65 to 1.15)	
P-value	-	0.9990		0.3098	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	19 (12.6)	23 (15.1)	1.0000
Number (%) of patients censored	2 (100.0)	2 (100.0)	132 (87.4)	129 (84.9)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.762 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.7403	
Hazard ratio (95% CI) vs Pd	-			1.11 (0.60 to 2.03)	
P-value	-			0.7412	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	60 (39.7)	37 (24.3)	0.9995
Number (%) of patients censored	2 (100.0)	2 (100.0)	91 (60.3)	115 (75.7)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	2.86 (1.610 to 4.830)	8.97 (6.012 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.462 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0009	
Hazard ratio (95% CI) vs Pd	-			0.51 (0.34 to 0.76)	
P-value	-			0.0011	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (34.8)	56 (47.5)	11 (28.9)	15 (41.7)	0.7626
Number (%) of patients censored	75 (65.2)	62 (52.5)	27 (71.1)	21 (58.3)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.61 (1.084 to 5.618)	1.97 (1.216 to 2.760)	1.94 (0.986 to NC)	2.04 (1.051 to 5.717)	
Median (95% CI)	NC (11.532 to NC)	11.99 (3.745 to NC)	NC (NC to NC)	NC (3.055 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1958		0.3551	
Hazard ratio (95% CI) vs Pd	-	1.31 (0.87 to 1.96)		1.44 (0.66 to 3.14)	
P-value	-	0.1971		0.3577	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	71 (61.7)	75 (63.6)	25 (65.8)	19 (52.8)	0.4936
Number (%) of patients censored	44 (38.3)	43 (36.4)	13 (34.2)	17 (47.2)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.12 (1.018 to 1.906)	1.51 (1.084 to 1.938)	1.12 (0.986 to 1.971)	1.10 (0.953 to 2.037)	
Median (95% CI)	3.84 (2.793 to 5.454)	4.44 (2.891 to 6.965)	2.83 (1.610 to 5.848)	4.11 (1.873 to NC)	
75% quantile (95% CI)	NC (8.608 to NC)	NC (9.495 to NC)	NC (3.811 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6300		0.3676	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.67 to 1.28)		0.76 (0.42 to 1.38)	
P-value	-	0.6294		0.3691	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (14.8)	20 (16.9)	2 (5.3)	3 (8.3)	0.6057
Number (%) of patients censored	98 (85.2)	98 (83.1)	36 (94.7)	33 (91.7)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (10.251 to NC)	14.32 (10.251 to NC)	NC (NC to NC)	NC (9.396 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9902		0.6118	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.52 to 1.90)		1.58 (0.26 to 9.48)	
P-value	-	0.9902		0.6149	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (35.7)	27 (22.9)	19 (50.0)	10 (27.8)	0.8380
Number (%) of patients censored	74 (64.3)	91 (77.1)	19 (50.0)	26 (72.2)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	3.15 (1.873 to 6.669)	8.97 (6.012 to NC)	2.53 (1.018 to 5.618)	9.00 (1.840 to NC)	
Median (95% CI)	NC (10.973 to NC)	NC (NC to NC)	9.46 (3.811 to NC)	NC (12.123 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.339 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0079		0.0586	
Hazard ratio (95% CI) vs Pd	-	0.52 (0.32 to 0.85)		0.48 (0.23 to 1.04)	
P-value	-	0.0090		0.0642	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (31.9)	66 (44.9)	5 (55.6)	5 (71.4)	0.9945
Number (%) of patients censored	98 (68.1)	81 (55.1)	4 (44.4)	2 (28.6)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.94 (1.150 to 8.312)	2.04 (1.380 to 2.760)	1.08 (0.986 to 2.990)	1.02 (0.986 to 3.055)	
Median (95% CI)	NC (NC to NC)	13.83 (5.421 to NC)	2.99 (0.986 to NC)	3.06 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.248 to NC)	NC (1.971 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1020		0.7387	
Hazard ratio (95% CI) vs Pd	-	1.37 (0.94 to 1.99)		1.23 (0.36 to 4.27)	
P-value	-	0.1034		0.7392	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_impl_refr1_de_i_t_x.rtf (08APR2021 14:34)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	91 (63.2)	91 (61.9)	5 (55.6)	3 (42.9)	0.9306
Number (%) of patients censored	53 (36.8)	56 (38.1)	4 (44.4)	4 (57.1)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.12 (1.018 to 1.873)	1.51 (1.084 to 1.938)	5.16 (0.986 to 8.608)	1.12 (1.018 to NC)	
Median (95% CI)	3.42 (2.464 to 4.205)	4.11 (2.858 to 6.702)	8.61 (0.986 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (8.345 to NC)	NC (10.185 to NC)	NC (5.848 to NC)	NC (4.928 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3365		0.7784	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.65 to 1.16)		0.81 (0.19 to 3.42)	
P-value	-	0.3369		0.7788	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (12.5)	21 (14.3)	1 (11.1)	2 (28.6)	0.3489
Number (%) of patients censored	126 (87.5)	126 (85.7)	8 (88.9)	5 (71.4)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (11.466 to NC)	NC (11.795 to NC)	NC (8.575 to NC)	10.25 (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (8.575 to NC)	NC (1.971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.251 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9439		0.2966	
Hazard ratio (95% CI) vs Pd	-	1.02 (0.54 to 1.92)		3.35 (0.30 to 37.31)	
P-value	-	0.9439		0.3251	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	57 (39.6)	35 (23.8)	3 (33.3)	2 (28.6)	0.4767
Number (%) of patients censored	87 (60.4)	112 (76.2)	6 (66.7)	5 (71.4)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.83 (1.610 to 4.205)	9.00 (6.472 to NC)	10.68 (0.986 to NC)	4.93 (1.018 to NC)	
Median (95% CI)	NC (8.936 to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.678 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0006		0.9331	
Hazard ratio (95% CI) vs Pd	-	0.48 (0.32 to 0.74)		0.93 (0.15 to 5.57)	
P-value	-	0.0008		0.9331	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (34.1)	39 (41.9)	21 (32.3)	32 (52.5)	0.5265
Number (%) of patients censored	58 (65.9)	54 (58.1)	44 (67.7)	29 (47.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.94 (1.117 to 5.651)	2.20 (1.380 to 2.990)	1.51 (1.018 to 9.725)	1.87 (1.018 to 2.530)	
Median (95% CI)	NC (11.532 to NC)	NC (4.797 to NC)	NC (9.725 to NC)	6.54 (2.530 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.832 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4086		0.1207	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.76 to 1.97)		1.54 (0.89 to 2.67)	
P-value	-	0.4094		0.1236	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	56 (63.6)	53 (57.0)	40 (61.5)	41 (67.2)	0.4348
Number (%) of patients censored	32 (36.4)	40 (43.0)	25 (38.5)	20 (32.8)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.08 (1.018 to 1.873)	1.84 (1.018 to 2.070)	1.35 (1.018 to 2.924)	1.28 (1.084 to 1.938)	
Median (95% CI)	2.83 (1.938 to 4.501)	4.47 (2.793 to 8.608)	3.98 (2.924 to 6.834)	4.44 (2.136 to 7.556)	
75% quantile (95% CI)	NC (7.655 to NC)	NC (NC to NC)	NC (6.834 to NC)	13.01 (7.556 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2503		0.9526	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.55 to 1.17)		0.99 (0.64 to 1.53)	
P-value	-	0.2513		0.9526	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (14.8)	12 (12.9)	6 (9.2)	11 (18.0)	0.2657
Number (%) of patients censored	75 (85.2)	81 (87.1)	59 (90.8)	50 (82.0)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (9.758 to NC)	NC (11.762 to NC)	NC (11.466 to NC)	14.32 (8.444 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.324 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6410		0.2872	
Hazard ratio (95% CI) vs Pd	-	0.83 (0.38 to 1.82)		1.71 (0.63 to 4.61)	
P-value	-	0.6408		0.2929	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Role functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (42.0)	20 (21.5)	23 (35.4)	17 (27.9)	0.3505
Number (%) of patients censored	51 (58.0)	73 (78.5)	42 (64.6)	44 (72.1)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.46 (1.084 to 4.862)	NC (6.012 to NC)	3.75 (2.267 to 10.678)	7.89 (4.698 to NC)	
Median (95% CI)	13.34 (5.618 to NC)	NC (NC to NC)	NC (10.678 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0020		0.1290	
Hazard ratio (95% CI) vs Pd	-	0.43 (0.25 to 0.75)		0.62 (0.33 to 1.16)	
P-value	-	0.0026		0.1327	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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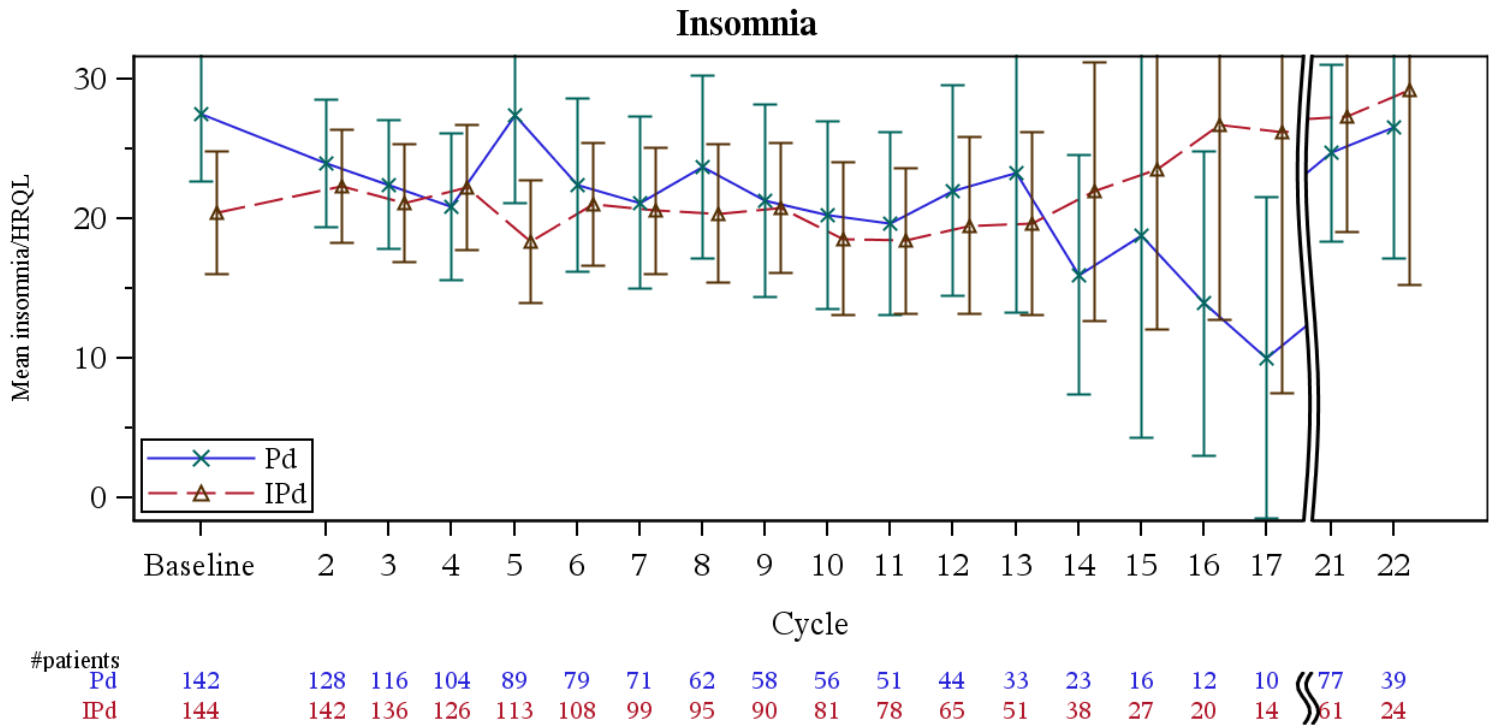
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Insomnia
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-C30 - Mean and 95% CI for insomnia score over time (LOCF) - ITT population



A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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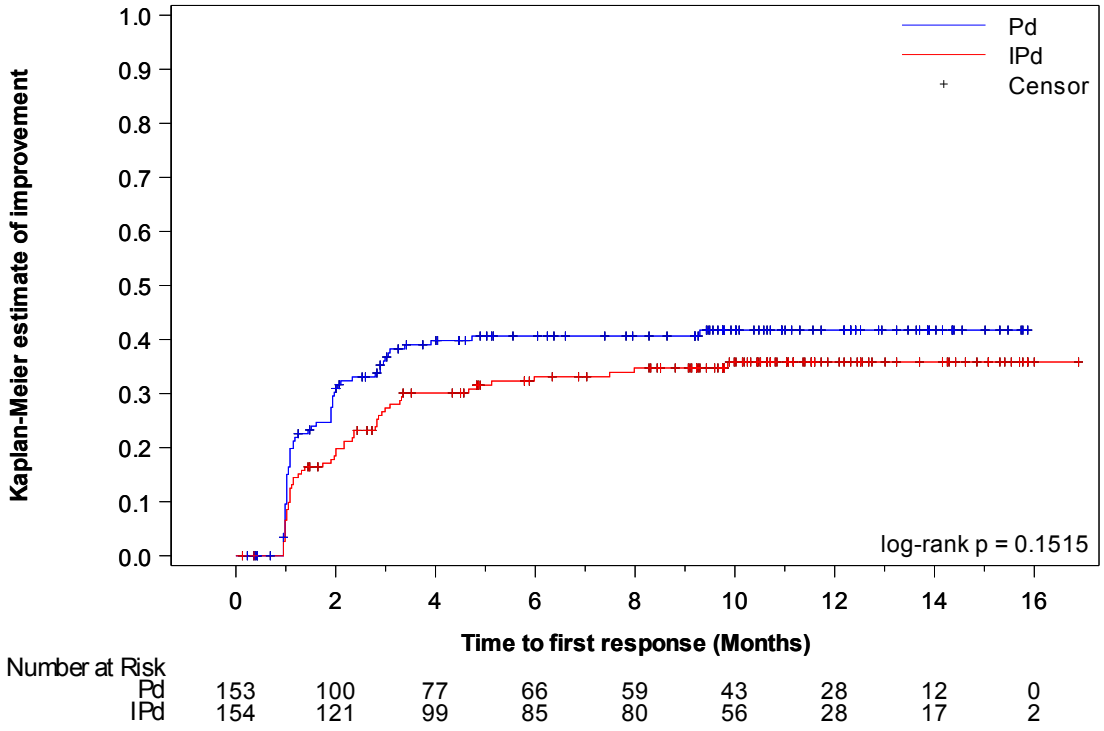
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Insomnia
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-C30 - Time to first improvement by 15 pt in insomnia (LOCF) - ITT population

First improvement 15 points Insomnia (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	59 (38.6)	52 (33.8)
Number (%) of patients censored	94 (61.4)	102 (66.2)
Kaplan-Meier estimates of insomnia in months		
25% quantile (95% CI)	1.91 (1.084 to 2.103)	2.83 (1.971 to 5.125)
Median (95% CI)	NC (9.298 to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1515
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.76 (0.52 to 1.11)
P-value	-	0.1528
Probability (95% CI)[c]		
2 Months	0.30 (0.230 to 0.378)	0.18 (0.128 to 0.250)
4 Months	0.40 (0.317 to 0.477)	0.30 (0.229 to 0.376)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_imp15l_de_i_t_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Insomnia
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-C30 - Time to first improvement by 15 pt in insomnia - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_imp15l_de_i_f_x.rtf (08APR2021 15:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Insomnia
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-C30 - Time to first deterioration by 15 pt in insomnia (LOCF) - ITT population

First deterioration 15 points Insomnia (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	69 (45.1)	87 (56.5)
Number (%) of patients censored	84 (54.9)	67 (43.5)
Kaplan-Meier estimates of insomnia in months		
25% quantile (95% CI)	2.23 (1.281 to 3.088)	1.91 (1.380 to 2.628)
Median (95% CI)	9.72 (4.665 to NC)	6.57 (4.698 to 9.495)
75% quantile (95% CI)	NC (NC to NC)	15.31 (13.864 to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1576
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.26 (0.92 to 1.72)
P-value	-	0.1585
Probability (95% CI)[c]		
2 Months	0.77 (0.697 to 0.834)	0.72 (0.643 to 0.786)
4 Months	0.61 (0.528 to 0.688)	0.60 (0.519 to 0.677)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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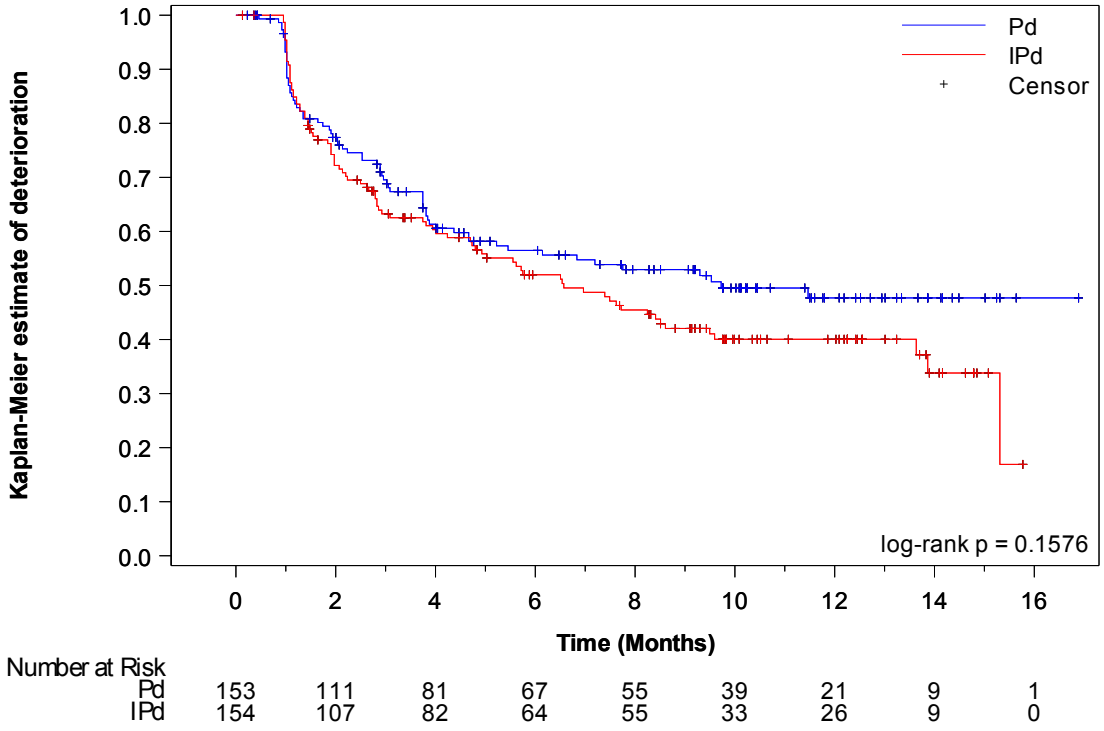
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Insomnia
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-C30 - Time to first deterioration by 15 pt in insomnia - Kaplan-Meier curve (LOCF) - ITT population



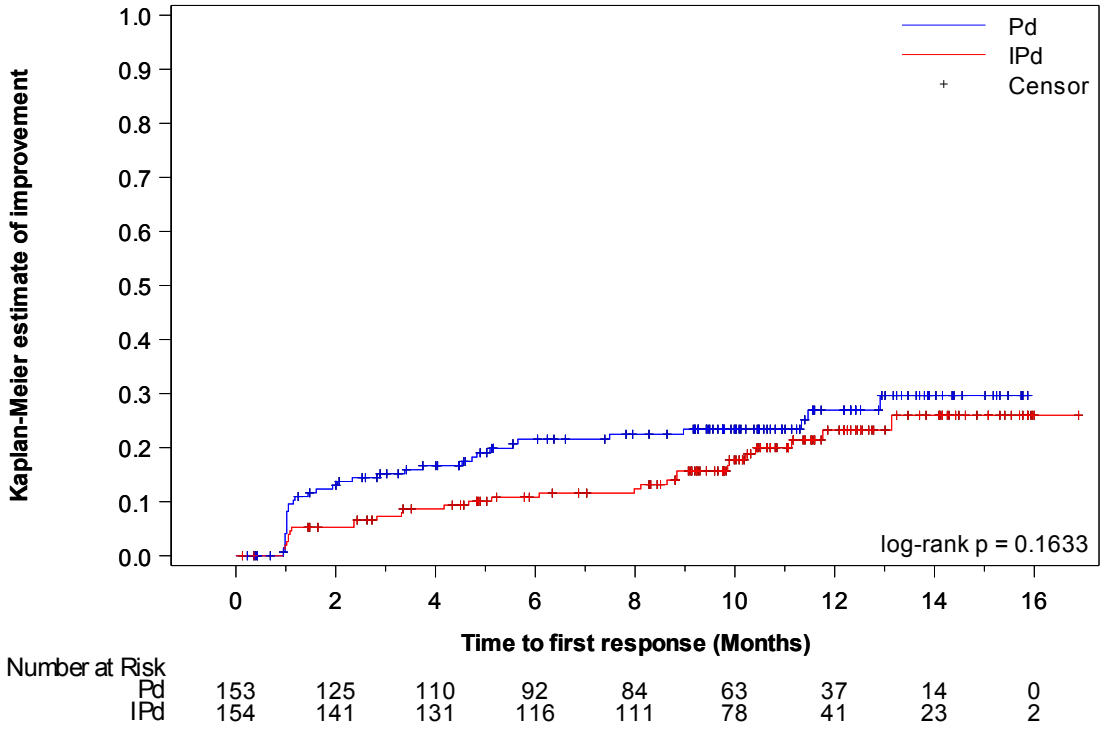
A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_det15l_de_i_f_x.rtf (08APR2021 15:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Insomnia
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in insomnia (LOCF) - ITT population

First permanent improvement 15 points Insomnia (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	35 (22.9)	29 (18.8)
Number (%) of patients censored	118 (77.1)	125 (81.2)
Kaplan-Meier estimates of insomnia in months		
25% quantile (95% CI)	11.33 (4.731 to NC)	13.14 (9.889 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1633
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.71 (0.43 to 1.16)
P-value	-	0.1654
Probability (95% CI)[c]		
2 Months	0.13 (0.082 to 0.190)	0.05 (0.025 to 0.096)
4 Months	0.17 (0.111 to 0.232)	0.09 (0.049 to 0.138)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_imp15pl_de_i_t_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Insomnia
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-C30 - Time until permanent improvement by 15 pt in insomnia - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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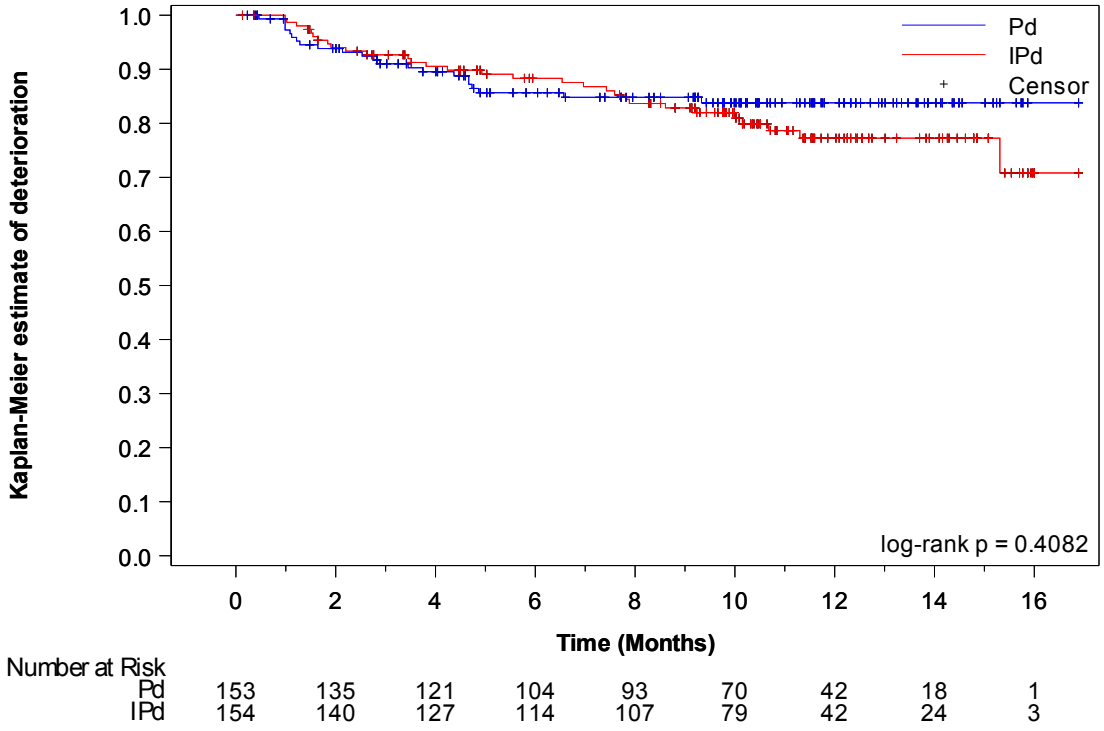
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Insomnia
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in insomnia (LOCF) - ITT population

First permanent deterioration 15 points Insomnia (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	22 (14.4)	30 (19.5)
Number (%) of patients censored	131 (85.6)	124 (80.5)
Kaplan-Meier estimates of insomnia in months		
25% quantile (95% CI)	NC (NC to NC)	15.31 (9.232 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4082
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.26 (0.73 to 2.19)
P-value	-	0.4093
Probability (95% CI)[c]		
2 Months	0.94 (0.885 to 0.967)	0.94 (0.888 to 0.968)
4 Months	0.90 (0.832 to 0.936)	0.91 (0.846 to 0.943)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_det15pl_de_i_t_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Insomnia
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-C30 - Time until permanent deterioration by 15 pt in insomnia - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_det15pl_de_i_f_x.rtf (08APR2021 15:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (38.6)	18 (33.3)	22 (40.7)	19 (27.9)	10 (34.5)	15 (46.9)	0.4553
Number (%) of patients censored	43 (61.4)	36 (66.7)	32 (59.3)	49 (72.1)	19 (65.5)	17 (53.1)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	1.91 (1.084 to 2.990)	2.00 (1.051 to NC)	1.51 (0.986 to 2.891)	3.35 (1.150 to NC)	1.08 (0.986 to NC)	2.60 (1.117 to 5.979)	
Median (95% CI)	NC (3.088 to NC)	NC (NC to NC)	NC (2.891 to NC)	NC (NC to NC)	NC (1.183 to NC)	7.98 (3.318 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4980		0.0873		0.8249	
Hazard ratio (95% CI) vs Pd	-	0.81 (0.45 to 1.48)		0.59 (0.32 to 1.09)		1.09 (0.49 to 2.44)	
P-value	-	0.4988		0.0910		0.8249	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_impl_age_de_i_t_x.rtf (08APR2021 14:48)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (48.6)	30 (55.6)	22 (40.7)	42 (61.8)	13 (44.8)	15 (46.9)	0.2209
Number (%) of patients censored	36 (51.4)	24 (44.4)	32 (59.3)	26 (38.2)	16 (55.2)	17 (53.1)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	1.87 (1.051 to 2.924)	1.97 (1.117 to 2.858)	3.75 (1.741 to 6.144)	1.51 (1.084 to 2.793)	1.18 (0.953 to 2.891)	2.45 (1.084 to 4.238)	
Median (95% CI)	7.75 (3.745 to NC)	8.51 (2.825 to 15.310)	NC (5.224 to NC)	5.75 (2.793 to 8.411)	6.83 (1.938 to NC)	7.72 (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	15.31 (13.864 to 15.310)	NC (NC to NC)	NC (9.495 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7621		0.0303		0.7574	
Hazard ratio (95% CI) vs Pd	-	1.08 (0.66 to 1.76)		1.76 (1.05 to 2.95)		0.89 (0.42 to 1.87)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (24.3)	10 (18.5)	10 (18.5)	10 (14.7)	8 (27.6)	9 (28.1)	0.9501
Number (%) of patients censored	53 (75.7)	44 (81.5)	44 (81.5)	58 (85.3)	21 (72.4)	23 (71.9)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	11.33 (2.891 to NC)	NC (4.172 to NC)	NC (2.037 to NC)	13.14 (10.218 to NC)	4.53 (1.018 to NC)	8.64 (2.366 to NC)	
Median (95% CI)	NC (12.912 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.969 to NC)	NC (9.889 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3578		0.3677		0.6963	
Hazard ratio (95% CI) vs Pd	-	0.69 (0.32 to 1.52)		0.67 (0.28 to 1.61)		0.83 (0.32 to 2.15)	
P-value	-	0.3605		0.3709		0.6967	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (18.6)	12 (22.2)	4 (7.4)	16 (23.5)	5 (17.2)	2 (6.3)	0.0521
Number (%) of patients censored	57 (81.4)	42 (77.8)	50 (92.6)	52 (76.5)	24 (82.8)	30 (93.8)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	NC (4.370 to NC)	15.31 (3.811 to NC)	NC (NC to NC)	10.15 (4.928 to NC)	NC (1.117 to NC)	NC (10.678 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.310 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.310 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8113		0.0314		0.1027	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.50 to 2.42)		3.13 (1.05 to 9.36)		0.28 (0.05 to 1.44)	
P-value	-	0.8107		0.0414		0.1265	
Hazard ratio inverted (95% CI) vs IPd		-		0.32 (0.11 to 0.96)		3.61 (0.70 to 18.78)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_detpl_age_de_i_t_x.rtf (08APR2021 14:49)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	38 (37.6)	33 (32.4)	21 (40.4)	19 (36.5)	0.7128
Number (%) of patients censored	63 (62.4)	69 (67.6)	31 (59.6)	33 (63.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.94 (1.150 to 2.990)	2.79 (1.117 to 9.856)	1.08 (1.018 to 2.037)	2.92 (1.906 to 7.491)	
Median (95% CI)	NC (9.298 to NC)	NC (NC to NC)	NC (2.037 to NC)	NC (5.979 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3595		0.2369	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.50 to 1.28)		0.69 (0.37 to 1.28)	
P-value	-	0.3603		0.2396	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (42.6)	55 (53.9)	26 (50.0)	32 (61.5)	0.8701
Number (%) of patients censored	58 (57.4)	47 (46.1)	26 (50.0)	20 (38.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.23 (1.183 to 3.811)	1.91 (1.446 to 2.793)	2.53 (1.018 to 2.957)	1.36 (1.051 to 2.825)	
Median (95% CI)	NC (4.665 to NC)	7.49 (4.008 to NC)	7.75 (2.924 to NC)	4.93 (2.825 to 9.593)	
75% quantile (95% CI)	NC (NC to NC)	15.31 (15.310 to NC)	NC (11.466 to NC)	13.86 (9.495 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2409		0.5089	
Hazard ratio (95% CI) vs Pd	-	1.27 (0.85 to 1.89)		1.19 (0.71 to 2.00)	
P-value	-	0.2420		0.5094	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	20 (19.8)	20 (19.6)	15 (28.8)	9 (17.3)	0.1977
Number (%) of patients censored	81 (80.2)	82 (80.4)	37 (71.2)	43 (82.7)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	12.91 (5.092 to NC)	13.14 (9.856 to NC)	4.83 (1.018 to NC)	NC (5.125 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.466 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7730		0.0626	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.49 to 1.70)		0.46 (0.20 to 1.06)	
P-value	-	0.7728		0.0691	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (13.9)	20 (19.6)	8 (15.4)	10 (19.2)	0.6902
Number (%) of patients censored	87 (86.1)	82 (80.4)	44 (84.6)	42 (80.8)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (9.331 to NC)	15.31 (7.589 to NC)	NC (2.891 to NC)	11.30 (6.538 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.310 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4008		0.8857	
Hazard ratio (95% CI) vs Pd	-	1.34 (0.68 to 2.66)		1.07 (0.42 to 2.71)	
P-value	-	0.4024		0.8860	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (28.6)	27 (30.3)	39 (47.0)	25 (38.5)	0.2802
Number (%) of patients censored	50 (71.4)	62 (69.7)	44 (53.0)	40 (61.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.79 (1.051 to NC)	2.83 (1.314 to NC)	1.18 (1.018 to 1.938)	2.79 (1.117 to 7.491)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	4.73 (2.103 to NC)	NC (7.491 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9697		0.0905	
Hazard ratio (95% CI) vs Pd	-	1.01 (0.57 to 1.80)		0.65 (0.39 to 1.07)	
P-value	-	0.9697		0.0930	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (51.4)	48 (53.9)	33 (39.8)	39 (60.0)	0.3256
Number (%) of patients censored	34 (48.6)	41 (46.1)	50 (60.2)	26 (40.0)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.87 (1.051 to 3.023)	1.97 (1.117 to 2.858)	2.89 (1.183 to 3.811)	1.91 (1.216 to 2.793)	
Median (95% CI)	9.30 (3.745 to NC)	6.57 (3.943 to 13.864)	NC (3.877 to NC)	6.54 (2.793 to 13.634)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.864 to NC)	NC (NC to NC)	15.31 (13.634 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7805		0.1026	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.69 to 1.64)		1.47 (0.92 to 2.34)	
P-value	-	0.7813		0.1047	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (11.4)	15 (16.9)	27 (32.5)	14 (21.5)	0.0724
Number (%) of patients censored	62 (88.6)	74 (83.1)	56 (67.5)	51 (78.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (12.912 to NC)	13.14 (10.218 to NC)	4.53 (1.446 to 11.335)	11.14 (4.665 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.335 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4014		0.0598	
Hazard ratio (95% CI) vs Pd	-	1.44 (0.61 to 3.40)		0.54 (0.28 to 1.04)	
P-value	-	0.4041		0.0638	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (14.3)	16 (18.0)	12 (14.5)	14 (21.5)	0.8824
Number (%) of patients censored	60 (85.7)	73 (82.0)	71 (85.5)	51 (78.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (4.731 to NC)	NC (7.589 to NC)	NC (6.571 to NC)	15.31 (7.819 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.310 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6143		0.5067	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.56 to 2.70)		1.30 (0.60 to 2.81)	
P-value	-	0.6150		0.5073	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (36.5)	40 (33.9)	12 (63.2)	9 (37.5)	0.3185
Number (%) of patients censored	80 (63.5)	78 (66.1)	7 (36.8)	15 (62.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.91 (1.084 to 2.793)	2.92 (1.971 to 7.491)	1.05 (0.953 to 2.103)	1.66 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	2.89 (1.051 to NC)	NC (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.891 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3028		0.1075	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.52 to 1.22)		0.50 (0.21 to 1.18)	
P-value	-	0.3036		0.1146	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	58 (46.0)	72 (61.0)	7 (36.8)	11 (45.8)	0.7551
Number (%) of patients censored	68 (54.0)	46 (39.0)	12 (63.2)	13 (54.2)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.94 (1.150 to 2.957)	1.91 (1.216 to 2.793)	4.37 (2.037 to 11.466)	2.14 (1.018 to 7.491)	
Median (95% CI)	9.53 (4.008 to NC)	5.72 (3.943 to 8.411)	11.47 (4.370 to NC)	NC (2.234 to NC)	
75% quantile (95% CI)	NC (NC to NC)	15.31 (13.634 to NC)	NC (11.466 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1677		0.3942	
Hazard ratio (95% CI) vs Pd	-	1.27 (0.90 to 1.80)		1.51 (0.58 to 3.92)	
P-value	-	0.1687		0.3974	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (21.4)	26 (22.0)	7 (36.8)	2 (8.3)	0.0366
Number (%) of patients censored	99 (78.6)	92 (78.0)	12 (63.2)	22 (91.7)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	11.47 (5.092 to NC)	11.76 (8.838 to NC)	1.05 (0.953 to NC)	NC (8.115 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7499		0.0129	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.53 to 1.57)		0.17 (0.03 to 0.82)	
P-value	-	0.7498		0.0277	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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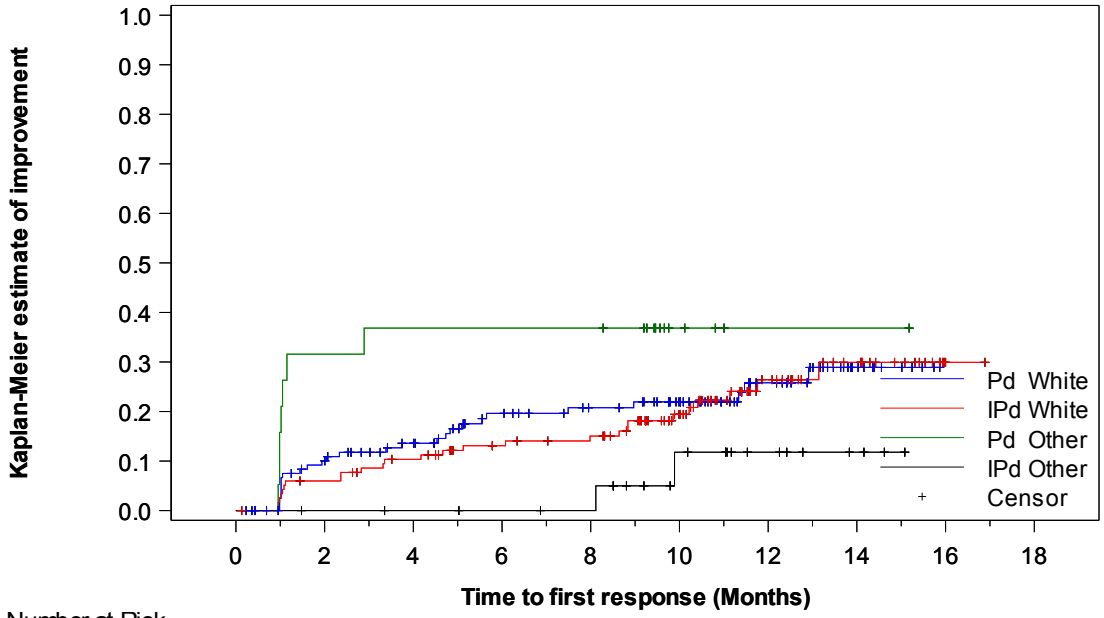
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to race (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd White	126	99	76	66	34	5	0
IPd White	118	104	90	79	30	11	0
Pd Other	19	12	12	11	1	1	0
IPd Other	24	23	21	16	7	1	0

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_imppl_race_de_i_f_x.rtf (08APR2021 14:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.7 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (15.1)	24 (20.3)	2 (10.5)	3 (12.5)	0.9662
Number (%) of patients censored	107 (84.9)	94 (79.7)	17 (89.5)	21 (87.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (9.331 to NC)	15.31 (9.232 to NC)	NC (2.825 to NC)	NC (4.928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5351		0.8188	
Hazard ratio (95% CI) vs Pd	-	1.21 (0.66 to 2.21)		1.23 (0.21 to 7.38)	
P-value	-	0.5357		0.8191	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (25.0)	53 (39.6)	47 (36.2)	0.9854
Number (%) of patients censored	3 (100.0)	3 (75.0)	81 (60.4)	83 (63.8)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (NC to NC)	NC (1.018 to NC)	1.91 (1.084 to 2.333)	2.83 (1.906 to 4.830)	
Median (95% CI)	NC (NC to NC)	NC (1.018 to NC)	NC (4.731 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.2852	
Hazard ratio (95% CI) vs Pd	-			0.81 (0.54 to 1.20)	
P-value	-	0.9985		0.2856	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_impl_ethn_de_i_t_x.rtf (08APR2021 14:49)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	2 (50.0)	60 (44.8)	75 (57.7)	0.5631
Number (%) of patients censored	2 (66.7)	2 (50.0)	74 (55.2)	55 (42.3)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.35 (1.347 to NC)	1.76 (1.018 to NC)	2.83 (1.643 to 3.745)	1.97 (1.380 to 2.825)	
Median (95% CI)	NC (1.347 to NC)	NC (1.018 to NC)	11.47 (5.224 to NC)	6.97 (4.797 to 9.495)	
75% quantile (95% CI)	NC (1.347 to NC)	NC (1.018 to NC)	NC (NC to NC)	15.31 (13.864 to 15.310)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9835		0.1423	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.09 to 10.98)		1.29 (0.92 to 1.81)	
P-value	-	0.9834		0.1434	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_detl_ethn_de_i_t_x.rtf (08APR2021 14:48)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	32 (23.9)	27 (20.8)	0.9999
Number (%) of patients censored	3 (100.0)	4 (100.0)	102 (76.1)	103 (79.2)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	11.33 (3.745 to NC)	11.76 (8.838 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.3136	
Hazard ratio (95% CI) vs Pd	-			0.77 (0.46 to 1.28)	
P-value	-			0.3148	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_imppl_ethn_de_i_t_x.rtf (08APR2021 14:49)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (25.0)	20 (14.9)	24 (18.5)	0.9874
Number (%) of patients censored	3 (100.0)	3 (75.0)	114 (85.1)	106 (81.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (NC to NC)	NC (1.018 to NC)	NC (NC to NC)	15.31 (10.021 to NC)	
Median (95% CI)	NC (NC to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.7501	
Hazard ratio (95% CI) vs Pd	-			1.10 (0.61 to 2.00)	
P-value	-	0.9985		0.7508	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	27 (35.5)	16 (29.1)	5 (25.0)	10 (35.7)	4 (80.0)	3 (42.9)	8 (53.3)	7 (33.3)	15 (40.5)	16 (37.2)	0.7197
Number (%) of patients censored	49 (64.5)	39 (70.9)	15 (75.0)	18 (64.3)	1 (20.0)	4 (57.1)	7 (46.7)	14 (66.7)	22 (59.5)	27 (62.8)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	1.97 (1.018 to 3.384)	5.13 (1.084 to NC)	4.73 (0.953 to NC)	2.83 (0.986 to NC)	0.99 (0.986 to 2.957)	0.95 (0.953 to NC)	1.15 (1.018 to 2.891)	2.00 (0.986 to NC)	1.48 (1.018 to 1.938)	2.33 (1.380 to 9.856)	
Median (95% CI)	NC (3.910 to NC)	NC (NC to NC)	NC (4.731 to NC)	NC (3.318 to NC)	1.91 (0.986 to NC)	NC (0.953 to NC)	2.89 (1.084 to NC)	NC (2.004 to NC)	NC (1.906 to NC)	NC (2.924 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	2.96 (0.986 to NC)	NC (1.248 to NC)	NC (2.891 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.2297		0.5788		0.4280		0.3202		0.4680	
Hazard ratio (95% CI) vs Pd	-	0.69 (0.37 to 1.27)		1.35 (0.46 to 3.96)		0.55 (0.12 to 2.47)		0.60 (0.22 to 1.66)		0.77 (0.38 to 1.56)	
P-value	-	0.2325		0.5803		0.4346		0.3254		0.4692	
Improvement probability (95% CI)[b]											
2 Months	0.254 (0.160 to 0.359)	0.148 (0.069 to 0.255)	0.211 (0.066 to 0.410)	0.143 (0.045 to 0.295)	0.600 (0.126 to 0.882)	0.429 (0.098 to 0.734)	0.333 (0.122 to 0.564)	0.238 (0.087 to 0.431)	0.394 (0.236 to 0.549)	0.192 (0.090 to 0.323)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	28 (36.8)	28 (50.9)	11 (55.0)	14 (50.0)	2 (40.0)	4 (57.1)	6 (40.0)	9 (42.9)	22 (59.5)	32 (74.4)	0.7009
Number (%) of patients censored	48 (63.2)	27 (49.1)	9 (45.0)	14 (50.0)	3 (60.0)	3 (42.9)	9 (60.0)	12 (57.1)	15 (40.5)	11 (25.6)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	1.35 (1.051 to 3.745)	1.51 (1.084 to 2.201)	1.91 (0.986 to 6.144)	3.09 (1.018 to 6.965)	3.88 (1.347 to NC)	1.15 (1.018 to 2.924)	4.37 (2.037 to 11.466)	2.23 (1.018 to 8.509)	2.14 (1.018 to 3.088)	1.91 (1.084 to 2.825)	
Median (95% CI)	NC (5.224 to NC)	4.93 (2.201 to NC)	6.14 (1.906 to NC)	9.59 (5.552 to NC)	NC (1.347 to NC)	2.92 (1.018 to NC)	11.47 (3.745 to 11.466)	NC (2.234 to NC)	3.84 (2.530 to 9.528)	4.80 (2.628 to 7.721)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.195 to NC)	13.63 (13.634 to NC)	NC (1.347 to NC)	NC (2.858 to NC)	11.47 (NC to NC)	NC (NC to NC)	NC (5.454 to NC)	13.86 (6.538 to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.2251		0.4167		0.4663		0.6896		0.6953	
Hazard ratio (95% CI) vs Pd	-	1.38 (0.82 to 2.33)		0.72 (0.32 to 1.60)		1.87 (0.34 to 10.27)		1.24 (0.43 to 3.53)		1.11 (0.65 to 1.92)	
P-value	-	0.2271		0.4188		0.4734		0.6901		0.6955	
Deterioration probability (95% CI)[b]											

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	18 (23.7)	10 (18.2)	4 (20.0)	6 (21.4)	0 (0.0)	2 (28.6)	4 (26.7)	1 (4.8)	9 (24.3)	10 (23.3)	0.6479
Number (%) of patients censored	58 (76.3)	45 (81.8)	16 (80.0)	22 (78.6)	5 (100.0)	5 (71.4)	11 (73.3)	20 (95.2)	28 (75.7)	33 (76.7)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	11.33 (4.534 to NC)	13.14 (5.125 to NC)	NC (0.986 to NC)	NC (1.051 to NC)	NC (NC to NC)	8.84 (0.953 to NC)	2.89 (1.018 to NC)	NC (8.115 to NC)	5.65 (1.018 to NC)	11.14 (8.641 to NC)	
Median (95% CI)	NC (12.912 to NC)	NC (13.142 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (1.150 to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.762 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.838 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.3652		0.9570		0.1917		0.0605		0.5191	
Hazard ratio (95% CI) vs Pd	-	0.70 (0.32 to 1.52)		1.04 (0.29 to 3.67)				0.16 (0.02 to 1.43)		0.74 (0.30 to 1.84)	
P-value	-	0.3677		0.9571		0.9977		0.1013		0.5206	
Improvement probability (95% CI)[b]											

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	6 (7.9)	12 (21.8)	5 (25.0)	5 (17.9)	0 (0.0)	2 (28.6)	2 (13.3)	2 (9.5)	9 (24.3)	9 (20.9)	0.2159
Number (%) of patients censored	70 (92.1)	43 (78.2)	15 (75.0)	23 (82.1)	5 (100.0)	5 (71.4)	13 (86.7)	19 (90.5)	28 (75.7)	34 (79.1)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (NC to NC)	11.30 (2.201 to NC)	9.33 (1.216 to NC)	10.68 (4.928 to NC)	NC (NC to NC)	3.45 (1.018 to NC)	NC (2.825 to NC)	NC (5.552 to NC)	6.57 (2.136 to NC)	15.31 (6.538 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.331 to NC)	NC (10.678 to NC)	NC (NC to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.310 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.0347		0.4154		0.2137		0.7659		0.4011	
Hazard ratio (95% CI) vs Pd	-	2.75 (1.03 to 7.34)		0.60 (0.17 to 2.08)				0.74 (0.10 to 5.28)		0.67 (0.26 to 1.71)	
P-value	-	0.0429		0.4204		0.9978		0.7667		0.4041	
Hazard ratio inverted (95% CI) vs IPd		-		1.67 (0.48 to 5.77)		0.9978		1.35 (0.19 to 9.55)		1.49 (0.59 to 3.78)	
Deterioration probability (95% CI)[b]											
2 Months	0.944 (0.857 to 0.979)	0.889 (0.769 to 0.948)	0.895 (0.641 to 0.973)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.857 (0.334 to 0.979)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.917 (0.763 to 0.972)	0.952 (0.821 to 0.988)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (40.2)	23 (29.9)	20 (35.7)	29 (37.7)	0.1669
Number (%) of patients censored	58 (59.8)	54 (70.1)	36 (64.3)	48 (62.3)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.25 (1.018 to 2.037)	4.67 (1.248 to NC)	1.91 (1.084 to 4.731)	2.17 (1.314 to 3.318)	
Median (95% CI)	NC (3.088 to NC)	NC (NC to NC)	NC (4.731 to NC)	NC (7.984 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0559		0.9258	
Hazard ratio (95% CI) vs Pd	-	0.61 (0.36 to 1.02)		1.03 (0.58 to 1.82)	
P-value	-	0.0585		0.9260	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (41.2)	44 (57.1)	29 (51.8)	43 (55.8)	0.2357
Number (%) of patients censored	57 (58.8)	33 (42.9)	27 (48.2)	34 (44.2)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.87 (1.084 to 2.957)	1.38 (1.084 to 1.971)	3.75 (1.643 to 4.665)	2.66 (1.906 to 5.027)	
Median (95% CI)	NC (3.811 to NC)	4.70 (2.201 to NC)	9.30 (4.370 to NC)	8.41 (5.618 to 13.864)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.466 to NC)	15.31 (13.864 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0994		0.9825	
Hazard ratio (95% CI) vs Pd	-	1.43 (0.93 to 2.20)		0.99 (0.62 to 1.60)	
P-value	-	0.1012		0.9825	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (22.7)	14 (18.2)	13 (23.2)	15 (19.5)	0.8700
Number (%) of patients censored	75 (77.3)	63 (81.8)	43 (76.8)	62 (80.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	11.33 (4.534 to NC)	13.14 (8.838 to NC)	NC (1.610 to NC)	11.76 (9.856 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2917		0.4542	
Hazard ratio (95% CI) vs Pd	-	0.70 (0.36 to 1.37)		0.75 (0.36 to 1.58)	
P-value	-	0.2943		0.4557	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (10.3)	18 (23.4)	12 (21.4)	12 (15.6)	0.0273
Number (%) of patients censored	87 (89.7)	59 (76.6)	44 (78.6)	65 (84.4)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (NC to NC)	11.30 (3.811 to NC)	NC (3.745 to NC)	15.31 (10.152 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.310 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0390		0.2190	
Hazard ratio (95% CI) vs Pd	-	2.21 (1.02 to 4.79)		0.61 (0.27 to 1.36)	
P-value	-	0.0444		0.2237	
Hazard ratio inverted (95% CI) vs IPd		-		1.65 (0.74 to 3.68)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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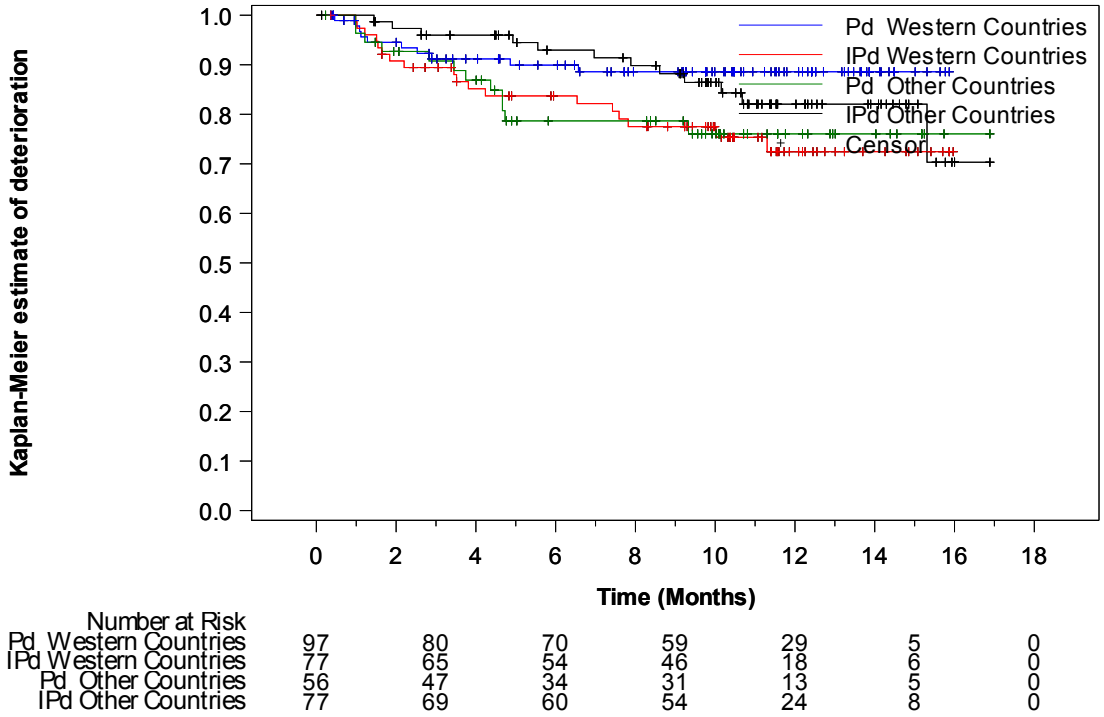
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.7 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to regulatory region (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd Western Countries	97	80	70	59	29	5	0
IPd Western Countries	77	65	54	46	18	6	0
Pd Other Countries	56	47	34	31	13	5	0
IPd Other Countries	77	69	60	54	24	8	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	54 (39.4)	47 (34.1)	5 (31.3)	5 (31.3)	0.5272
Number (%) of patients censored	83 (60.6)	91 (65.9)	11 (68.8)	11 (68.8)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.91 (1.084 to 2.103)	2.86 (2.004 to 5.979)	1.15 (0.953 to NC)	1.08 (0.953 to NC)	
Median (95% CI)	NC (4.731 to NC)	NC (NC to NC)	NC (1.018 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1223		0.9325	
Hazard ratio (95% CI) vs Pd	-	0.74 (0.50 to 1.09)		1.06 (0.30 to 3.65)	
P-value	-	0.1238		0.9325	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	61 (44.5)	85 (61.6)	8 (50.0)	2 (12.5)	0.0125
Number (%) of patients censored	76 (55.5)	53 (38.4)	8 (50.0)	14 (87.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.23 (1.281 to 3.745)	1.91 (1.281 to 2.234)	1.87 (0.986 to 3.745)	NC (1.018 to NC)	
Median (95% CI)	11.47 (5.224 to NC)	5.72 (3.811 to 8.246)	4.67 (1.084 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	15.31 (13.634 to 15.310)	NC (4.665 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0335		0.0440	
Hazard ratio (95% CI) vs Pd	-	1.43 (1.03 to 1.98)		0.23 (0.05 to 1.09)	
P-value	-	0.0344		0.0646	
Hazard ratio inverted (95% CI) vs IPd		-		4.33 (0.91 to 20.50)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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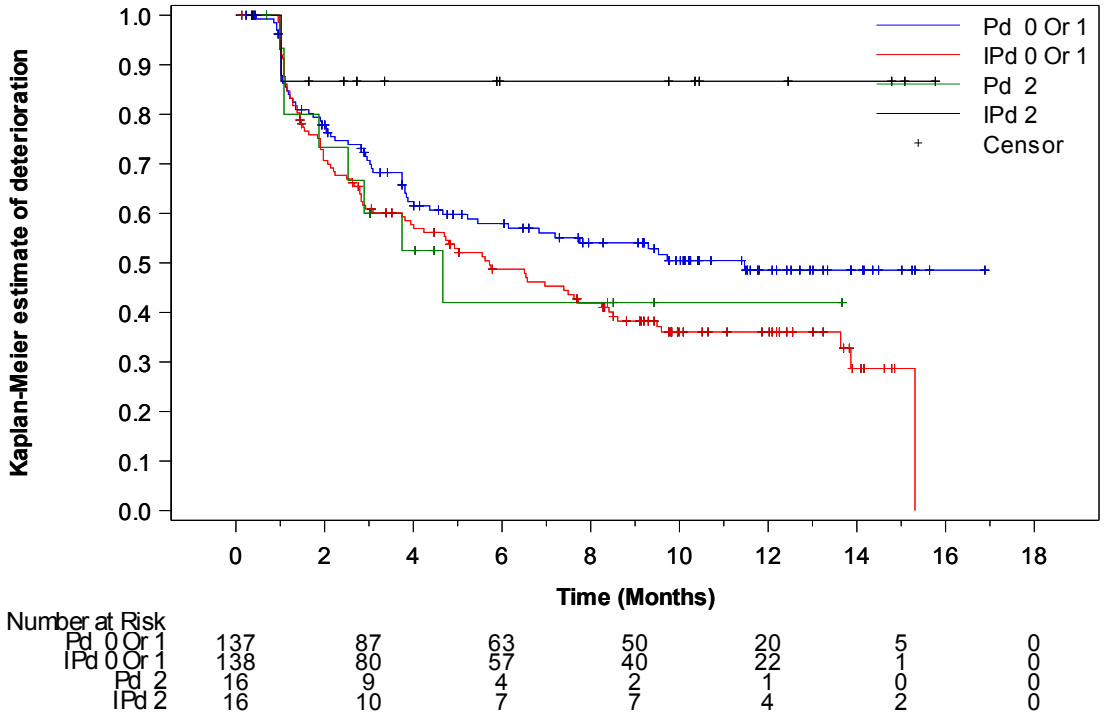
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to baseline ECOG PS (LOCF) - Kaplan-Meier curve - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (21.9)	24 (17.4)	5 (31.3)	5 (31.3)	0.5636
Number (%) of patients censored	107 (78.1)	114 (82.6)	11 (68.8)	11 (68.8)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	11.47 (4.731 to NC)	NC (9.889 to NC)	5.09 (0.986 to NC)	11.14 (0.953 to 13.142)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	12.91 (1.150 to NC)	13.14 (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.912 to NC)	NC (11.138 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1581		0.9621	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.40 to 1.16)		1.03 (0.30 to 3.59)	
P-value	-	0.1606		0.9621	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.7 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (12.4)	28 (20.3)	5 (31.3)	2 (12.5)	0.1049
Number (%) of patients censored	120 (87.6)	110 (79.7)	11 (68.8)	14 (87.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (NC to NC)	15.31 (9.232 to NC)	2.89 (0.986 to NC)	NC (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.530 to NC)	NC (3.515 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1803		0.2550	
Hazard ratio (95% CI) vs Pd	-	1.51 (0.82 to 2.75)		0.40 (0.08 to 2.06)	
P-value	-	0.1834		0.2717	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (47.1)	24 (37.5)	22 (39.3)	18 (34.0)	12 (27.9)	9 (26.5)	0.9876
Number (%) of patients censored	27 (52.9)	40 (62.5)	34 (60.7)	35 (66.0)	31 (72.1)	25 (73.5)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	1.91 (1.018 to 2.891)	2.17 (1.084 to 7.984)	1.18 (1.018 to 2.037)	2.92 (1.248 to NC)	1.91 (1.018 to NC)	4.67 (1.117 to NC)	
Median (95% CI)	NC (2.891 to NC)	NC (7.984 to NC)	NC (1.971 to NC)	NC (5.979 to NC)	NC (3.910 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3588		0.3221		0.5769	
Hazard ratio (95% CI) vs Pd	-	0.77 (0.44 to 1.35)		0.73 (0.39 to 1.36)		0.78 (0.33 to 1.86)	
P-value	-	0.3602		0.3238		0.5779	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_impl_seiss_de_i_t_x.rtf (08APR2021 14:49)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (45.1)	35 (54.7)	24 (42.9)	30 (56.6)	20 (46.5)	19 (55.9)	0.6020
Number (%) of patients censored	28 (54.9)	29 (45.3)	32 (57.1)	23 (43.4)	23 (53.5)	15 (44.1)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	2.89 (1.150 to 5.224)	1.97 (1.117 to 4.238)	2.83 (1.018 to 3.811)	1.45 (1.150 to 2.497)	1.74 (0.986 to 3.088)	2.66 (1.018 to 3.943)	
Median (95% CI)	NC (3.877 to NC)	7.39 (4.797 to NC)	NC (3.745 to NC)	6.97 (2.234 to 13.864)	6.14 (2.136 to NC)	6.54 (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	15.31 (15.310 to NC)	NC (NC to NC)	13.86 (13.634 to NC)	NC (7.195 to NC)	NC (8.411 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2796		0.2291		0.7115	
Hazard ratio (95% CI) vs Pd	-	1.34 (0.79 to 2.26)		1.39 (0.81 to 2.38)		0.89 (0.47 to 1.67)	
P-value	-	0.2813		0.2314		0.7115	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (27.5)	11 (17.2)	15 (26.8)	13 (24.5)	5 (11.6)	5 (14.7)	0.7436
Number (%) of patients censored	37 (72.5)	53 (82.8)	41 (73.2)	40 (75.5)	38 (88.4)	29 (85.3)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	11.47 (2.333 to NC)	NC (9.856 to NC)	5.65 (1.018 to NC)	10.41 (3.318 to NC)	NC (4.534 to NC)	NC (1.117 to NC)	
Median (95% CI)	NC (12.912 to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.142 to NC)	NC (11.335 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2342		0.5187		0.8870	
Hazard ratio (95% CI) vs Pd	-	0.62 (0.28 to 1.37)		0.78 (0.37 to 1.65)		1.09 (0.32 to 3.79)	
P-value	-	0.2385		0.5192		0.8869	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_imppl_seiss_de_i_t_x.rtf (08APR2021 14:49)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (9.8)	12 (18.8)	7 (12.5)	9 (17.0)	9 (20.9)	7 (20.6)	0.3806
Number (%) of patients censored	46 (90.2)	52 (81.3)	49 (87.5)	44 (83.0)	34 (79.1)	27 (79.4)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	NC (NC to NC)	15.31 (7.885 to NC)	NC (4.862 to NC)	NC (6.965 to NC)	9.33 (1.117 to NC)	11.30 (3.515 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.310 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.302 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1828		0.6341		0.5894	
Hazard ratio (95% CI) vs Pd	-	2.00 (0.71 to 5.70)		1.27 (0.47 to 3.42)		0.76 (0.28 to 2.05)	
P-value	-	0.1918		0.6349		0.5905	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (38.7)	16 (41.0)	40 (40.8)	31 (31.3)	7 (29.2)	5 (31.3)	0.4738
Number (%) of patients censored	19 (61.3)	23 (59.0)	58 (59.2)	68 (68.7)	17 (70.8)	11 (68.8)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	2.79 (1.018 to NC)	1.91 (0.986 to 7.491)	1.25 (1.018 to 2.004)	2.99 (2.004 to NC)	1.51 (0.986 to NC)	2.00 (0.953 to NC)	
Median (95% CI)	NC (2.957 to NC)	NC (3.088 to NC)	NC (3.088 to NC)	NC (NC to NC)	NC (1.511 to NC)	NC (1.380 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7903		0.0714		0.8313	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.52 to 2.34)		0.65 (0.41 to 1.04)		0.88 (0.28 to 2.79)	
P-value	-	0.7904		0.0736		0.8314	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (45.2)	19 (48.7)	48 (49.0)	59 (59.6)	7 (29.2)	9 (56.3)	0.9122
Number (%) of patients censored	17 (54.8)	20 (51.3)	50 (51.0)	40 (40.4)	17 (70.8)	7 (43.8)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	2.89 (1.051 to 9.528)	1.97 (1.084 to 6.505)	2.04 (1.183 to 3.023)	1.54 (1.150 to 2.497)	3.06 (0.953 to NC)	2.83 (1.018 to 6.538)	
Median (95% CI)	NC (3.877 to NC)	15.31 (4.928 to 15.310)	9.30 (3.811 to NC)	5.62 (2.924 to 8.411)	NC (3.055 to NC)	6.54 (1.840 to 9.495)	
75% quantile (95% CI)	NC (NC to NC)	15.31 (NC to NC)	NC (NC to NC)	13.86 (13.634 to NC)	NC (7.754 to NC)	9.49 (3.943 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6844		0.2236		0.4574	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.58 to 2.30)		1.27 (0.86 to 1.85)		1.45 (0.54 to 3.92)	
P-value	-	0.6846		0.2246		0.4600	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (22.6)	8 (20.5)	25 (25.5)	18 (18.2)	3 (12.5)	3 (18.8)	0.6304
Number (%) of patients censored	24 (77.4)	31 (79.5)	73 (74.5)	81 (81.8)	21 (87.5)	13 (81.3)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	12.91 (1.610 to NC)	11.76 (8.115 to NC)	7.49 (1.938 to NC)	13.14 (9.889 to NC)	NC (1.446 to NC)	NC (0.953 to NC)	
Median (95% CI)	NC (12.912 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.534 to NC)	NC (4.665 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8352		0.1264		0.7716	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.33 to 2.48)		0.63 (0.34 to 1.15)		1.27 (0.25 to 6.33)	
P-value	-	0.8352		0.1298		0.7721	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (9.7)	5 (12.8)	16 (16.3)	20 (20.2)	3 (12.5)	5 (31.3)	0.8388
Number (%) of patients censored	28 (90.3)	34 (87.2)	82 (83.7)	79 (79.8)	21 (87.5)	11 (68.8)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	NC (6.571 to NC)	15.31 (7.819 to NC)	NC (4.862 to NC)	NC (7.589 to NC)	NC (0.986 to NC)	6.54 (1.840 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.310 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.538 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.310 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.302 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7155		0.6285		0.4632	
Hazard ratio (95% CI) vs Pd	-	1.30 (0.31 to 5.48)		1.18 (0.61 to 2.27)		1.71 (0.40 to 7.24)	
P-value	-	0.7163		0.6289		0.4682	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (26.1)	2 (14.3)	37 (38.9)	43 (36.4)	0.4570
Number (%) of patients censored	17 (73.9)	12 (85.7)	58 (61.1)	75 (63.6)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	3.06 (0.986 to NC)	NC (2.990 to NC)	1.91 (1.084 to 2.793)	2.83 (1.248 to 4.830)	
Median (95% CI)	NC (3.055 to NC)	NC (3.318 to NC)	NC (3.910 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3008		0.4590	
Hazard ratio (95% CI) vs Pd	-	0.44 (0.09 to 2.18)		0.85 (0.55 to 1.32)	
P-value	-	0.3142		0.4595	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (26.1)	7 (50.0)	45 (47.4)	69 (58.5)	0.2633
Number (%) of patients censored	17 (73.9)	7 (50.0)	50 (52.6)	49 (41.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.89 (1.117 to NC)	1.84 (0.986 to 5.618)	1.94 (1.084 to 3.023)	1.97 (1.281 to 2.793)	
Median (95% CI)	NC (2.891 to NC)	5.62 (1.150 to 9.593)	11.47 (3.745 to NC)	6.54 (4.008 to 8.509)	
75% quantile (95% CI)	NC (NC to NC)	9.59 (5.618 to 9.593)	NC (NC to NC)	NC (13.864 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1049		0.2845	
Hazard ratio (95% CI) vs Pd	-	2.42 (0.80 to 7.27)		1.23 (0.84 to 1.79)	
P-value	-	0.1161		0.2853	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (21.7)	1 (7.1)	22 (23.2)	25 (21.2)	0.4093
Number (%) of patients censored	18 (78.3)	13 (92.9)	73 (76.8)	93 (78.8)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	8.97 (0.986 to NC)	NC (3.318 to NC)	11.47 (4.534 to NC)	13.14 (8.838 to NC)	
Median (95% CI)	NC (8.969 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2322		0.4556	
Hazard ratio (95% CI) vs Pd	-	0.29 (0.03 to 2.50)		0.80 (0.45 to 1.43)	
P-value	-	0.2615		0.4565	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (8.7)	2 (14.3)	15 (15.8)	24 (20.3)	0.7530
Number (%) of patients censored	21 (91.3)	12 (85.7)	80 (84.2)	94 (79.7)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (1.117 to NC)	NC (1.840 to NC)	NC (6.571 to NC)	NC (8.608 to NC)	
Median (95% CI)	NC (NC to NC)	NC (7.589 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6269		0.5623	
Hazard ratio (95% CI) vs Pd	-	1.62 (0.23 to 11.50)		1.21 (0.63 to 2.31)	
P-value	-	0.6302		0.5629	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (36.1)	4 (16.7)	29 (37.2)	39 (37.9)	0.1440
Number (%) of patients censored	23 (63.9)	20 (83.3)	49 (62.8)	64 (62.1)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.91 (1.018 to 4.731)	NC (2.990 to NC)	1.91 (1.018 to 2.891)	2.17 (1.117 to 4.830)	
Median (95% CI)	NC (2.037 to NC)	NC (NC to NC)	NC (3.910 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0545		0.7346	
Hazard ratio (95% CI) vs Pd	-	0.35 (0.11 to 1.07)		0.92 (0.57 to 1.49)	
P-value	-	0.0661		0.7347	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (33.3)	16 (66.7)	36 (46.2)	57 (55.3)	0.1100
Number (%) of patients censored	24 (66.7)	8 (33.3)	42 (53.8)	46 (44.7)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.89 (1.150 to NC)	1.84 (0.986 to 4.008)	2.14 (1.216 to 3.745)	1.91 (1.281 to 2.793)	
Median (95% CI)	NC (3.745 to NC)	4.80 (1.840 to 6.538)	11.47 (3.811 to NC)	7.39 (4.238 to NC)	
75% quantile (95% CI)	NC (NC to NC)	6.54 (4.797 to 9.593)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0162		0.3972	
Hazard ratio (95% CI) vs Pd	-	2.46 (1.15 to 5.25)		1.20 (0.79 to 1.82)	
P-value	-	0.0200		0.3978	
Hazard ratio inverted (95% CI) vs IPd		-		0.84 (0.55 to 1.27)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (27.8)	2 (8.3)	17 (21.8)	23 (22.3)	0.1467
Number (%) of patients censored	26 (72.2)	22 (91.7)	61 (78.2)	80 (77.7)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	4.53 (1.183 to NC)	NC (3.318 to NC)	11.47 (2.891 to NC)	11.76 (8.838 to NC)	
Median (95% CI)	NC (4.731 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0515		0.7794	
Hazard ratio (95% CI) vs Pd	-	0.25 (0.05 to 1.13)		0.91 (0.49 to 1.71)	
P-value	-	0.0720		0.7795	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (11.1)	6 (25.0)	12 (15.4)	20 (19.4)	0.3812
Number (%) of patients censored	32 (88.9)	18 (75.0)	66 (84.6)	83 (80.6)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (2.891 to NC)	7.89 (1.840 to NC)	NC (6.571 to NC)	NC (8.608 to NC)	
Median (95% CI)	NC (NC to NC)	NC (7.589 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2139		0.6367	
Hazard ratio (95% CI) vs Pd	-	2.19 (0.62 to 7.78)		1.19 (0.58 to 2.43)	
P-value	-	0.2255		0.6371	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (50.0)	26 (31.3)	14 (22.2)	26 (36.6)	0.0166
Number (%) of patients censored	45 (50.0)	57 (68.7)	49 (77.8)	45 (63.4)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.51 (1.051 to 1.938)	2.83 (1.150 to NC)	9.30 (1.018 to NC)	3.29 (1.380 to 7.491)	
Median (95% CI)	3.91 (2.333 to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.984 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0143		0.2355	
Hazard ratio (95% CI) vs Pd	-	0.55 (0.34 to 0.89)		1.48 (0.77 to 2.83)	
P-value	-	0.0157		0.2385	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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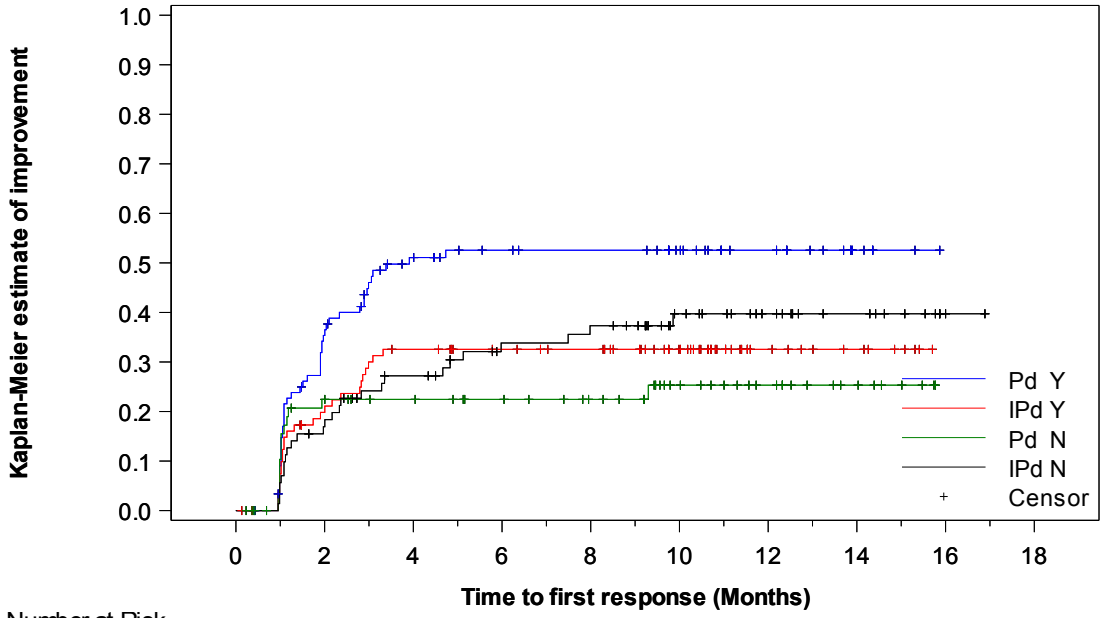
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to previous autologous stem-cell (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd Y	90	44	30	28	14	2	0
IPd Y	83	55	47	40	12	4	0
Pd N	63	41	36	29	14	4	0
IPd N	71	50	38	34	16	7	0

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (41.1)	44 (53.0)	32 (50.8)	43 (60.6)	0.4862
Number (%) of patients censored	53 (58.9)	39 (47.0)	31 (49.2)	28 (39.4)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.89 (1.216 to 3.811)	2.20 (1.150 to 3.088)	2.04 (1.018 to 3.745)	1.54 (1.216 to 2.793)	
Median (95% CI)	NC (5.224 to NC)	8.51 (4.698 to 13.864)	7.20 (3.745 to 9.725)	5.72 (2.825 to 7.721)	
75% quantile (95% CI)	NC (NC to NC)	15.31 (13.864 to NC)	NC (9.528 to NC)	NC (7.721 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1749		0.7109	
Hazard ratio (95% CI) vs Pd	-	1.35 (0.87 to 2.09)		1.09 (0.69 to 1.72)	
P-value	-	0.1765		0.7110	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (28.9)	14 (16.9)	9 (14.3)	15 (21.1)	0.1046
Number (%) of patients censored	64 (71.1)	69 (83.1)	54 (85.7)	56 (78.9)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	5.65 (2.333 to 12.912)	NC (10.415 to NC)	NC (4.534 to NC)	13.14 (8.115 to NC)	
Median (95% CI)	NC (12.912 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0500		0.5903	
Hazard ratio (95% CI) vs Pd	-	0.53 (0.28 to 1.01)		1.25 (0.55 to 2.87)	
P-value	-	0.0540		0.5911	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.7 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (13.3)	14 (16.9)	10 (15.9)	16 (22.5)	0.9790
Number (%) of patients censored	78 (86.7)	69 (83.1)	53 (84.1)	55 (77.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (NC to NC)	15.31 (7.425 to NC)	NC (4.665 to NC)	11.30 (7.819 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.310 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6215		0.6309	
Hazard ratio (95% CI) vs Pd	-	1.21 (0.56 to 2.63)		1.21 (0.55 to 2.68)	
P-value	-	0.6224		0.6315	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	1 (50.0)	57 (37.7)	51 (33.6)	0.2702
Number (%) of patients censored	0 (0.0)	1 (50.0)	94 (62.3)	101 (66.4)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.02 (1.018 to 1.084)	1.08 (1.084 to NC)	1.91 (1.084 to 2.333)	2.86 (1.971 to 5.125)	
Median (95% CI)	1.05 (1.018 to 1.084)	NC (1.084 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	1.08 (1.018 to 1.084)	NC (1.084 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.2025	
Hazard ratio (95% CI) vs Pd	-	0.31 (0.03 to 3.50)		0.78 (0.54 to 1.14)	
P-value	-	0.3429		0.2036	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	69 (45.7)	86 (56.6)	0.9810
Number (%) of patients censored	2 (100.0)	1 (50.0)	82 (54.3)	66 (43.4)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (NC to NC)	1.12 (1.117 to NC)	2.14 (1.281 to 3.055)	1.91 (1.380 to 2.661)	
Median (95% CI)	NC (NC to NC)	NC (1.117 to NC)	9.53 (4.665 to NC)	6.57 (4.698 to 9.495)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.117 to NC)	NC (NC to NC)	15.31 (13.864 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.2082	
Hazard ratio (95% CI) vs Pd	-			1.23 (0.89 to 1.68)	
P-value	-	0.9990		0.2089	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	0 (0.0)	33 (21.9)	29 (19.1)	0.9874
Number (%) of patients censored	0 (0.0)	2 (100.0)	118 (78.1)	123 (80.9)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	5.65 (5.651 to 11.466)	NC (NC to NC)	12.91 (4.534 to NC)	13.14 (9.889 to NC)	
Median (95% CI)	8.56 (5.651 to 11.466)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	11.47 (5.651 to 11.466)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.2901	
Hazard ratio (95% CI) vs Pd	-			0.76 (0.46 to 1.26)	
P-value	-	0.9990		0.2915	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	22 (14.6)	30 (19.7)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	129 (85.4)	122 (80.3)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	15.31 (9.232 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.4314	
Hazard ratio (95% CI) vs Pd	-			1.25 (0.72 to 2.16)	
P-value	-			0.4323	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (43.6)	32 (30.8)	12 (29.3)	13 (39.4)	0.1695
Number (%) of patients censored	57 (56.4)	72 (69.2)	29 (70.7)	20 (60.6)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.51 (1.018 to 2.037)	3.09 (1.741 to NC)	2.00 (1.051 to NC)	2.37 (1.084 to 7.984)	
Median (95% CI)	NC (2.957 to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.285 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0239		0.5792	
Hazard ratio (95% CI) vs Pd	-	0.59 (0.38 to 0.94)		1.25 (0.57 to 2.74)	
P-value	-	0.0255		0.5800	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (45.5)	61 (58.7)	18 (43.9)	18 (54.5)	0.9501
Number (%) of patients censored	55 (54.5)	43 (41.3)	23 (56.1)	15 (45.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.53 (1.084 to 3.745)	1.91 (1.281 to 2.793)	1.91 (1.051 to 3.745)	2.20 (1.150 to 4.797)	
Median (95% CI)	9.72 (4.008 to NC)	6.51 (3.943 to 9.495)	NC (2.924 to NC)	7.72 (2.924 to 15.310)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (NC to NC)	15.31 (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2022		0.7058	
Hazard ratio (95% CI) vs Pd	-	1.28 (0.87 to 1.88)		1.13 (0.59 to 2.18)	
P-value	-	0.2034		0.7052	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (24.8)	19 (18.3)	7 (17.1)	6 (18.2)	0.8288
Number (%) of patients censored	76 (75.2)	85 (81.7)	34 (82.9)	27 (81.8)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	11.33 (4.534 to NC)	13.14 (9.889 to NC)	NC (1.150 to NC)	NC (4.665 to NC)	
Median (95% CI)	NC (12.912 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1318		0.8718	
Hazard ratio (95% CI) vs Pd	-	0.63 (0.35 to 1.15)		0.91 (0.31 to 2.72)	
P-value	-	0.1352		0.8721	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (13.9)	20 (19.2)	7 (17.1)	6 (18.2)	0.6806
Number (%) of patients censored	87 (86.1)	84 (80.8)	34 (82.9)	27 (81.8)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (NC to NC)	NC (9.232 to NC)	NC (4.665 to NC)	15.31 (3.450 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	15.31 (15.310 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.310 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4691		0.9300	
Hazard ratio (95% CI) vs Pd	-	1.29 (0.65 to 2.55)		0.95 (0.32 to 2.84)	
P-value	-	0.4703		0.9301	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (44.0)	31 (30.4)	15 (28.8)	21 (41.2)	0.0354
Number (%) of patients censored	56 (56.0)	71 (69.6)	37 (71.2)	30 (58.8)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.51 (1.018 to 1.971)	3.09 (1.741 to NC)	2.00 (1.051 to NC)	2.17 (1.117 to 4.665)	
Median (95% CI)	NC (2.957 to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.285 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0186		0.3654	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.37 to 0.92)		1.36 (0.70 to 2.63)	
P-value	-	0.0201		0.3672	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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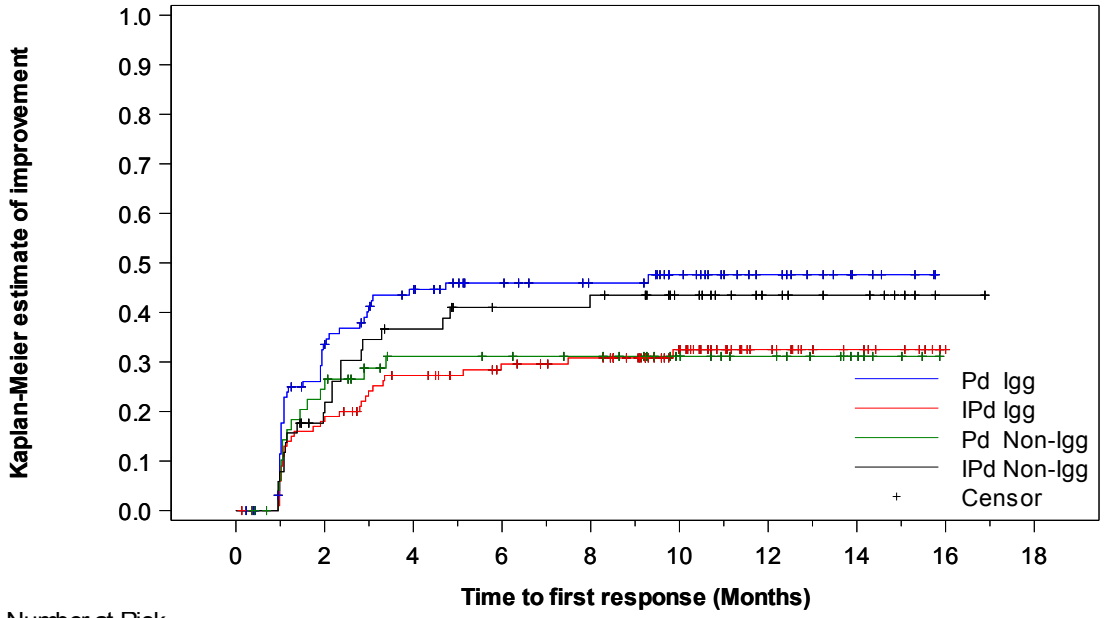
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to MM type at initial diagnosis (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd Igg	100	53	38	33	14	3	0
IPd Igg	102	73	60	51	18	7	0
Pd Non-Igg	52	31	27	23	13	3	0
IPd Non-Igg	51	31	24	22	10	4	0

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (45.0)	59 (57.8)	23 (44.2)	27 (52.9)	0.8456
Number (%) of patients censored	55 (55.0)	43 (42.2)	29 (55.8)	24 (47.1)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.14 (1.084 to 3.745)	1.94 (1.281 to 2.793)	2.23 (1.150 to 3.745)	1.64 (1.084 to 4.008)	
Median (95% CI)	11.47 (3.877 to NC)	6.54 (3.943 to 9.593)	9.30 (3.088 to NC)	7.72 (3.745 to 15.310)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (NC to NC)	15.31 (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2218		0.5363	
Hazard ratio (95% CI) vs Pd	-	1.27 (0.86 to 1.88)		1.19 (0.68 to 2.08)	
P-value	-	0.2229		0.5376	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (25.0)	19 (18.6)	10 (19.2)	10 (19.6)	0.5286
Number (%) of patients censored	75 (75.0)	83 (81.4)	42 (80.8)	41 (80.4)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	11.33 (4.534 to NC)	13.14 (9.889 to NC)	NC (1.150 to NC)	NC (4.665 to NC)	
Median (95% CI)	NC (12.912 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1360		0.8173	
Hazard ratio (95% CI) vs Pd	-	0.64 (0.35 to 1.16)		0.90 (0.38 to 2.17)	
P-value	-	0.1393		0.8171	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.7 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (14.0)	18 (17.6)	8 (15.4)	11 (21.6)	0.7921
Number (%) of patients censored	86 (86.0)	84 (82.4)	44 (84.6)	40 (78.4)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (NC to NC)	NC (9.232 to NC)	NC (4.731 to NC)	15.31 (4.238 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.310 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.310 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6796		0.5613	
Hazard ratio (95% CI) vs Pd	-	1.16 (0.58 to 2.33)		1.31 (0.53 to 3.26)	
P-value	-	0.6799		0.5625	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (30.0)	5 (35.7)	56 (39.2)	47 (33.6)	0.6875
Number (%) of patients censored	7 (70.0)	9 (64.3)	87 (60.8)	93 (66.4)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	3.38 (1.018 to NC)	1.91 (0.986 to NC)	1.61 (1.084 to 2.004)	2.86 (2.004 to 5.979)	
Median (95% CI)	NC (1.018 to NC)	NC (1.380 to NC)	NC (9.298 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (3.384 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9531		0.1499	
Hazard ratio (95% CI) vs Pd	-	1.04 (0.25 to 4.38)		0.75 (0.51 to 1.11)	
P-value	-	0.9533		0.1509	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (50.0)	11 (78.6)	64 (44.8)	76 (54.3)	0.7798
Number (%) of patients censored	5 (50.0)	3 (21.4)	79 (55.2)	64 (45.7)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.28 (0.920 to 3.745)	1.84 (0.986 to 2.825)	2.53 (1.347 to 3.745)	1.91 (1.281 to 2.793)	
Median (95% CI)	3.75 (0.920 to NC)	4.70 (1.544 to 9.593)	11.47 (5.224 to NC)	6.97 (4.731 to 13.634)	
75% quantile (95% CI)	NC (1.741 to NC)	11.73 (2.825 to NC)	NC (NC to NC)	15.31 (15.310 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9522		0.2196	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.36 to 3.00)		1.23 (0.88 to 1.72)	
P-value	-	0.9525		0.2212	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (20.0)	2 (14.3)	33 (23.1)	27 (19.3)	0.5249
Number (%) of patients censored	8 (80.0)	12 (85.7)	110 (76.9)	113 (80.7)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (1.018 to NC)	NC (2.825 to NC)	11.47 (4.731 to NC)	13.14 (9.856 to NC)	
Median (95% CI)	NC (1.018 to NC)	NC (10.415 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3100		0.2708	
Hazard ratio (95% CI) vs Pd	-	0.36 (0.05 to 2.77)		0.75 (0.45 to 1.25)	
P-value	-	0.3276		0.2727	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (20.0)	3 (21.4)	20 (14.0)	27 (19.3)	0.5233
Number (%) of patients censored	8 (80.0)	11 (78.6)	123 (86.0)	113 (80.7)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	3.75 (1.281 to NC)	NC (1.544 to NC)	NC (NC to NC)	15.31 (9.232 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (8.608 to NC)	NC (NC to NC)	NC (15.310 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7516		0.3803	
Hazard ratio (95% CI) vs Pd	-	0.75 (0.12 to 4.60)		1.29 (0.73 to 2.31)	
P-value	-	0.7524		0.3816	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (38.5)	31 (35.6)	21 (42.9)	18 (32.7)	0.3103
Number (%) of patients censored	59 (61.5)	56 (64.4)	28 (57.1)	37 (67.3)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.00 (1.150 to 2.957)	2.92 (1.150 to 5.979)	1.05 (0.986 to 1.906)	2.37 (1.380 to NC)	
Median (95% CI)	NC (4.731 to NC)	NC (NC to NC)	NC (1.446 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4900		0.0843	
Hazard ratio (95% CI) vs Pd	-	0.85 (0.52 to 1.36)		0.58 (0.31 to 1.09)	
P-value	-	0.4905		0.0881	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (43.8)	52 (59.8)	23 (46.9)	31 (56.4)	0.5191
Number (%) of patients censored	54 (56.3)	35 (40.2)	26 (53.1)	24 (43.6)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.14 (1.150 to 3.745)	1.91 (1.216 to 2.793)	2.89 (1.018 to 3.844)	1.97 (1.150 to 3.745)	
Median (95% CI)	NC (4.370 to NC)	6.57 (3.811 to 13.634)	6.14 (3.745 to NC)	6.51 (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	15.31 (13.634 to NC)	NC (NC to NC)	NC (9.495 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1140		0.7056	
Hazard ratio (95% CI) vs Pd	-	1.39 (0.92 to 2.08)		1.11 (0.65 to 1.90)	
P-value	-	0.1155		0.7057	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (24.0)	19 (21.8)	11 (22.4)	9 (16.4)	0.5536
Number (%) of patients censored	73 (76.0)	68 (78.2)	38 (77.6)	46 (83.6)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	11.33 (4.830 to NC)	11.76 (8.115 to NC)	NC (1.018 to NC)	NC (8.838 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4858		0.2530	
Hazard ratio (95% CI) vs Pd	-	0.81 (0.44 to 1.48)		0.60 (0.25 to 1.45)	
P-value	-	0.4866		0.2581	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (16.7)	17 (19.5)	5 (10.2)	10 (18.2)	0.6067
Number (%) of patients censored	80 (83.3)	70 (80.5)	44 (89.8)	45 (81.8)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (4.862 to NC)	15.31 (7.819 to NC)	NC (4.665 to NC)	NC (8.608 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.310 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8150		0.4204	
Hazard ratio (95% CI) vs Pd	-	1.09 (0.55 to 2.15)		1.55 (0.53 to 4.53)	
P-value	-	0.8151		0.4242	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_detpl_crcl_de_i_t_x.rtf (08APR2021 14:49)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	59 (39.1)	51 (33.6)	0.9847
Number (%) of patients censored	2 (100.0)	1 (50.0)	92 (60.9)	101 (66.4)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (NC to NC)	1.91 (1.906 to NC)	1.61 (1.084 to 2.037)	2.86 (1.971 to 5.125)	
Median (95% CI)	NC (NC to NC)	NC (1.906 to NC)	NC (9.298 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.906 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.1293	
Hazard ratio (95% CI) vs Pd	-			0.75 (0.51 to 1.09)	
P-value	-	0.9990		0.1306	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	69 (45.7)	86 (56.6)	0.9755
Number (%) of patients censored	2 (100.0)	1 (50.0)	82 (54.3)	66 (43.4)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (NC to NC)	2.83 (2.825 to NC)	2.14 (1.281 to 3.055)	1.91 (1.281 to 2.628)	
Median (95% CI)	NC (NC to NC)	NC (2.825 to NC)	9.72 (4.665 to NC)	6.57 (4.698 to 9.495)	
75% quantile (95% CI)	NC (NC to NC)	NC (2.825 to NC)	NC (NC to NC)	15.31 (13.864 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.1911	
Hazard ratio (95% CI) vs Pd	-			1.23 (0.90 to 1.70)	
P-value	-	0.9990		0.1919	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	35 (23.2)	29 (19.1)	0.9998
Number (%) of patients censored	2 (100.0)	2 (100.0)	116 (76.8)	123 (80.9)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	11.33 (4.534 to NC)	13.14 (9.889 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.1994	
Hazard ratio (95% CI) vs Pd	-			0.73 (0.44 to 1.19)	
P-value	-			0.2014	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	22 (14.6)	30 (19.7)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	129 (85.4)	122 (80.3)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	15.31 (9.232 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.4157	
Hazard ratio (95% CI) vs Pd	-			1.26 (0.72 to 2.18)	
P-value	-			0.4167	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (39.1)	42 (35.6)	14 (36.8)	10 (27.8)	0.9153
Number (%) of patients censored	70 (60.9)	76 (64.4)	24 (63.2)	26 (72.2)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.45 (1.051 to 1.938)	2.83 (1.741 to 4.830)	2.89 (1.018 to 9.298)	4.67 (1.084 to NC)	
Median (95% CI)	NC (3.088 to NC)	NC (NC to NC)	NC (3.910 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2297		0.4289	
Hazard ratio (95% CI) vs Pd	-	0.77 (0.51 to 1.18)		0.72 (0.32 to 1.63)	
P-value	-	0.2310		0.4310	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	52 (45.2)	66 (55.9)	17 (44.7)	21 (58.3)	0.6102
Number (%) of patients censored	63 (54.8)	52 (44.1)	21 (55.3)	15 (41.7)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.23 (1.347 to 3.055)	1.91 (1.216 to 2.825)	2.53 (1.018 to 4.665)	1.84 (1.084 to 2.793)	
Median (95% CI)	9.53 (4.008 to NC)	6.97 (4.731 to 9.593)	11.47 (3.745 to NC)	4.93 (2.497 to 15.310)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.864 to NC)	NC (NC to NC)	15.31 (7.622 to 15.310)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3506		0.2762	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.83 to 1.71)		1.43 (0.75 to 2.71)	
P-value	-	0.3512		0.2787	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (24.3)	24 (20.3)	7 (18.4)	5 (13.9)	0.9713
Number (%) of patients censored	87 (75.7)	94 (79.7)	31 (81.6)	31 (86.1)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	8.97 (3.384 to NC)	11.76 (9.856 to NC)	NC (1.610 to NC)	NC (4.665 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2114		0.5704	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.41 to 1.22)		0.72 (0.23 to 2.26)	
P-value	-	0.2137		0.5721	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (14.8)	22 (18.6)	5 (13.2)	8 (22.2)	0.4897
Number (%) of patients censored	98 (85.2)	96 (81.4)	33 (86.8)	28 (77.8)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (9.331 to NC)	NC (7.885 to NC)	NC (4.665 to NC)	15.31 (2.201 to 15.310)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	15.31 (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	15.31 (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6930		0.2868	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.60 to 2.14)		1.82 (0.59 to 5.60)	
P-value	-	0.6932		0.2939	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	54 (37.5)	50 (34.0)	5 (55.6)	2 (28.6)	0.5112
Number (%) of patients censored	90 (62.5)	97 (66.0)	4 (44.4)	5 (71.4)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.91 (1.084 to 2.103)	2.83 (1.971 to 5.125)	1.25 (0.986 to 3.088)	1.12 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	3.09 (0.986 to NC)	NC (1.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.990 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2383		0.3587	
Hazard ratio (95% CI) vs Pd	-	0.79 (0.54 to 1.17)		0.47 (0.09 to 2.44)	
P-value	-	0.2393		0.3699	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	63 (43.8)	82 (55.8)	6 (66.7)	5 (71.4)	0.9210
Number (%) of patients censored	81 (56.3)	65 (44.2)	3 (33.3)	2 (28.6)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.23 (1.347 to 3.745)	1.91 (1.281 to 2.628)	3.06 (0.986 to 6.144)	1.45 (0.986 to 4.928)	
Median (95% CI)	11.47 (4.665 to NC)	6.57 (4.698 to 9.593)	6.14 (0.986 to NC)	4.93 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	15.31 (13.864 to NC)	NC (3.088 to NC)	NC (3.088 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1629		0.7753	
Hazard ratio (95% CI) vs Pd	-	1.26 (0.91 to 1.75)		1.19 (0.36 to 3.96)	
P-value	-	0.1638		0.7756	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (24.3)	27 (18.4)	0 (0.0)	2 (28.6)	0.9831
Number (%) of patients censored	109 (75.7)	120 (81.6)	9 (100.0)	5 (71.4)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	8.97 (3.745 to NC)	13.14 (9.889 to NC)	NC (NC to NC)	1.12 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0743		0.0954	
Hazard ratio (95% CI) vs Pd	-	0.64 (0.38 to 1.05)			
P-value	-	0.0768		0.9977	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (14.6)	29 (19.7)	1 (11.1)	1 (14.3)	0.9344
Number (%) of patients censored	123 (85.4)	118 (80.3)	8 (88.9)	6 (85.7)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (NC to NC)	15.31 (9.232 to NC)	NC (3.450 to NC)	NC (4.928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.450 to NC)	NC (4.928 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4702		0.8917	
Hazard ratio (95% CI) vs Pd	-	1.23 (0.70 to 2.16)		1.21 (0.08 to 19.40)	
P-value	-	0.4709		0.8918	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_detpl_refr1_de_i_t_x.rtf (08APR2021 14:49)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (40.9)	28 (30.1)	23 (35.4)	24 (39.3)	0.3929
Number (%) of patients censored	52 (59.1)	65 (69.9)	42 (64.6)	37 (60.7)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.61 (1.018 to 2.891)	2.83 (1.314 to NC)	1.91 (1.084 to 2.990)	2.92 (1.248 to 4.830)	
Median (95% CI)	NC (3.384 to NC)	NC (NC to NC)	NC (2.990 to NC)	NC (4.830 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1100		0.7692	
Hazard ratio (95% CI) vs Pd	-	0.67 (0.41 to 1.10)		0.92 (0.52 to 1.63)	
P-value	-	0.1124		0.7688	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (46.6)	48 (51.6)	28 (43.1)	39 (63.9)	0.2012
Number (%) of patients censored	47 (53.4)	45 (48.4)	37 (56.9)	22 (36.1)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.87 (1.084 to 3.745)	2.20 (1.511 to 3.943)	2.92 (1.741 to 3.844)	1.38 (1.084 to 2.136)	
Median (95% CI)	11.47 (3.811 to NC)	8.41 (4.731 to NC)	9.72 (3.844 to NC)	4.93 (2.793 to 7.491)	
75% quantile (95% CI)	NC (NC to NC)	15.31 (15.310 to NC)	NC (NC to NC)	13.86 (7.491 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7935		0.0593	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.70 to 1.60)		1.59 (0.98 to 2.59)	
P-value	-	0.7938		0.0616	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (27.3)	16 (17.2)	11 (16.9)	13 (21.3)	0.2160
Number (%) of patients censored	64 (72.7)	77 (82.8)	54 (83.1)	48 (78.7)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	7.49 (2.333 to NC)	NC (9.856 to NC)	NC (3.384 to NC)	13.14 (5.125 to NC)	
Median (95% CI)	NC (12.912 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0716		0.8525	
Hazard ratio (95% CI) vs Pd	-	0.56 (0.30 to 1.06)		1.08 (0.48 to 2.41)	
P-value	-	0.0755		0.8529	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Insomnia
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (14.8)	17 (18.3)	9 (13.8)	13 (21.3)	0.9369
Number (%) of patients censored	75 (85.2)	76 (81.7)	56 (86.2)	48 (78.7)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (9.331 to NC)	15.31 (9.232 to NC)	NC (4.370 to NC)	NC (6.538 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.310 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6033		0.5763	
Hazard ratio (95% CI) vs Pd	-	1.21 (0.59 to 2.49)		1.27 (0.54 to 2.98)	
P-value	-	0.6038		0.5772	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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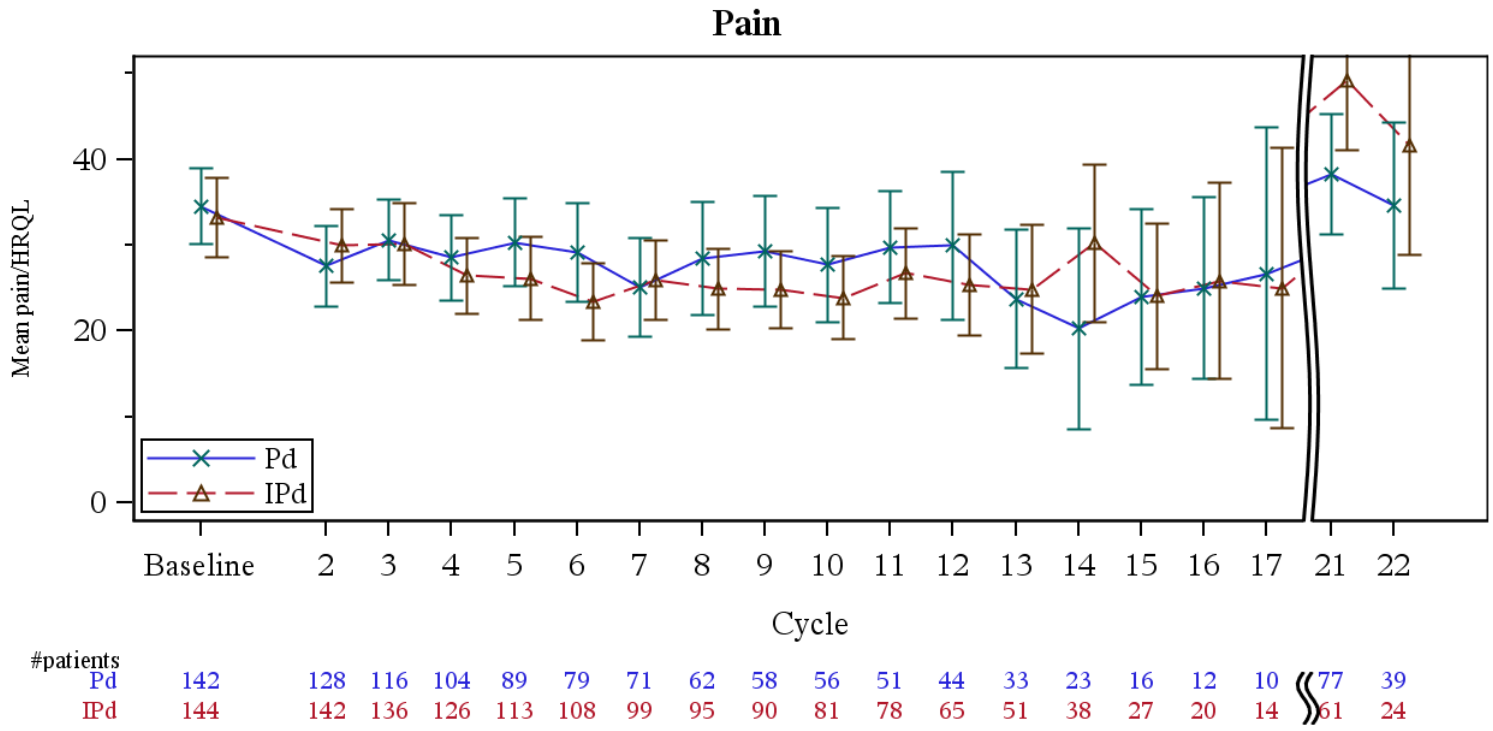
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Pain
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-C30 - Mean and 95% CI for pain score over time (LOCF) - ITT population



A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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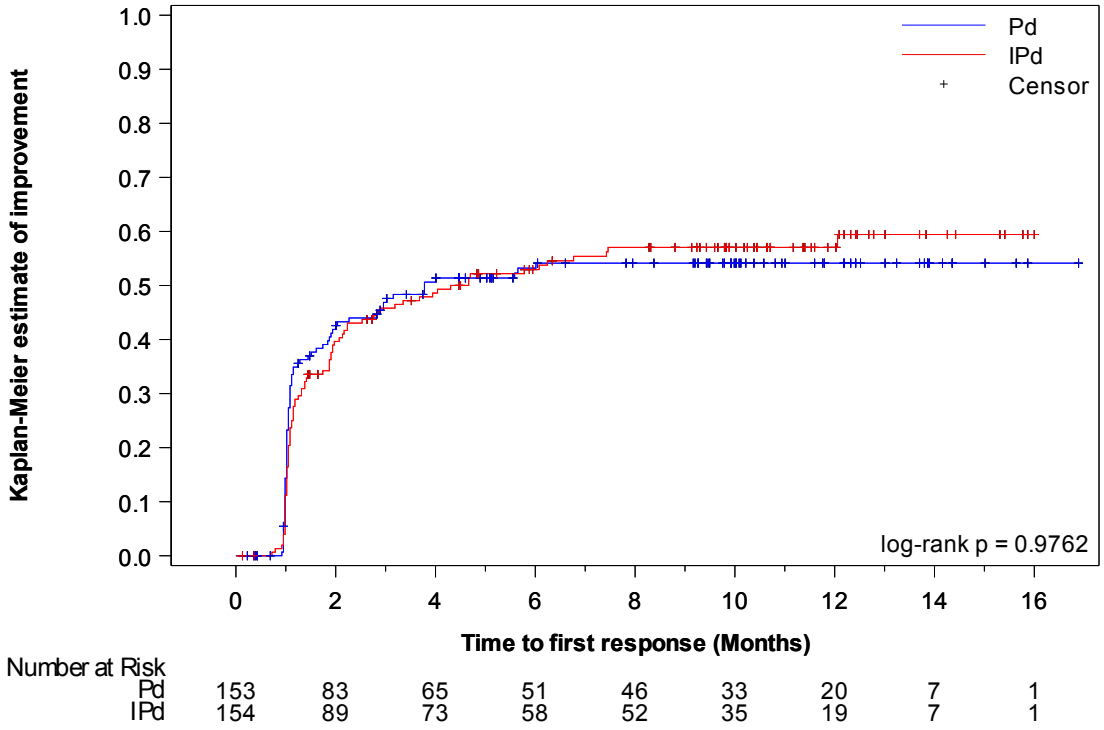
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Pain
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-C30 - Time to first improvement by 15 pt in pain (LOCF) - ITT population

First improvement 15 points Pain (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	77 (50.3)	85 (55.2)
Number (%) of patients censored	76 (49.7)	69 (44.8)
Kaplan-Meier estimates of pain in months		
25% quantile (95% CI)	1.05 (1.018 to 1.117)	1.13 (1.051 to 1.380)
Median (95% CI)	3.78 (1.938 to NC)	4.30 (2.234 to 12.057)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9762
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.00 (0.74 to 1.37)
P-value	-	0.9763
Probability (95% CI)[c]		
2 Months	0.42 (0.338 to 0.497)	0.40 (0.318 to 0.473)
4 Months	0.51 (0.422 to 0.585)	0.49 (0.404 to 0.563)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_imp15l_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Pain
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-C30 - Time to first improvement by 15 pt in pain - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Pain
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-C30 - Time to first deterioration by 15 pt in pain (LOCF) - ITT population

First deterioration 15 points Pain (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	80 (52.3)	93 (60.4)
Number (%) of patients censored	73 (47.7)	61 (39.6)
Kaplan-Meier estimates of pain in months		
25% quantile (95% CI)	2.00 (1.216 to 2.595)	1.91 (1.216 to 2.168)
Median (95% CI)	6.14 (3.778 to 9.823)	5.55 (3.187 to 7.655)
75% quantile (95% CI)	NC (NC to NC)	NC (12.485 to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5791
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.09 (0.81 to 1.47)
P-value	-	0.5798
Probability (95% CI)[c]		
2 Months	0.75 (0.674 to 0.815)	0.69 (0.609 to 0.756)
4 Months	0.55 (0.466 to 0.631)	0.54 (0.460 to 0.620)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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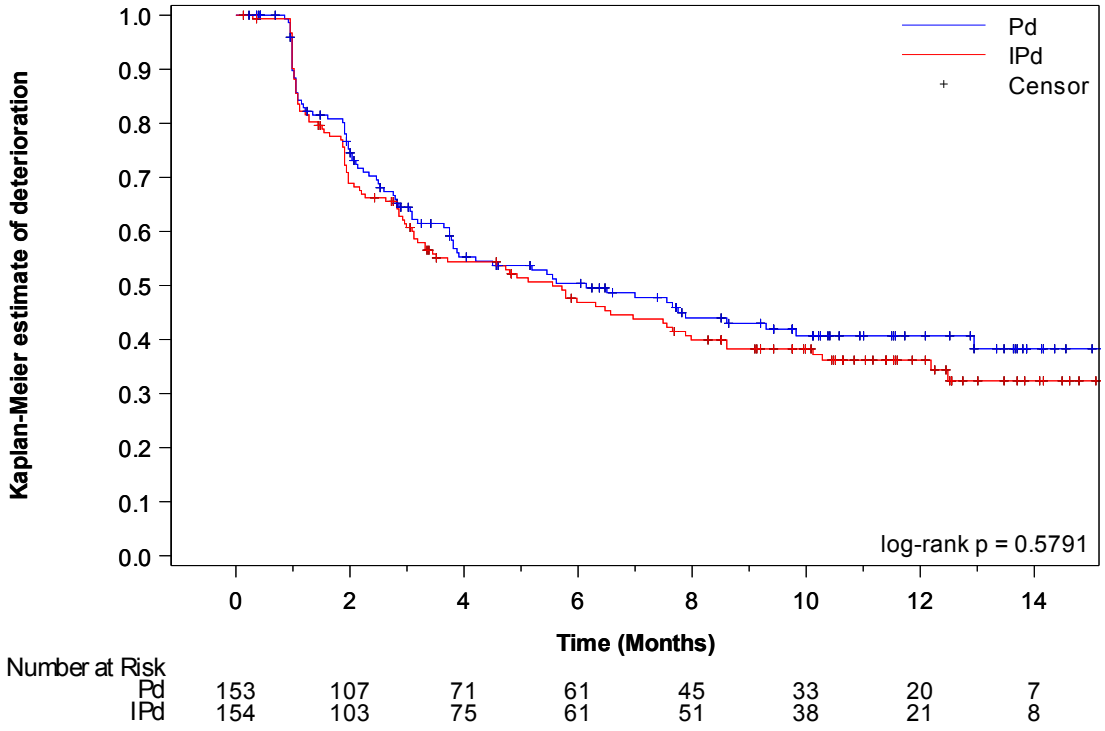
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Pain
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-C30 - Time to first deterioration by 15 pt in pain - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_det15l_de_i_f_x.rtf (08APR2021 15:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Pain
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in pain (LOCF) - ITT population

First permanent improvement 15 points Pain (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	34 (22.2)	43 (27.9)
Number (%) of patients censored	119 (77.8)	111 (72.1)
Kaplan-Meier estimates of pain in months		
25% quantile (95% CI)	11.47 (7.754 to NC)	8.64 (4.698 to 13.142)
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4111
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.21 (0.77 to 1.90)
P-value	-	0.4118
Probability (95% CI)[c]		
2 Months	0.12 (0.076 to 0.182)	0.16 (0.106 to 0.221)
4 Months	0.15 (0.099 to 0.216)	0.17 (0.111 to 0.229)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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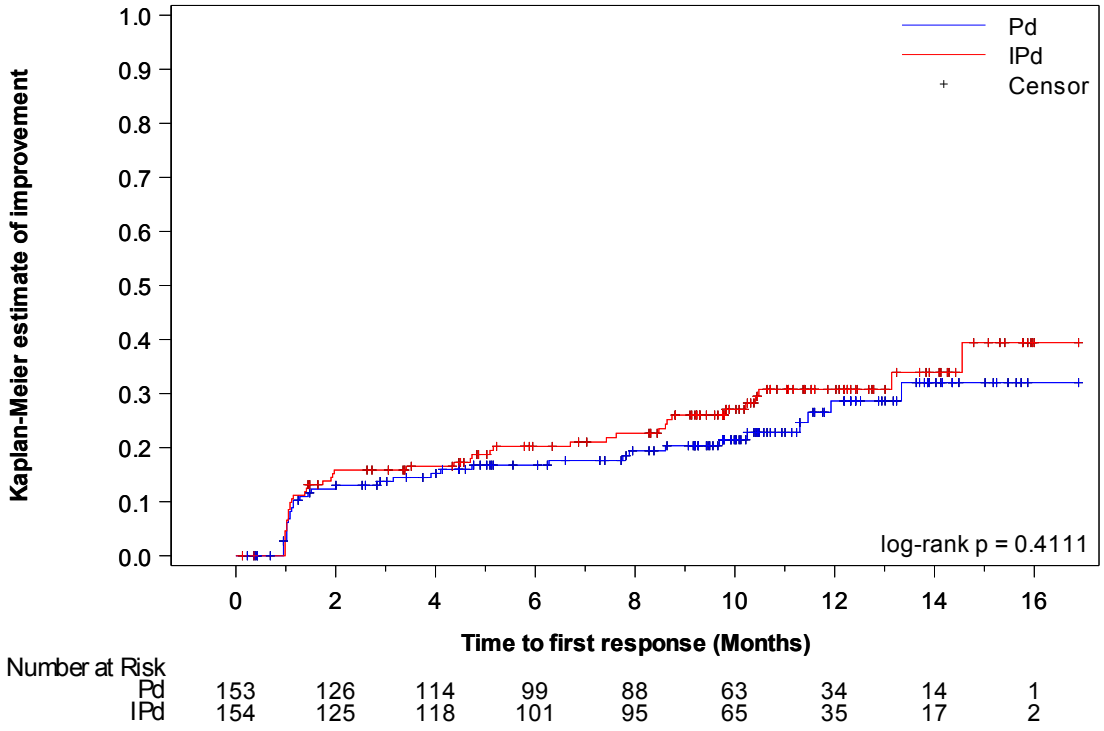
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Pain
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-C30 - Time until permanent improvement by 15 pt in pain - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Pain
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in pain (LOCF) - ITT population

First permanent deterioration 15 points Pain (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	48 (31.4)	34 (22.1)
Number (%) of patients censored	105 (68.6)	120 (77.9)
Kaplan-Meier estimates of pain in months		
25% quantile (95% CI)	5.55 (2.793 to 9.528)	12.32 (6.571 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0260
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.61 (0.39 to 0.95)
P-value	-	0.0275
Probability (95% CI)[c]		
2 Months	0.88 (0.819 to 0.926)	0.91 (0.849 to 0.944)
4 Months	0.79 (0.713 to 0.848)	0.87 (0.801 to 0.912)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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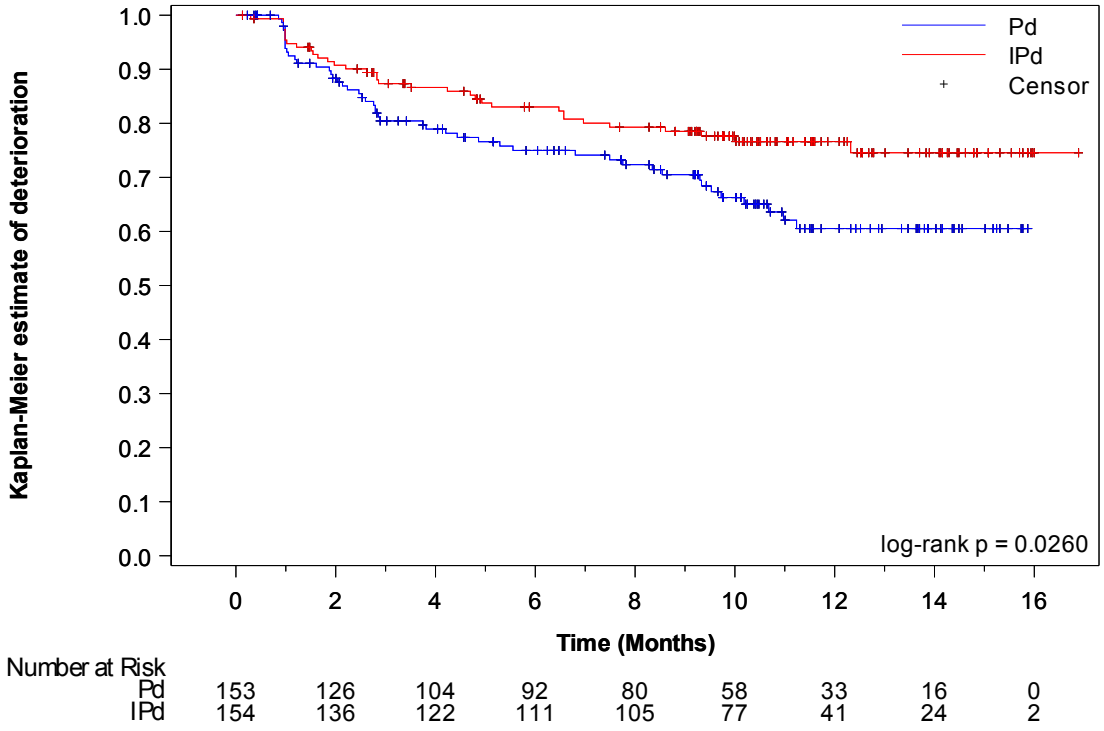
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Pain
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-C30 - Time until permanent deterioration by 15 pt in pain - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_det15pl_de_i_f_x.rtf (08APR2021 15:32)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (54.3)	31 (57.4)	26 (48.1)	36 (52.9)	13 (44.8)	18 (56.3)	0.9204
Number (%) of patients censored	32 (45.7)	23 (42.6)	28 (51.9)	32 (47.1)	16 (55.2)	14 (43.8)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	1.02 (0.986 to 1.051)	1.08 (0.986 to 1.413)	1.15 (1.018 to 2.267)	1.18 (1.051 to 2.234)	1.02 (0.986 to 1.906)	1.08 (0.986 to 2.168)	
Median (95% CI)	2.04 (1.084 to NC)	2.14 (1.413 to NC)	6.01 (2.267 to NC)	4.70 (2.530 to NC)	NC (1.084 to NC)	5.78 (1.314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.768 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8470		0.8394		0.7636	
Hazard ratio (95% CI) vs Pd	-	0.95 (0.59 to 1.53)		1.05 (0.64 to 1.74)		1.12 (0.55 to 2.28)	
P-value	-	0.8473		0.8400		0.7638	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_impl_age_de_i_t_x.rtf (08APR2021 14:45)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (45.7)	25 (46.3)	28 (51.9)	47 (69.1)	20 (69.0)	21 (65.6)	0.0688
Number (%) of patients censored	38 (54.3)	29 (53.7)	26 (48.1)	21 (30.9)	9 (31.0)	11 (34.4)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	2.79 (1.906 to 4.205)	1.97 (1.117 to 3.121)	1.97 (1.051 to 3.088)	1.28 (1.018 to 1.971)	1.02 (0.953 to 1.938)	1.94 (1.051 to 3.318)	
Median (95% CI)	9.30 (5.454 to NC)	NC (3.088 to NC)	5.62 (3.088 to NC)	3.52 (2.267 to 6.571)	2.46 (1.018 to 3.187)	5.98 (2.168 to 12.189)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.823 to NC)	NC (6.965 to NC)	3.81 (2.497 to NC)	12.48 (7.655 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8663		0.1552		0.0718	
Hazard ratio (95% CI) vs Pd	-	1.05 (0.62 to 1.77)		1.40 (0.88 to 2.24)		0.57 (0.31 to 1.06)	
P-value	-	0.8659		0.1572		0.0754	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_detl_age_de_i_t_x.rtf (08APR2021 14:45)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (31.4)	15 (27.8)	7 (13.0)	21 (30.9)	5 (17.2)	7 (21.9)	0.1918
Number (%) of patients censored	48 (68.6)	39 (72.2)	47 (87.0)	47 (69.1)	24 (82.8)	25 (78.1)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	4.73 (1.084 to 13.339)	8.48 (1.018 to NC)	NC (7.885 to NC)	7.62 (4.370 to 14.554)	11.93 (7.754 to NC)	NC (1.051 to NC)	
Median (95% CI)	NC (11.466 to NC)	NC (10.415 to NC)	NC (NC to NC)	NC (13.142 to NC)	NC (9.692 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.926 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7117		0.0417		0.9410	
Hazard ratio (95% CI) vs Pd	-	0.88 (0.46 to 1.71)		2.37 (1.01 to 5.57)		1.04 (0.33 to 3.31)	
P-value	-	0.7119		0.0483		0.9412	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_imppl_age_de_i_t_x.rtf (08APR2021 14:45)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (24.3)	14 (25.9)	17 (31.5)	14 (20.6)	14 (48.3)	6 (18.8)	0.0851
Number (%) of patients censored	53 (75.7)	40 (74.1)	37 (68.5)	54 (79.4)	15 (51.7)	26 (81.3)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	9.33 (4.205 to NC)	8.61 (2.628 to NC)	5.55 (1.938 to 11.236)	NC (4.928 to NC)	2.46 (0.986 to 4.435)	12.32 (1.216 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.725 to NC)	NC (NC to NC)	10.18 (2.530 to NC)	NC (12.320 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.973 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9399		0.1018		0.0053	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.51 to 2.08)		0.56 (0.27 to 1.13)		0.28 (0.11 to 0.73)	
P-value	-	0.9398		0.1067		0.0091	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_detpl_age_de_i_t_x.rtf (08APR2021 14:45)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (49.5)	51 (50.0)	27 (51.9)	34 (65.4)	0.6349
Number (%) of patients censored	51 (50.5)	51 (50.0)	25 (48.1)	18 (34.6)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.08 (1.018 to 1.248)	1.15 (1.051 to 1.413)	1.02 (0.986 to 1.150)	1.08 (1.018 to 1.873)	
Median (95% CI)	5.59 (2.004 to NC)	7.46 (2.530 to NC)	2.96 (1.084 to NC)	2.23 (1.873 to 6.078)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.698 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7728		0.6834	
Hazard ratio (95% CI) vs Pd	-	0.94 (0.64 to 1.39)		1.11 (0.67 to 1.84)	
P-value	-	0.7727		0.6835	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_impl_plne_de_i_t_x.rtf (08APR2021 14:45)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	53 (52.5)	61 (59.8)	27 (51.9)	32 (61.5)	0.9908
Number (%) of patients censored	48 (47.5)	41 (40.2)	25 (48.1)	20 (38.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.04 (1.150 to 3.055)	1.91 (1.084 to 2.825)	2.00 (1.051 to 2.530)	1.59 (1.051 to 2.168)	
Median (95% CI)	6.14 (3.778 to 12.945)	5.78 (3.121 to 7.885)	5.55 (2.497 to NC)	5.13 (2.168 to 12.485)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.189 to NC)	NC (8.608 to NC)	NC (10.283 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5230		0.6424	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.78 to 1.63)		1.13 (0.68 to 1.89)	
P-value	-	0.5240		0.6435	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_detl_plne_de_i_t_x.rtf (08APR2021 14:45)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	25 (24.8)	27 (26.5)	9 (17.3)	16 (30.8)	0.2839
Number (%) of patients censored	76 (75.2)	75 (73.5)	43 (82.7)	36 (69.2)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	10.25 (3.154 to NC)	8.74 (4.370 to 14.554)	11.93 (6.275 to NC)	5.09 (1.446 to NC)	
Median (95% CI)	NC (13.339 to NC)	NC (14.554 to NC)	NC (11.926 to NC)	NC (10.480 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9353		0.1650	
Hazard ratio (95% CI) vs Pd	-	1.02 (0.59 to 1.76)		1.77 (0.78 to 4.01)	
P-value	-	0.9354		0.1707	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_imppl_plne_de_i_t_x.rtf (08APR2021 14:46)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		**> 3 previous lines of therapy**		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (28.7)	24 (23.5)	19 (36.5)	10 (19.2)	0.2442
Number (%) of patients censored	72 (71.3)	78 (76.5)	33 (63.5)	42 (80.8)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	7.49 (2.595 to NC)	12.32 (2.858 to NC)	5.29 (2.136 to 10.678)	NC (5.125 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (8.345 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3119		0.0199	
Hazard ratio (95% CI) vs Pd	-	0.76 (0.44 to 1.30)		0.41 (0.19 to 0.89)	
P-value	-	0.3136		0.0241	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_detpl_plne_de_i_t_x.rtf (08APR2021 14:45)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (47.1)	53 (59.6)	44 (53.0)	32 (49.2)	0.2030
Number (%) of patients censored	37 (52.9)	36 (40.4)	39 (47.0)	33 (50.8)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.05 (0.986 to 1.248)	1.10 (1.018 to 1.380)	1.05 (1.018 to 1.150)	1.17 (1.018 to 1.938)	
Median (95% CI)	6.01 (1.511 to NC)	3.35 (1.906 to 6.768)	3.15 (1.610 to NC)	7.46 (2.168 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.057 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3746		0.3659	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.79 to 1.88)		0.81 (0.51 to 1.28)	
P-value	-	0.3754		0.3668	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_impl_sex_de_i_t_x.rtf (08APR2021 14:45)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (51.4)	52 (58.4)	44 (53.0)	41 (63.1)	0.9379
Number (%) of patients censored	34 (48.6)	37 (41.6)	39 (47.0)	24 (36.9)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.04 (1.084 to 3.647)	1.91 (1.281 to 2.858)	1.91 (1.018 to 2.530)	1.40 (0.986 to 2.070)	
Median (95% CI)	7.56 (3.745 to NC)	5.98 (3.121 to 10.283)	5.19 (3.055 to 12.945)	4.60 (2.267 to 8.608)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.189 to NC)	NC (12.945 to NC)	NC (8.608 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5663		0.4938	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.74 to 1.73)		1.16 (0.76 to 1.78)	
P-value	-	0.5666		0.4942	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (18.6)	28 (31.5)	21 (25.3)	15 (23.1)	0.1245
Number (%) of patients censored	57 (81.4)	61 (68.5)	62 (74.7)	50 (76.9)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	NC (7.885 to NC)	8.48 (1.741 to 13.142)	11.47 (1.446 to NC)	10.48 (1.938 to NC)	
Median (95% CI)	NC (NC to NC)	NC (13.142 to NC)	NC (13.339 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1027		0.5946	
Hazard ratio (95% CI) vs Pd	-	1.72 (0.89 to 3.32)		0.84 (0.43 to 1.62)	
P-value	-	0.1070		0.5951	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (28.6)	15 (16.9)	28 (33.7)	19 (29.2)	0.3899
Number (%) of patients censored	50 (71.4)	74 (83.1)	55 (66.3)	46 (70.8)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	5.55 (2.858 to NC)	NC (9.331 to NC)	8.34 (1.873 to 10.185)	5.13 (1.544 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.185 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0469		0.3774	
Hazard ratio (95% CI) vs Pd	-	0.51 (0.26 to 1.00)		0.77 (0.43 to 1.38)	
P-value	-	0.0511		0.3788	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	63 (50.0)	67 (56.8)	12 (63.2)	15 (62.5)	0.6220
Number (%) of patients censored	63 (50.0)	51 (43.2)	7 (36.8)	9 (37.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.05 (1.018 to 1.248)	1.15 (1.018 to 1.741)	0.99 (0.953 to 1.117)	1.08 (0.986 to 1.380)	
Median (95% CI)	4.01 (1.938 to NC)	4.04 (2.070 to 12.057)	1.15 (0.986 to NC)	2.23 (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.150 to NC)	NC (2.234 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7924		0.6369	
Hazard ratio (95% CI) vs Pd	-	1.05 (0.74 to 1.48)		0.83 (0.39 to 1.78)	
P-value	-	0.7925		0.6373	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_impl_race_de_i_t_x.rtf (08APR2021 14:45)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	68 (54.0)	75 (63.6)	9 (47.4)	14 (58.3)	0.7639
Number (%) of patients censored	58 (46.0)	43 (36.4)	10 (52.6)	10 (41.7)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.97 (1.150 to 2.497)	1.84 (1.051 to 1.971)	3.88 (1.018 to 7.754)	2.99 (1.117 to 6.571)	
Median (95% CI)	5.45 (3.088 to 9.298)	3.71 (2.924 to 6.965)	NC (3.877 to NC)	7.89 (4.797 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.189 to NC)	NC (NC to NC)	NC (8.608 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4108		0.5412	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.83 to 1.59)		1.30 (0.56 to 3.01)	
P-value	-	0.4113		0.5423	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (20.6)	36 (30.5)	6 (31.6)	5 (20.8)	0.1885
Number (%) of patients censored	100 (79.4)	82 (69.5)	13 (68.4)	19 (79.2)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	11.93 (7.885 to NC)	8.61 (4.370 to 13.142)	3.91 (0.953 to NC)	NC (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (13.142 to NC)	NC (3.910 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1449		0.5312	
Hazard ratio (95% CI) vs Pd	-	1.45 (0.88 to 2.41)		0.69 (0.21 to 2.25)	
P-value	-	0.1472		0.5337	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (34.9)	28 (23.7)	3 (15.8)	3 (12.5)	0.7262
Number (%) of patients censored	82 (65.1)	90 (76.3)	16 (84.2)	21 (87.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	4.44 (2.530 to 9.298)	12.32 (5.125 to NC)	NC (4.205 to NC)	NC (4.797 to NC)	
Median (95% CI)	NC (10.678 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0209		0.8363	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.36 to 0.93)		0.84 (0.17 to 4.19)	
P-value	-	0.0226		0.8364	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	3 (75.0)	66 (49.3)	75 (57.7)	0.5391
Number (%) of patients censored	2 (66.7)	1 (25.0)	68 (50.7)	55 (42.3)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	1.02 (1.018 to 1.314)	1.05 (1.018 to 1.117)	1.12 (1.018 to 1.380)	
Median (95% CI)	NC (1.281 to NC)	1.17 (1.018 to NC)	5.59 (1.873 to NC)	3.94 (2.070 to 7.425)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6015		0.5821	
Hazard ratio (95% CI) vs Pd	-	1.82 (0.19 to 17.92)		1.10 (0.79 to 1.53)	
P-value	-	0.6066		0.5828	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_impl_ethn_de_i_t_x.rtf (08APR2021 14:45)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	0 (0.0)	70 (52.2)	83 (63.8)	0.9792
Number (%) of patients censored	2 (66.7)	4 (100.0)	64 (47.8)	47 (36.2)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.35 (1.347 to NC)	NC (NC to NC)	2.04 (1.610 to 2.760)	1.87 (1.084 to 1.971)	
Median (95% CI)	NC (1.347 to NC)	NC (NC to NC)	7.00 (3.745 to 12.945)	4.93 (3.088 to 7.491)	
75% quantile (95% CI)	NC (1.347 to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.283 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.2074	
Hazard ratio (95% CI) vs Pd	-			1.23 (0.89 to 1.69)	
P-value	-	0.9990		0.2090	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	3 (75.0)	29 (21.6)	36 (27.7)	0.8931
Number (%) of patients censored	2 (66.7)	1 (25.0)	105 (78.4)	94 (72.3)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	2.22 (1.018 to 5.158)	11.47 (7.754 to NC)	8.74 (4.698 to 14.554)	
Median (95% CI)	NC (1.281 to NC)	4.29 (1.018 to NC)	NC (NC to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7345		0.3641	
Hazard ratio (95% CI) vs Pd	-	1.48 (0.15 to 14.39)		1.25 (0.77 to 2.04)	
P-value	-	0.7362		0.3651	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	44 (32.8)	30 (23.1)	0.9998
Number (%) of patients censored	3 (100.0)	4 (100.0)	90 (67.2)	100 (76.9)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	5.29 (2.793 to 9.528)	12.32 (6.472 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.973 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0348	
Hazard ratio (95% CI) vs Pd	-			0.61 (0.38 to 0.97)	
P-value	-			0.0366	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	35 (46.1)	27 (49.1)	7 (35.0)	17 (60.7)	1 (20.0)	4 (57.1)	9 (60.0)	13 (61.9)	25 (67.6)	24 (55.8)	0.1661
Number (%) of patients censored	41 (53.9)	28 (50.9)	13 (65.0)	11 (39.3)	4 (80.0)	3 (42.9)	6 (40.0)	8 (38.1)	12 (32.4)	19 (44.2)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	1.08 (1.018 to 1.938)	1.18 (1.018 to 1.938)	1.08 (0.986 to NC)	1.03 (0.986 to 1.971)	NC (6.012 to NC)	1.02 (0.953 to 1.938)	1.05 (0.986 to 1.150)	1.08 (0.986 to 2.168)	1.02 (0.986 to 1.018)	1.18 (1.018 to 1.906)	
Median (95% CI)	3.78 (2.267 to NC)	6.77 (1.938 to NC)	NC (1.084 to NC)	4.48 (1.084 to NC)	NC (6.012 to NC)	1.94 (0.953 to NC)	1.15 (1.051 to NC)	2.23 (1.084 to NC)	1.48 (1.018 to 5.585)	4.70 (1.741 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.078 to NC)	NC (6.012 to NC)	NC (1.150 to NC)	NC (1.150 to NC)	NC (2.234 to NC)	NC (1.906 to NC)	NC (12.057 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.9426		0.1968		0.1328		0.8894		0.0804	
Hazard ratio (95% CI) vs Pd	-	0.98 (0.59 to 1.62)		1.77 (0.73 to 4.27)		4.79 (0.51 to 44.66)		0.94 (0.40 to 2.20)		0.61 (0.34 to 1.07)	
P-value	-	0.9427		0.2031		0.1687		0.8887		0.0835	
Improvement probability (95% CI)[b]											
2 Months	0.352 (0.244 to 0.463)	0.372 (0.245 to 0.499)	0.316 (0.129 to 0.522)	0.429 (0.246 to 0.600)		0.571 (0.172 to 0.837)	0.533 (0.263 to 0.744)	0.381 (0.183 to 0.578)	0.618 (0.438 to 0.755)	0.383 (0.238 to 0.526)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_impl_greg_de_i_t_x.rtf (08APR2021 14:45)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	32 (42.1)	28 (50.9)	14 (70.0)	17 (60.7)	4 (80.0)	5 (71.4)	7 (46.7)	12 (57.1)	23 (62.2)	31 (72.1)	0.8260
Number (%) of patients censored	44 (57.9)	27 (49.1)	6 (30.0)	11 (39.3)	1 (20.0)	2 (28.6)	8 (53.3)	9 (42.9)	14 (37.8)	12 (27.9)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	2.10 (1.150 to 3.778)	2.07 (1.216 to 5.125)	0.99 (0.953 to 1.906)	1.03 (0.953 to 2.168)	1.35 (0.986 to 3.877)	1.08 (0.953 to 3.450)	3.75 (1.018 to 7.754)	2.99 (1.117 to 6.571)	2.14 (1.610 to 3.088)	1.91 (0.986 to 1.971)	
Median (95% CI)	12.94 (5.191 to NC)	7.98 (4.731 to NC)	2.50 (0.986 to 9.823)	2.86 (1.084 to NC)	2.60 (0.986 to NC)	3.45 (0.953 to NC)	NC (1.971 to NC)	7.89 (2.990 to NC)	3.75 (2.530 to 8.608)	2.92 (1.938 to 5.552)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.189 to NC)	NC (2.497 to NC)	NC (4.928 to NC)	3.88 (0.986 to NC)	NC (3.318 to NC)	NC (NC to NC)	NC (8.608 to NC)	NC (4.501 to NC)	12.48 (3.713 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_detl_greg_de_i_t_x.rtf (08APR2021 14:45)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.6810		0.5587		0.6560		0.5966		0.3887	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.67 to 1.85)		0.81 (0.40 to 1.64)		0.74 (0.20 to 2.79)		1.29 (0.50 to 3.30)		1.27 (0.74 to 2.18)	
P-value	-	0.6812		0.5594		0.6571		0.5975		0.3898	
Deterioration probability (95% CI)[b]											
2 Months	0.774 (0.658 to 0.855)	0.760 (0.622 to 0.853)	0.526 (0.287 to 0.719)	0.607 (0.404 to 0.760)	0.600 (0.126 to 0.882)	0.714 (0.258 to 0.920)	0.800 (0.500 to 0.931)	0.804 (0.558 to 0.922)	0.831 (0.661 to 0.920)	0.589 (0.425 to 0.721)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_detl_greg_de_i_t_x.rtf (08APR2021 14:45)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	18 (23.7)	15 (27.3)	2 (10.0)	9 (32.1)	0 (0.0)	2 (28.6)	4 (26.7)	4 (19.0)	10 (27.0)	13 (30.2)	0.5443
Number (%) of patients censored	58 (76.3)	40 (72.7)	18 (90.0)	19 (67.9)	5 (100.0)	5 (71.4)	11 (73.3)	17 (81.0)	27 (73.0)	30 (69.8)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	9.69 (3.154 to NC)	8.74 (1.938 to NC)	NC (4.731 to NC)	3.35 (0.986 to NC)	NC (NC to NC)	5.16 (4.370 to NC)	3.91 (1.117 to NC)	NC (0.986 to NC)	10.25 (1.018 to NC)	8.64 (1.446 to NC)	
Median (95% CI)	NC (13.339 to NC)	NC (13.142 to NC)	NC (11.926 to NC)	NC (8.608 to NC)	NC (NC to NC)	NC (4.370 to NC)	NC (1.150 to NC)	NC (NC to NC)	NC (10.251 to NC)	NC (10.480 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.6583		0.0679		0.2137		0.7462		0.9709	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.59 to 2.32)		3.80 (0.82 to 17.74)				0.80 (0.20 to 3.18)		0.98 (0.43 to 2.25)	
P-value	-	0.6586		0.0890		0.9978		0.7467		0.9709	
Improvement probability (95% CI)[b]											

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	19 (25.0)	14 (25.5)	11 (55.0)	8 (28.6)	2 (40.0)	1 (14.3)	3 (20.0)	2 (9.5)	13 (35.1)	9 (20.9)	0.6241
Number (%) of patients censored	57 (75.0)	41 (74.5)	9 (45.0)	20 (71.4)	3 (60.0)	6 (85.7)	12 (80.0)	19 (90.5)	24 (64.9)	34 (79.1)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	7.49 (2.793 to NC)	7.49 (1.643 to NC)	1.02 (0.953 to 9.331)	6.47 (1.018 to NC)	9.72 (2.595 to NC)	NC (0.953 to NC)	NC (4.205 to NC)	NC (4.797 to NC)	3.81 (1.938 to 9.528)	NC (4.698 to NC)	
Median (95% CI)	NC (NC to NC)	NC (12.320 to NC)	10.97 (1.018 to NC)	NC (6.965 to NC)	9.72 (2.595 to NC)	NC (0.953 to NC)	NC (8.345 to NC)	NC (NC to NC)	NC (6.801 to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.973 to NC)	NC (NC to NC)	NC (2.595 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.9107		0.0995		0.3940		0.4528		0.0637	
Hazard ratio (95% CI) vs Pd	-	0.96 (0.48 to 1.92)		0.47 (0.19 to 1.18)		0.37 (0.03 to 4.06)		0.51 (0.09 to 3.06)		0.45 (0.19 to 1.07)	
P-value	-	0.9109		0.1073		0.4134		0.4612		0.0705	
Deterioration probability (95% CI)[b]											

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_detpl_greg_de_i_t_x.rtf (08APR2021 14:45)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	47 (48.5)	39 (50.6)	30 (53.6)	46 (59.7)	0.9035
Number (%) of patients censored	50 (51.5)	38 (49.4)	26 (46.4)	31 (40.3)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.05 (1.018 to 1.741)	1.15 (1.018 to 1.741)	1.05 (0.986 to 1.117)	1.08 (1.018 to 1.906)	
Median (95% CI)	3.78 (2.004 to NC)	4.70 (1.873 to NC)	3.02 (1.117 to NC)	4.30 (1.971 to 7.458)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.057 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8879		0.9877	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.63 to 1.48)		1.00 (0.63 to 1.59)	
P-value	-	0.8880		0.9877	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_impl_rreg_de_i_t_x.rtf (08APR2021 14:45)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (44.3)	42 (54.5)	37 (66.1)	51 (66.2)	0.8183
Number (%) of patients censored	54 (55.7)	35 (45.5)	19 (33.9)	26 (33.8)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.14 (1.873 to 3.055)	1.97 (1.281 to 3.318)	1.61 (1.018 to 2.497)	1.87 (1.018 to 1.971)	
Median (95% CI)	12.94 (3.877 to NC)	7.56 (3.450 to NC)	3.81 (2.497 to 7.885)	3.71 (2.628 to 6.571)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.485 to NC)	NC (7.754 to NC)	NC (7.491 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5491		0.8359	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.74 to 1.74)		1.05 (0.68 to 1.60)	
P-value	-	0.5493		0.8364	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (22.7)	22 (28.6)	12 (21.4)	21 (27.3)	0.8833
Number (%) of patients censored	75 (77.3)	55 (71.4)	44 (78.6)	56 (72.7)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	11.47 (3.154 to NC)	8.48 (3.417 to NC)	11.30 (4.731 to NC)	10.41 (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (13.142 to NC)	NC (11.926 to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5126		0.4809	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.67 to 2.20)		1.29 (0.63 to 2.62)	
P-value	-	0.5132		0.4821	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (27.8)	18 (23.4)	21 (37.5)	16 (20.8)	0.3739
Number (%) of patients censored	70 (72.2)	59 (76.6)	35 (62.5)	61 (79.2)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	5.55 (2.760 to NC)	12.32 (4.238 to NC)	6.80 (1.216 to 9.331)	NC (4.928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.298 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3338		0.0307	
Hazard ratio (95% CI) vs Pd	-	0.75 (0.41 to 1.35)		0.50 (0.26 to 0.95)	
P-value	-	0.3355		0.0342	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_detpl_rreg_de_i_t_x.rtf (08APR2021 14:45)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	68 (49.6)	75 (54.3)	9 (56.3)	10 (62.5)	0.9525
Number (%) of patients censored	69 (50.4)	63 (45.7)	7 (43.8)	6 (37.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.05 (1.018 to 1.117)	1.15 (1.051 to 1.380)	0.99 (0.953 to 1.281)	1.05 (0.986 to 3.351)	
Median (95% CI)	4.01 (2.037 to NC)	4.67 (2.168 to NC)	1.91 (0.986 to NC)	3.68 (1.018 to 7.458)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.906 to NC)	7.46 (3.351 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9572		0.9591	
Hazard ratio (95% CI) vs Pd	-	1.01 (0.73 to 1.40)		0.98 (0.40 to 2.41)	
P-value	-	0.9572		0.9591	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_impl_ecog_de_i_t_x.rtf (08APR2021 14:45)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	72 (52.6)	87 (63.0)	8 (50.0)	6 (37.5)	0.2525
Number (%) of patients censored	65 (47.4)	51 (37.0)	8 (50.0)	10 (62.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.04 (1.610 to 2.760)	1.91 (1.216 to 1.971)	1.05 (0.986 to 2.793)	3.52 (0.296 to NC)	
Median (95% CI)	6.51 (3.811 to 9.823)	5.13 (2.990 to 7.491)	3.75 (1.018 to NC)	NC (3.515 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.189 to NC)	NC (3.745 to NC)	NC (7.984 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2691		0.5470	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.87 to 1.63)		0.72 (0.25 to 2.09)	
P-value	-	0.2697		0.5487	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (21.2)	37 (26.8)	5 (31.3)	6 (37.5)	0.9074
Number (%) of patients censored	108 (78.8)	101 (73.2)	11 (68.8)	10 (62.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	11.47 (7.885 to NC)	8.74 (4.698 to NC)	1.28 (0.953 to NC)	5.16 (0.986 to 13.142)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (1.150 to NC)	13.14 (1.938 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.823 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4116		0.8931	
Hazard ratio (95% CI) vs Pd	-	1.23 (0.75 to 1.99)		1.08 (0.33 to 3.58)	
P-value	-	0.4124		0.8934	
Improvement probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (30.7)	31 (22.5)	6 (37.5)	3 (18.8)	0.6439
Number (%) of patients censored	95 (69.3)	107 (77.5)	10 (62.5)	13 (81.3)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	7.49 (2.858 to 10.185)	12.32 (6.571 to NC)	2.79 (0.986 to NC)	NC (0.296 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.530 to NC)	NC (3.515 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0541		0.3401	
Hazard ratio (95% CI) vs Pd	-	0.64 (0.40 to 1.01)		0.52 (0.13 to 2.06)	
P-value	-	0.0562		0.3489	
Deterioration probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (56.9)	31 (48.4)	24 (42.9)	29 (54.7)	21 (48.8)	24 (70.6)	0.2012
Number (%) of patients censored	22 (43.1)	33 (51.6)	32 (57.1)	24 (45.3)	22 (51.2)	10 (29.4)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	1.05 (0.986 to 1.117)	1.15 (1.018 to 2.530)	1.08 (1.018 to 2.825)	1.38 (1.051 to 1.971)	1.08 (0.986 to 1.446)	1.02 (0.986 to 1.051)	
Median (95% CI)	3.15 (1.084 to NC)	12.06 (3.187 to NC)	NC (2.267 to NC)	3.94 (1.938 to NC)	3.02 (1.117 to NC)	1.38 (1.051 to 3.351)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.760 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3000		0.4054		0.2022	
Hazard ratio (95% CI) vs Pd	-	0.77 (0.46 to 1.27)		1.26 (0.73 to 2.16)		1.46 (0.81 to 2.63)	
P-value	-	0.3014		0.4064		0.2049	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (54.9)	39 (60.9)	35 (62.5)	34 (64.2)	15 (34.9)	18 (52.9)	0.6609
Number (%) of patients censored	23 (45.1)	25 (39.1)	21 (37.5)	19 (35.8)	28 (65.1)	16 (47.1)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	1.97 (1.216 to 3.055)	1.97 (1.117 to 2.858)	1.35 (0.986 to 2.136)	1.28 (1.018 to 2.070)	3.09 (0.986 to 6.505)	1.94 (0.986 to 4.928)	
Median (95% CI)	7.66 (2.858 to NC)	4.73 (2.858 to 12.189)	3.78 (2.037 to 6.144)	5.55 (1.971 to 6.965)	12.94 (3.745 to NC)	7.98 (3.318 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.189 to NC)	NC (6.144 to NC)	NC (6.308 to NC)	NC (12.945 to NC)	NC (8.608 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4904		0.8257		0.3540	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.73 to 1.93)		0.95 (0.59 to 1.52)		1.38 (0.69 to 2.76)	
P-value	-	0.4909		0.8257		0.3560	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (27.5)	15 (23.4)	9 (16.1)	15 (28.3)	10 (23.3)	12 (35.3)	0.5160
Number (%) of patients censored	37 (72.5)	49 (76.6)	47 (83.9)	38 (71.7)	33 (76.7)	22 (64.7)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	7.75 (1.150 to NC)	14.55 (1.084 to NC)	NC (7.885 to NC)	10.22 (3.417 to NC)	11.30 (1.084 to NC)	4.70 (1.018 to 10.480)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (13.142 to NC)	13.34 (11.302 to NC)	NC (8.641 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.339 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7450		0.2152		0.4203	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.43 to 1.84)		1.68 (0.73 to 3.84)		1.41 (0.61 to 3.27)	
P-value	-	0.7452		0.2203		0.4225	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (33.3)	14 (21.9)	23 (41.1)	13 (24.5)	7 (16.3)	7 (20.6)	0.4903
Number (%) of patients censored	34 (66.7)	50 (78.1)	33 (58.9)	40 (75.5)	36 (83.7)	27 (79.4)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	6.80 (2.234 to NC)	NC (2.825 to NC)	2.89 (1.183 to 8.542)	10.02 (5.125 to NC)	9.53 (3.745 to NC)	NC (1.840 to NC)	
Median (95% CI)	NC (11.236 to NC)	NC (NC to NC)	10.97 (7.491 to NC)	NC (12.320 to NC)	NC (9.528 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2259		0.0332		0.9538	
Hazard ratio (95% CI) vs Pd	-	0.65 (0.32 to 1.31)		0.48 (0.24 to 0.96)		1.03 (0.36 to 2.95)	
P-value	-	0.2295		0.0371		0.9538	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (51.6)	18 (46.2)	51 (52.0)	57 (57.6)	10 (41.7)	10 (62.5)	0.5339
Number (%) of patients censored	15 (48.4)	21 (53.8)	47 (48.0)	42 (42.4)	14 (58.3)	6 (37.5)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	1.05 (0.986 to 2.037)	1.08 (0.986 to 3.187)	1.05 (1.018 to 1.117)	1.18 (1.051 to 1.873)	1.08 (0.953 to 1.511)	1.02 (0.723 to 1.117)	
Median (95% CI)	5.65 (1.117 to NC)	12.06 (1.906 to NC)	3.78 (1.840 to NC)	3.94 (1.971 to 7.458)	3.78 (1.084 to NC)	1.31 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.778 to NC)	NC (1.314 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6290		0.9524		0.3185	
Hazard ratio (95% CI) vs Pd	-	0.85 (0.43 to 1.66)		1.01 (0.69 to 1.48)		1.56 (0.65 to 3.75)	
P-value	-	0.6294		0.9525		0.3224	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (58.1)	24 (61.5)	56 (57.1)	61 (61.6)	6 (25.0)	8 (50.0)	0.7337
Number (%) of patients censored	13 (41.9)	15 (38.5)	42 (42.9)	38 (38.4)	18 (75.0)	8 (50.0)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	1.91 (1.051 to 3.745)	2.27 (1.051 to 3.088)	2.00 (1.150 to 2.530)	1.51 (1.051 to 1.971)	2.83 (0.953 to NC)	1.91 (0.986 to 3.515)	
Median (95% CI)	7.56 (2.234 to NC)	6.47 (2.858 to NC)	5.55 (3.088 to 9.823)	5.55 (2.957 to 7.655)	NC (2.825 to NC)	3.52 (1.840 to NC)	
75% quantile (95% CI)	NC (8.608 to NC)	NC (10.119 to NC)	NC (12.945 to NC)	NC (10.283 to NC)	NC (5.191 to NC)	NC (3.515 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9101		0.5999		0.3310	
Hazard ratio (95% CI) vs Pd	-	1.04 (0.56 to 1.91)		1.10 (0.77 to 1.58)		1.68 (0.58 to 4.87)	
P-value	-	0.9103		0.6003		0.3364	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (25.8)	12 (30.8)	19 (19.4)	27 (27.3)	7 (29.2)	4 (25.0)	0.5709
Number (%) of patients censored	23 (74.2)	27 (69.2)	79 (80.6)	72 (72.7)	17 (70.8)	12 (75.0)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	11.47 (1.117 to NC)	8.61 (1.018 to NC)	11.93 (7.885 to NC)	9.82 (3.417 to NC)	1.51 (0.953 to NC)	10.48 (0.986 to NC)	
Median (95% CI)	NC (11.466 to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (13.142 to NC)	NC (1.511 to NC)	NC (4.698 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.692 to NC)	NC (10.480 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6154		0.2485		0.5385	
Hazard ratio (95% CI) vs Pd	-	1.26 (0.51 to 3.08)		1.41 (0.78 to 2.54)		0.68 (0.20 to 2.34)	
P-value	-	0.6162		0.2508		0.5410	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (35.5)	6 (15.4)	34 (34.7)	23 (23.2)	3 (12.5)	5 (31.3)	0.1772
Number (%) of patients censored	20 (64.5)	33 (84.6)	64 (65.3)	76 (76.8)	21 (87.5)	11 (68.8)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	2.86 (1.610 to NC)	NC (2.825 to NC)	5.29 (2.760 to 9.528)	12.32 (4.928 to NC)	NC (0.986 to NC)	4.70 (0.986 to NC)	
Median (95% CI)	NC (8.345 to NC)	NC (NC to NC)	NC (10.185 to NC)	NC (NC to NC)	NC (7.754 to NC)	NC (3.515 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.608 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0522		0.0568		0.3688	
Hazard ratio (95% CI) vs Pd	-	0.39 (0.14 to 1.05)		0.60 (0.35 to 1.02)		1.91 (0.45 to 8.06)	
P-value	-	0.0614		0.0595		0.3769	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (47.8)	7 (50.0)	49 (51.6)	68 (57.6)	0.8317
Number (%) of patients censored	12 (52.2)	7 (50.0)	46 (48.4)	50 (42.4)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.25 (0.953 to 1.610)	1.31 (0.986 to 4.698)	1.05 (1.018 to 1.084)	1.08 (1.018 to 1.248)	
Median (95% CI)	2.96 (1.248 to NC)	4.70 (1.150 to NC)	3.78 (1.511 to NC)	3.68 (1.971 to 12.057)	
75% quantile (95% CI)	NC (2.957 to NC)	NC (4.698 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8399		0.8083	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.35 to 2.34)		1.05 (0.72 to 1.51)	
P-value	-	0.8400		0.8089	
Improvement probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (43.5)	5 (35.7)	50 (52.6)	75 (63.6)	0.3144
Number (%) of patients censored	13 (56.5)	9 (64.3)	45 (47.4)	43 (36.4)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.83 (0.953 to 3.811)	1.84 (0.296 to NC)	1.94 (1.084 to 2.760)	1.91 (1.084 to 2.168)	
Median (95% CI)	3.81 (2.103 to NC)	NC (1.051 to NC)	7.00 (3.745 to NC)	5.55 (2.957 to 7.655)	
75% quantile (95% CI)	NC (3.811 to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.189 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5813		0.2585	
Hazard ratio (95% CI) vs Pd	-	0.74 (0.25 to 2.17)		1.23 (0.86 to 1.76)	
P-value	-	0.5827		0.2593	
Deterioration probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (26.1)	2 (14.3)	21 (22.1)	38 (32.2)	0.2140
Number (%) of patients censored	17 (73.9)	12 (85.7)	74 (77.9)	80 (67.8)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	7.89 (0.953 to NC)	8.48 (4.698 to NC)	11.47 (4.731 to NC)	7.62 (1.906 to 10.480)	
Median (95% CI)	NC (7.885 to NC)	NC (4.698 to NC)	NC (NC to NC)	NC (13.142 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3078		0.1668	
Hazard ratio (95% CI) vs Pd	-	0.44 (0.09 to 2.21)		1.45 (0.85 to 2.48)	
P-value	-	0.3209		0.1693	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (26.1)	4 (28.6)	29 (30.5)	24 (20.3)	0.3615
Number (%) of patients censored	17 (73.9)	10 (71.4)	66 (69.5)	94 (79.7)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	4.44 (0.953 to NC)	2.86 (0.296 to NC)	7.75 (2.037 to 11.236)	NC (6.571 to NC)	
Median (95% CI)	NC (4.435 to NC)	NC (1.840 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (10.185 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8698		0.0516	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.31 to 3.95)		0.59 (0.34 to 1.01)	
P-value	-	0.8698		0.0544	
Deterioration probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (44.4)	9 (37.5)	42 (53.8)	65 (63.1)	0.3823
Number (%) of patients censored	20 (55.6)	15 (62.5)	36 (46.2)	38 (36.9)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.08 (1.018 to 1.610)	1.31 (0.986 to NC)	1.02 (0.986 to 1.084)	1.05 (1.018 to 1.183)	
Median (95% CI)	NC (1.248 to NC)	NC (1.938 to NC)	2.96 (1.117 to NC)	2.83 (1.906 to 5.782)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.057 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4306		0.6332	
Hazard ratio (95% CI) vs Pd	-	0.72 (0.32 to 1.63)		1.10 (0.75 to 1.62)	
P-value	-	0.4327		0.6334	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (52.8)	13 (54.2)	38 (48.7)	65 (63.1)	0.3468
Number (%) of patients censored	17 (47.2)	11 (45.8)	40 (51.3)	38 (36.9)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.35 (0.986 to 2.825)	1.28 (0.296 to 2.957)	1.97 (1.084 to 3.745)	1.91 (1.084 to 2.201)	
Median (95% CI)	3.81 (2.103 to NC)	5.72 (1.840 to NC)	7.89 (5.191 to NC)	5.13 (2.924 to 7.984)	
75% quantile (95% CI)	NC (3.811 to NC)	NC (5.782 to NC)	NC (NC to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8095		0.1221	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.45 to 1.86)		1.37 (0.92 to 2.05)	
P-value	-	0.8096		0.1236	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (25.0)	2 (8.3)	18 (23.1)	37 (35.9)	0.0407
Number (%) of patients censored	27 (75.0)	22 (91.7)	60 (76.9)	66 (64.1)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	7.89 (1.084 to NC)	NC (4.698 to NC)	11.47 (3.910 to NC)	5.16 (1.150 to 10.218)	
Median (95% CI)	NC (7.885 to NC)	NC (NC to NC)	NC (13.339 to NC)	14.55 (13.142 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0747		0.1012	
Hazard ratio (95% CI) vs Pd	-	0.27 (0.06 to 1.26)		1.60 (0.91 to 2.80)	
P-value	-	0.0962		0.1044	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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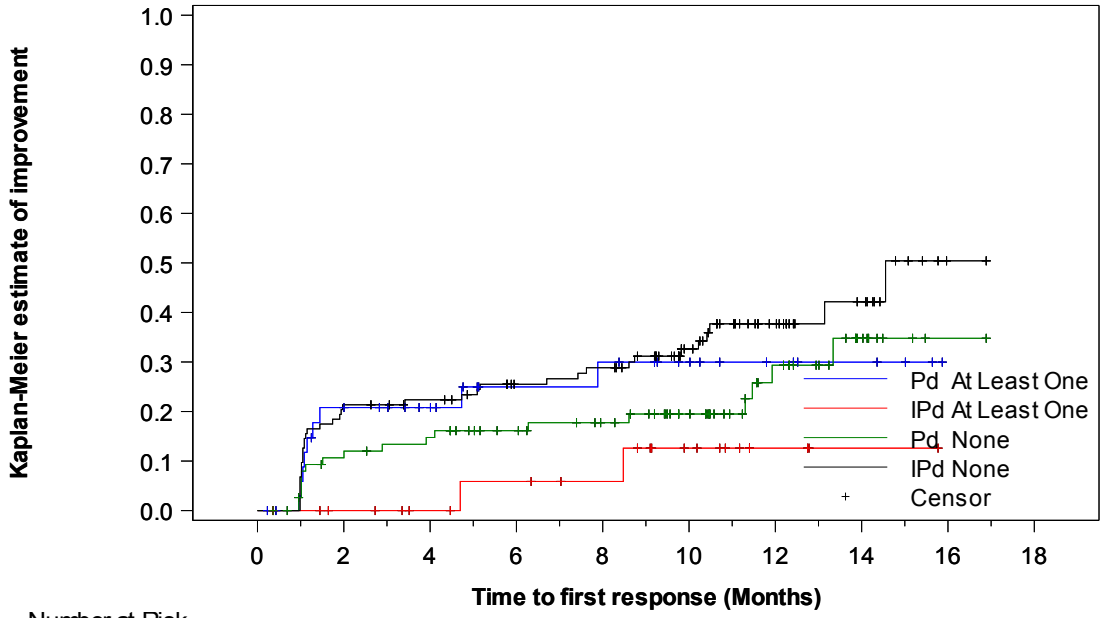
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to cytogenetic abnormality (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd At Least One	36	24	15	13	6	3	0
IPd At Least One	24	20	16	12	3	1	0
Pd None	78	63	54	45	20	3	0
IPd None	103	80	67	58	23	5	0

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.7 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (27.8)	8 (33.3)	23 (29.5)	20 (19.4)	0.2105
Number (%) of patients censored	26 (72.2)	16 (66.7)	55 (70.5)	83 (80.6)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	4.44 (2.037 to NC)	4.24 (0.296 to NC)	8.34 (2.760 to 11.236)	NC (6.571 to NC)	
Median (95% CI)	NC (4.862 to NC)	NC (4.238 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7463		0.0752	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.46 to 2.96)		0.58 (0.32 to 1.06)	
P-value	-	0.7465		0.0787	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (51.1)	45 (54.2)	31 (49.2)	40 (56.3)	0.7848
Number (%) of patients censored	44 (48.9)	38 (45.8)	32 (50.8)	31 (43.7)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.05 (0.986 to 1.084)	1.08 (1.018 to 1.314)	1.08 (1.018 to 1.610)	1.18 (1.051 to 2.168)	
Median (95% CI)	5.59 (1.511 to NC)	2.89 (1.873 to NC)	3.02 (1.610 to NC)	4.67 (2.760 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8621		0.8155	
Hazard ratio (95% CI) vs Pd	-	1.04 (0.69 to 1.56)		0.95 (0.59 to 1.51)	
P-value	-	0.8621		0.8148	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (51.1)	39 (47.0)	34 (54.0)	54 (76.1)	0.1008
Number (%) of patients censored	44 (48.9)	44 (53.0)	29 (46.0)	17 (23.9)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.00 (1.610 to 3.055)	2.20 (1.840 to 3.121)	1.94 (0.986 to 2.595)	1.12 (0.986 to 1.906)	
Median (95% CI)	6.14 (3.745 to NC)	10.28 (3.713 to NC)	4.50 (2.595 to 9.823)	3.45 (1.906 to 5.979)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.298 to NC)	8.61 (6.472 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5469		0.1007	
Hazard ratio (95% CI) vs Pd	-	0.88 (0.57 to 1.34)		1.43 (0.93 to 2.20)	
P-value	-	0.5482		0.1025	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (26.7)	22 (26.5)	10 (15.9)	21 (29.6)	0.2848
Number (%) of patients censored	66 (73.3)	61 (73.5)	53 (84.1)	50 (70.4)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	7.75 (1.446 to NC)	10.22 (3.417 to NC)	11.30 (8.608 to NC)	7.62 (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (11.926 to NC)	NC (13.142 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9918		0.1822	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.56 to 1.78)		1.66 (0.78 to 3.54)	
P-value	-	0.9918		0.1869	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (32.2)	15 (18.1)	19 (30.2)	19 (26.8)	0.4323
Number (%) of patients censored	61 (67.8)	68 (81.9)	44 (69.8)	52 (73.2)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	7.75 (2.760 to 10.185)	NC (4.928 to NC)	4.44 (2.464 to 11.236)	9.33 (3.515 to NC)	
Median (95% CI)	NC (10.678 to NC)	NC (NC to NC)	NC (11.236 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0286		0.3657	
Hazard ratio (95% CI) vs Pd	-	0.50 (0.27 to 0.94)		0.75 (0.39 to 1.41)	
P-value	-	0.0318		0.3674	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	2 (100.0)	75 (49.7)	83 (54.6)	0.7730
Number (%) of patients censored	0 (0.0)	0 (0.0)	76 (50.3)	69 (45.4)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.02 (1.018 to 1.084)	1.08 (1.084 to 1.117)	1.05 (1.018 to 1.117)	1.15 (1.051 to 1.413)	
Median (95% CI)	1.05 (1.018 to 1.084)	1.10 (1.084 to 1.117)	4.01 (2.004 to NC)	4.67 (2.234 to 12.057)	
75% quantile (95% CI)	1.08 (1.018 to 1.084)	1.12 (1.084 to 1.117)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.9486	
Hazard ratio (95% CI) vs Pd	-	0.31 (0.03 to 3.50)		1.01 (0.74 to 1.38)	
P-value	-	0.3429		0.9487	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	80 (53.0)	92 (60.5)	0.9800
Number (%) of patients censored	2 (100.0)	1 (50.0)	71 (47.0)	60 (39.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	NC (NC to NC)	3.19 (3.187 to NC)	1.97 (1.216 to 2.530)	1.91 (1.117 to 2.070)	
Median (95% CI)	NC (NC to NC)	NC (3.187 to NC)	5.62 (3.745 to 9.298)	5.55 (3.121 to 7.655)	
75% quantile (95% CI)	NC (NC to NC)	NC (3.187 to NC)	NC (NC to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.4940	
Hazard ratio (95% CI) vs Pd	-			1.11 (0.82 to 1.50)	
P-value	-	0.9990		0.4949	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	0 (0.0)	32 (21.2)	43 (28.3)	0.9849
Number (%) of patients censored	0 (0.0)	2 (100.0)	119 (78.8)	109 (71.7)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.02 (1.018 to 11.466)	NC (NC to NC)	11.93 (7.754 to NC)	8.64 (4.698 to 13.142)	
Median (95% CI)	6.24 (1.018 to 11.466)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	11.47 (1.018 to 11.466)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.2642	
Hazard ratio (95% CI) vs Pd	-			1.30 (0.82 to 2.05)	
P-value	-	0.9990		0.2656	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	48 (31.8)	34 (22.4)	0.9997
Number (%) of patients censored	2 (100.0)	2 (100.0)	103 (68.2)	118 (77.6)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	5.55 (2.793 to 9.528)	12.32 (6.472 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.236 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0279	
Hazard ratio (95% CI) vs Pd	-			0.61 (0.40 to 0.95)	
P-value	-			0.0294	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (49.5)	57 (54.8)	21 (51.2)	19 (57.6)	0.7740
Number (%) of patients censored	51 (50.5)	47 (45.2)	20 (48.8)	14 (42.4)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.05 (1.018 to 1.117)	1.12 (1.018 to 1.446)	1.12 (0.986 to 1.906)	1.15 (0.986 to 2.530)	
Median (95% CI)	3.78 (1.840 to NC)	4.04 (1.938 to NC)	5.65 (1.446 to NC)	4.30 (1.248 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.768 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9443		0.7794	
Hazard ratio (95% CI) vs Pd	-	1.01 (0.69 to 1.48)		1.09 (0.59 to 2.03)	
P-value	-	0.9443		0.7787	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	56 (55.4)	59 (56.7)	19 (46.3)	22 (66.7)	0.1147
Number (%) of patients censored	45 (44.6)	45 (43.3)	22 (53.7)	11 (33.3)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.94 (1.051 to 2.595)	1.94 (1.281 to 2.858)	2.04 (1.051 to 5.552)	1.12 (0.986 to 1.971)	
Median (95% CI)	4.21 (3.055 to 8.608)	5.78 (3.515 to 10.283)	7.75 (3.088 to NC)	3.32 (1.544 to 10.119)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.731 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6120		0.1215	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.63 to 1.31)		1.62 (0.87 to 2.99)	
P-value	-	0.6111		0.1250	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (22.8)	30 (28.8)	7 (17.1)	9 (27.3)	0.4327
Number (%) of patients censored	78 (77.2)	74 (71.2)	34 (82.9)	24 (72.7)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	11.47 (7.754 to NC)	8.48 (1.938 to 14.554)	NC (1.446 to NC)	8.64 (1.084 to NC)	
Median (95% CI)	NC (13.339 to NC)	NC (13.142 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4605		0.4006	
Hazard ratio (95% CI) vs Pd	-	1.23 (0.71 to 2.11)		1.52 (0.57 to 4.09)	
P-value	-	0.4613		0.4040	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (34.7)	20 (19.2)	11 (26.8)	9 (27.3)	0.1495
Number (%) of patients censored	66 (65.3)	84 (80.8)	30 (73.2)	24 (72.7)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	3.81 (2.136 to 9.298)	NC (6.571 to NC)	9.33 (2.464 to NC)	12.32 (0.986 to NC)	
Median (95% CI)	NC (10.678 to NC)	NC (NC to NC)	NC (11.236 to NC)	NC (12.320 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0040		0.9837	
Hazard ratio (95% CI) vs Pd	-	0.45 (0.26 to 0.79)		0.99 (0.41 to 2.40)	
P-value	-	0.0050		0.9837	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (49.0)	55 (53.9)	27 (51.9)	29 (56.9)	0.9915
Number (%) of patients censored	51 (51.0)	47 (46.1)	25 (48.1)	22 (43.1)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.05 (1.018 to 1.117)	1.10 (1.018 to 1.446)	1.08 (0.986 to 1.741)	1.15 (1.018 to 2.530)	
Median (95% CI)	3.78 (1.840 to NC)	4.04 (1.938 to NC)	4.01 (1.446 to NC)	4.67 (1.873 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9356		0.9869	
Hazard ratio (95% CI) vs Pd	-	1.02 (0.69 to 1.49)		1.00 (0.59 to 1.70)	
P-value	-	0.9356		0.9869	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	55 (55.0)	58 (56.9)	24 (46.2)	35 (68.6)	0.0390
Number (%) of patients censored	45 (45.0)	44 (43.1)	28 (53.8)	16 (31.4)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.91 (1.051 to 2.497)	1.94 (1.281 to 2.858)	2.46 (1.347 to 5.552)	1.22 (1.018 to 1.971)	
Median (95% CI)	4.21 (3.055 to 8.608)	5.78 (3.515 to 10.283)	9.30 (5.454 to NC)	3.12 (1.906 to 7.556)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	12.48 (6.472 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6623		0.0208	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.64 to 1.33)		1.84 (1.09 to 3.10)	
P-value	-	0.6617		0.0227	
Hazard ratio inverted (95% CI) vs IPd		-		0.54 (0.32 to 0.92)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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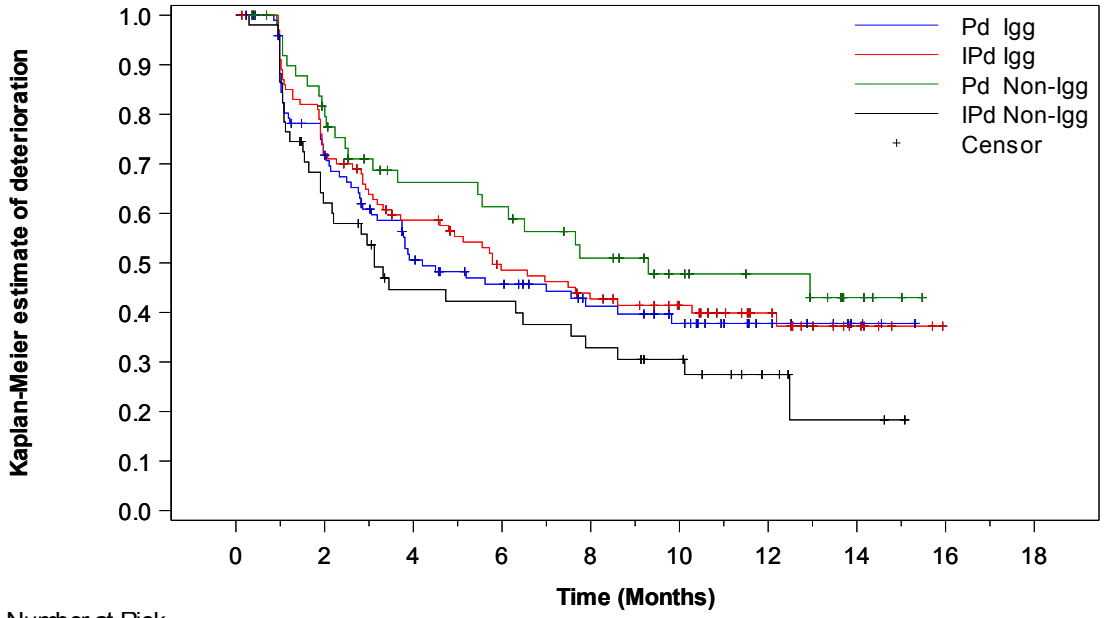
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-C30 - Time to first deterioration by 10 pt in pain according to MM type at initial diagnosis (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd Igg	100	55	36	25	10	1	0
IPd Igg	102	62	42	32	16	2	0
Pd Non-Igg	52	31	25	17	10	2	0
IPd Non-Igg	51	25	18	13	5	1	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (22.0)	30 (29.4)	11 (21.2)	13 (25.5)	0.7774
Number (%) of patients censored	78 (78.0)	72 (70.6)	41 (78.8)	38 (74.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	11.47 (4.731 to NC)	8.48 (1.938 to 13.142)	10.25 (1.150 to NC)	8.74 (4.370 to NC)	
Median (95% CI)	NC (13.339 to NC)	NC (13.142 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3415		0.7866	
Hazard ratio (95% CI) vs Pd	-	1.31 (0.75 to 2.26)		1.12 (0.50 to 2.49)	
P-value	-	0.3429		0.7872	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.7 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (35.0)	20 (19.6)	13 (25.0)	14 (27.5)	0.0701
Number (%) of patients censored	65 (65.0)	82 (80.4)	39 (75.0)	37 (72.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	3.81 (2.136 to 9.298)	NC (6.571 to NC)	9.33 (2.530 to NC)	8.61 (1.511 to NC)	
Median (95% CI)	NC (10.678 to NC)	NC (NC to NC)	NC (11.236 to NC)	NC (12.320 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0043		0.7974	
Hazard ratio (95% CI) vs Pd	-	0.46 (0.26 to 0.79)		1.10 (0.52 to 2.35)	
P-value	-	0.0054		0.7976	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (70.0)	9 (64.3)	70 (49.0)	76 (54.3)	0.1496
Number (%) of patients censored	3 (30.0)	5 (35.7)	73 (51.0)	64 (45.7)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	0.95 (0.920 to 1.018)	1.12 (0.986 to 1.906)	1.05 (1.018 to 1.150)	1.15 (1.051 to 1.446)	
Median (95% CI)	1.02 (0.920 to NC)	2.33 (1.084 to NC)	5.59 (2.267 to NC)	4.67 (2.234 to NC)	
75% quantile (95% CI)	1.94 (0.986 to NC)	NC (1.906 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2089		0.7905	
Hazard ratio (95% CI) vs Pd	-	0.53 (0.20 to 1.44)		1.04 (0.76 to 1.45)	
P-value	-	0.2160		0.7906	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (30.0)	9 (64.3)	77 (53.8)	84 (60.0)	0.5025
Number (%) of patients censored	7 (70.0)	5 (35.7)	66 (46.2)	56 (40.0)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	3.75 (0.920 to NC)	1.84 (0.986 to 3.187)	2.00 (1.216 to 2.530)	1.91 (1.117 to 2.201)	
Median (95% CI)	NC (0.920 to NC)	5.90 (1.544 to NC)	5.62 (3.778 to 9.298)	5.72 (3.318 to 7.655)	
75% quantile (95% CI)	NC (3.745 to NC)	12.19 (3.187 to NC)	NC (NC to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5190		0.5496	
Hazard ratio (95% CI) vs Pd	-	1.56 (0.40 to 6.04)		1.10 (0.81 to 1.50)	
P-value	-	0.5224		0.5499	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_detl_mri_de_i_t_x.rtf (08APR2021 14:45)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (20.0)	4 (28.6)	32 (22.4)	39 (27.9)	0.8057
Number (%) of patients censored	8 (80.0)	10 (71.4)	111 (77.6)	101 (72.1)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	NC (0.953 to NC)	10.41 (0.986 to NC)	11.47 (7.754 to NC)	8.64 (4.370 to 14.554)	
Median (95% CI)	NC (0.953 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.415 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9417		0.3841	
Hazard ratio (95% CI) vs Pd	-	1.07 (0.19 to 5.85)		1.23 (0.77 to 1.96)	
P-value	-	0.9418		0.3850	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (30.0)	5 (35.7)	45 (31.5)	29 (20.7)	0.9061
Number (%) of patients censored	7 (70.0)	9 (64.3)	98 (68.5)	111 (79.3)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	3.75 (0.920 to NC)	8.61 (1.544 to NC)	6.80 (2.793 to 9.725)	NC (6.571 to NC)	
Median (95% CI)	NC (0.920 to NC)	NC (2.825 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (3.745 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4478		0.0248	
Hazard ratio (95% CI) vs Pd	-	0.54 (0.11 to 2.70)		0.59 (0.37 to 0.94)	
P-value	-	0.4547		0.0265	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (52.1)	50 (57.5)	25 (51.0)	32 (58.2)	0.9821
Number (%) of patients censored	46 (47.9)	37 (42.5)	24 (49.0)	23 (41.8)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.05 (0.986 to 1.117)	1.15 (1.018 to 1.873)	1.02 (0.986 to 1.610)	1.05 (1.018 to 1.380)	
Median (95% CI)	3.78 (1.281 to NC)	3.94 (2.070 to NC)	2.96 (1.446 to NC)	4.70 (1.380 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.057 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9390		0.9143	
Hazard ratio (95% CI) vs Pd	-	1.02 (0.69 to 1.50)		1.03 (0.61 to 1.74)	
P-value	-	0.9390		0.9144	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (51.0)	55 (63.2)	28 (57.1)	34 (61.8)	0.3750
Number (%) of patients censored	47 (49.0)	32 (36.8)	21 (42.9)	21 (38.2)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.23 (1.610 to 3.088)	1.91 (1.117 to 2.628)	1.91 (0.986 to 2.464)	1.91 (1.051 to 2.924)	
Median (95% CI)	7.66 (3.745 to NC)	5.72 (3.088 to 7.885)	4.50 (2.333 to 9.823)	3.52 (2.924 to 8.608)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.283 to NC)	NC (6.998 to NC)	NC (8.608 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2389		0.9118	
Hazard ratio (95% CI) vs Pd	-	1.26 (0.86 to 1.85)		0.97 (0.59 to 1.61)	
P-value	-	0.2400		0.9116	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (27.1)	25 (28.7)	6 (12.2)	16 (29.1)	0.1351
Number (%) of patients censored	70 (72.9)	62 (71.3)	43 (87.8)	39 (70.9)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	10.25 (3.154 to 13.339)	9.82 (5.092 to 14.554)	NC (8.608 to NC)	4.70 (1.380 to NC)	
Median (95% CI)	NC (13.339 to NC)	NC (13.142 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9243		0.0655	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.59 to 1.78)		2.35 (0.92 to 6.01)	
P-value	-	0.9243		0.0740	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (31.3)	17 (19.5)	17 (34.7)	14 (25.5)	0.9097
Number (%) of patients censored	66 (68.8)	70 (80.5)	32 (65.3)	41 (74.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	7.49 (2.858 to 10.973)	NC (6.472 to NC)	2.89 (1.906 to 9.725)	10.02 (3.515 to NC)	
Median (95% CI)	NC (11.236 to NC)	NC (NC to NC)	NC (9.298 to NC)	NC (12.320 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0461		0.1239	
Hazard ratio (95% CI) vs Pd	-	0.55 (0.30 to 1.00)		0.58 (0.28 to 1.17)	
P-value	-	0.0494		0.1286	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	2 (100.0)	76 (50.3)	83 (54.6)	0.6168
Number (%) of patients censored	1 (50.0)	0 (0.0)	75 (49.7)	69 (45.4)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	1.91 (1.906 to 6.768)	1.05 (1.018 to 1.117)	1.12 (1.051 to 1.380)	
Median (95% CI)	NC (1.281 to NC)	4.34 (1.906 to 6.768)	3.78 (1.938 to NC)	4.30 (2.234 to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	6.77 (1.906 to 6.768)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.9787	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		1.00 (0.73 to 1.36)	
P-value	-	0.8092		0.9787	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (100.0)	80 (53.0)	91 (59.9)	0.9743
Number (%) of patients censored	2 (100.0)	0 (0.0)	71 (47.0)	61 (40.1)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	NC (NC to NC)	0.99 (0.986 to 1.971)	1.97 (1.216 to 2.530)	1.91 (1.216 to 2.201)	
Median (95% CI)	NC (NC to NC)	1.48 (0.986 to 1.971)	5.62 (3.745 to 9.298)	5.72 (3.318 to 7.885)	
75% quantile (95% CI)	NC (NC to NC)	1.97 (0.986 to 1.971)	NC (NC to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.5687	
Hazard ratio (95% CI) vs Pd	-			1.09 (0.81 to 1.47)	
P-value	-	0.9991		0.5694	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	33 (21.9)	42 (27.6)	0.5881
Number (%) of patients censored	1 (50.0)	1 (50.0)	118 (78.1)	110 (72.4)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	5.09 (5.092 to NC)	11.47 (7.754 to NC)	8.74 (4.698 to 14.554)	
Median (95% CI)	NC (1.281 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.3691	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		1.23 (0.78 to 1.94)	
P-value	-	0.8092		0.3700	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_imppl_prmab_de_i_t_x.rtf (08APR2021 14:46)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	48 (31.8)	33 (21.7)	0.9836
Number (%) of patients censored	2 (100.0)	1 (50.0)	103 (68.2)	119 (78.3)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	NC (NC to NC)	12.32 (NC to NC)	5.55 (2.793 to 9.528)	NC (6.472 to NC)	
Median (95% CI)	NC (NC to NC)	12.32 (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	12.32 (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0227	
Hazard ratio (95% CI) vs Pd	-			0.60 (0.39 to 0.94)	
P-value	-			0.0241	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	57 (49.6)	69 (58.5)	20 (52.6)	16 (44.4)	0.3364
Number (%) of patients censored	58 (50.4)	49 (41.5)	18 (47.4)	20 (55.6)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.05 (1.018 to 1.150)	1.10 (1.018 to 1.413)	1.05 (0.986 to 1.281)	1.18 (1.018 to 1.938)	
Median (95% CI)	3.78 (1.938 to NC)	3.94 (2.136 to 7.425)	4.01 (1.117 to NC)	NC (1.380 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6153		0.3806	
Hazard ratio (95% CI) vs Pd	-	1.09 (0.77 to 1.55)		0.75 (0.39 to 1.44)	
P-value	-	0.6164		0.3823	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	58 (50.4)	72 (61.0)	22 (57.9)	21 (58.3)	0.5849
Number (%) of patients censored	57 (49.6)	46 (39.0)	16 (42.1)	15 (41.7)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.14 (1.347 to 3.088)	1.91 (1.117 to 2.168)	1.94 (0.986 to 2.464)	1.54 (0.986 to 3.088)	
Median (95% CI)	7.56 (3.877 to 12.945)	5.55 (3.121 to 7.984)	3.75 (1.971 to NC)	5.72 (2.201 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.189 to NC)	NC (6.144 to NC)	NC (5.979 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3505		0.9322	
Hazard ratio (95% CI) vs Pd	-	1.18 (0.83 to 1.67)		0.97 (0.54 to 1.77)	
P-value	-	0.3511		0.9322	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (23.5)	34 (28.8)	7 (18.4)	9 (25.0)	0.5723
Number (%) of patients censored	88 (76.5)	84 (71.2)	31 (81.6)	27 (75.0)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	11.30 (3.154 to NC)	8.64 (4.370 to 14.554)	13.34 (3.910 to NC)	10.22 (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (13.339 to NC)	NC (10.218 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6512		0.3492	
Hazard ratio (95% CI) vs Pd	-	1.12 (0.68 to 1.86)		1.61 (0.59 to 4.43)	
P-value	-	0.6514		0.3532	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (28.7)	27 (22.9)	15 (39.5)	7 (19.4)	0.4769
Number (%) of patients censored	82 (71.3)	91 (77.1)	23 (60.5)	29 (80.6)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	7.75 (2.891 to 10.973)	12.32 (5.125 to NC)	2.86 (1.051 to 9.528)	NC (1.544 to NC)	
Median (95% CI)	NC (11.236 to NC)	NC (NC to NC)	NC (7.491 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1238		0.0870	
Hazard ratio (95% CI) vs Pd	-	0.67 (0.40 to 1.12)		0.47 (0.19 to 1.14)	
P-value	-	0.1262		0.0949	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	70 (48.6)	80 (54.4)	7 (77.8)	5 (71.4)	0.6437
Number (%) of patients censored	74 (51.4)	67 (45.6)	2 (22.2)	2 (28.6)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.05 (1.018 to 1.150)	1.15 (1.051 to 1.446)	0.99 (0.986 to 1.018)	1.02 (0.986 to 1.117)	
Median (95% CI)	5.59 (2.037 to NC)	4.67 (2.234 to NC)	1.02 (0.986 to NC)	1.12 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	4.01 (0.986 to NC)	NC (1.018 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8453		0.6439	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.75 to 1.42)		0.76 (0.24 to 2.42)	
P-value	-	0.8454		0.6448	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	72 (50.0)	90 (61.2)	8 (88.9)	3 (42.9)	0.0945
Number (%) of patients censored	72 (50.0)	57 (38.8)	1 (11.1)	4 (57.1)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.00 (1.347 to 2.530)	1.91 (1.117 to 2.070)	3.09 (0.986 to 5.191)	4.93 (1.446 to NC)	
Median (95% CI)	6.51 (3.745 to NC)	5.13 (3.121 to 7.556)	5.19 (0.986 to 9.823)	NC (1.446 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.189 to NC)	8.61 (3.910 to 9.823)	NC (6.571 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2267		0.1002	
Hazard ratio (95% CI) vs Pd	-	1.21 (0.89 to 1.65)		0.34 (0.09 to 1.31)	
P-value	-	0.2274		0.1158	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (23.6)	40 (27.2)	0 (0.0)	3 (42.9)	0.9812
Number (%) of patients censored	110 (76.4)	107 (72.8)	9 (100.0)	4 (57.1)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	11.30 (4.731 to NC)	8.74 (5.092 to 14.554)	NC (NC to NC)	1.12 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.971 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7683		0.0328	
Hazard ratio (95% CI) vs Pd	-	1.07 (0.68 to 1.69)			
P-value	-	0.7687		0.9972	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (30.6)	33 (22.4)	4 (44.4)	1 (14.3)	0.5482
Number (%) of patients censored	100 (69.4)	114 (77.6)	5 (55.6)	6 (85.7)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	5.29 (2.793 to 9.331)	12.32 (6.472 to NC)	9.72 (0.986 to NC)	NC (4.928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (4.928 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.678 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0502		0.3459	
Hazard ratio (95% CI) vs Pd	-	0.64 (0.41 to 1.00)		0.36 (0.04 to 3.27)	
P-value	-	0.0521		0.3659	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (52.3)	46 (49.5)	31 (47.7)	39 (63.9)	0.2177
Number (%) of patients censored	42 (47.7)	47 (50.5)	34 (52.3)	22 (36.1)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.05 (1.018 to 1.150)	1.31 (1.084 to 1.938)	1.08 (0.986 to 1.511)	1.05 (0.986 to 1.150)	
Median (95% CI)	3.78 (1.610 to NC)	7.46 (2.760 to NC)	4.01 (1.511 to NC)	2.53 (1.150 to 6.242)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.242 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4568		0.3519	
Hazard ratio (95% CI) vs Pd	-	0.86 (0.57 to 1.29)		1.25 (0.78 to 2.00)	
P-value	-	0.4572		0.3529	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	47 (53.4)	55 (59.1)	33 (50.8)	38 (62.3)	0.9754
Number (%) of patients censored	41 (46.6)	38 (40.9)	32 (49.2)	23 (37.7)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.97 (1.150 to 2.464)	1.87 (1.051 to 2.267)	2.04 (1.051 to 3.877)	1.91 (1.084 to 2.858)	
Median (95% CI)	4.50 (2.858 to NC)	4.80 (2.990 to 7.491)	7.75 (3.877 to NC)	6.57 (2.957 to 12.189)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.283 to NC)	NC (12.945 to NC)	NC (12.189 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5756		0.6187	
Hazard ratio (95% CI) vs Pd	-	1.12 (0.76 to 1.65)		1.13 (0.71 to 1.79)	
P-value	-	0.5767		0.6196	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (29.5)	23 (24.7)	8 (12.3)	20 (32.8)	0.0156
Number (%) of patients censored	62 (70.5)	70 (75.3)	57 (87.7)	41 (67.2)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	7.89 (2.891 to 13.339)	10.22 (4.698 to NC)	NC (11.466 to NC)	7.43 (1.117 to 13.142)	
Median (95% CI)	NC (13.339 to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (13.142 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3956		0.0134	
Hazard ratio (95% CI) vs Pd	-	0.78 (0.45 to 1.38)		2.70 (1.19 to 6.14)	
P-value	-	0.3968		0.0176	
Hazard ratio inverted (95% CI) vs IPd		-		0.37 (0.16 to 0.84)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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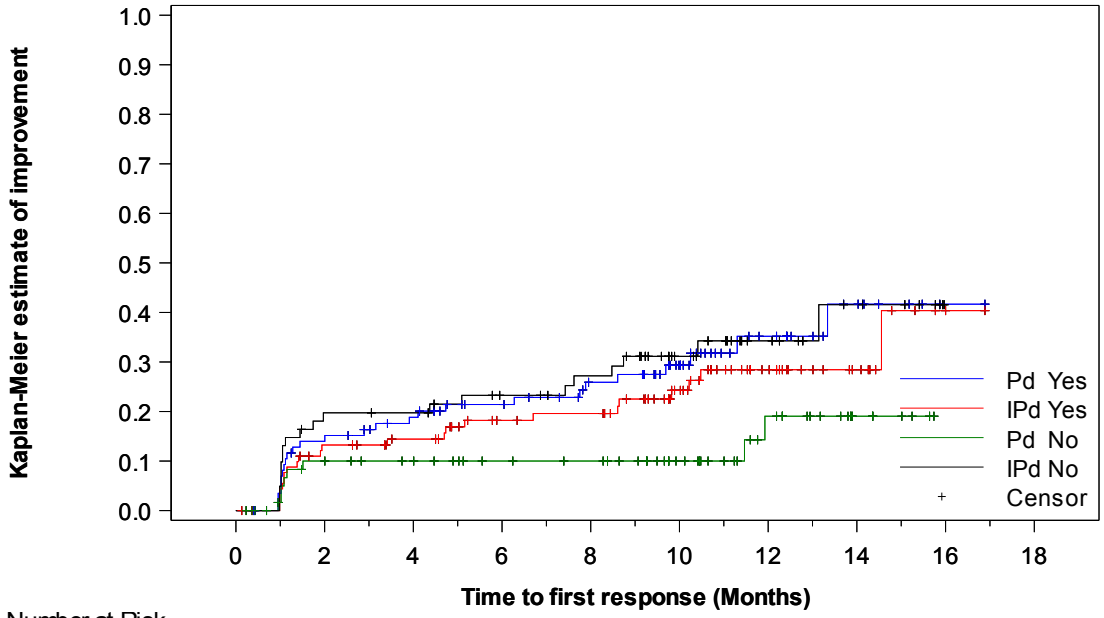
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to refractory to lenalidomide in last previous regimen (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd Yes	88	69	56	46	17	4	0
IPd Yes	93	75	60	52	22	4	0
Pd No	65	50	43	38	17	4	0
IPd No	61	48	41	34	13	6	0

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Pain
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.7 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (31.8)	21 (22.6)	20 (30.8)	13 (21.3)	0.7486
Number (%) of patients censored	60 (68.2)	72 (77.4)	45 (69.2)	48 (78.7)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	4.86 (2.595 to 9.331)	12.32 (6.472 to NC)	8.54 (2.530 to 10.973)	NC (4.698 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.678 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1412		0.0965	
Hazard ratio (95% CI) vs Pd	-	0.66 (0.37 to 1.16)		0.56 (0.28 to 1.12)	
P-value	-	0.1444		0.1012	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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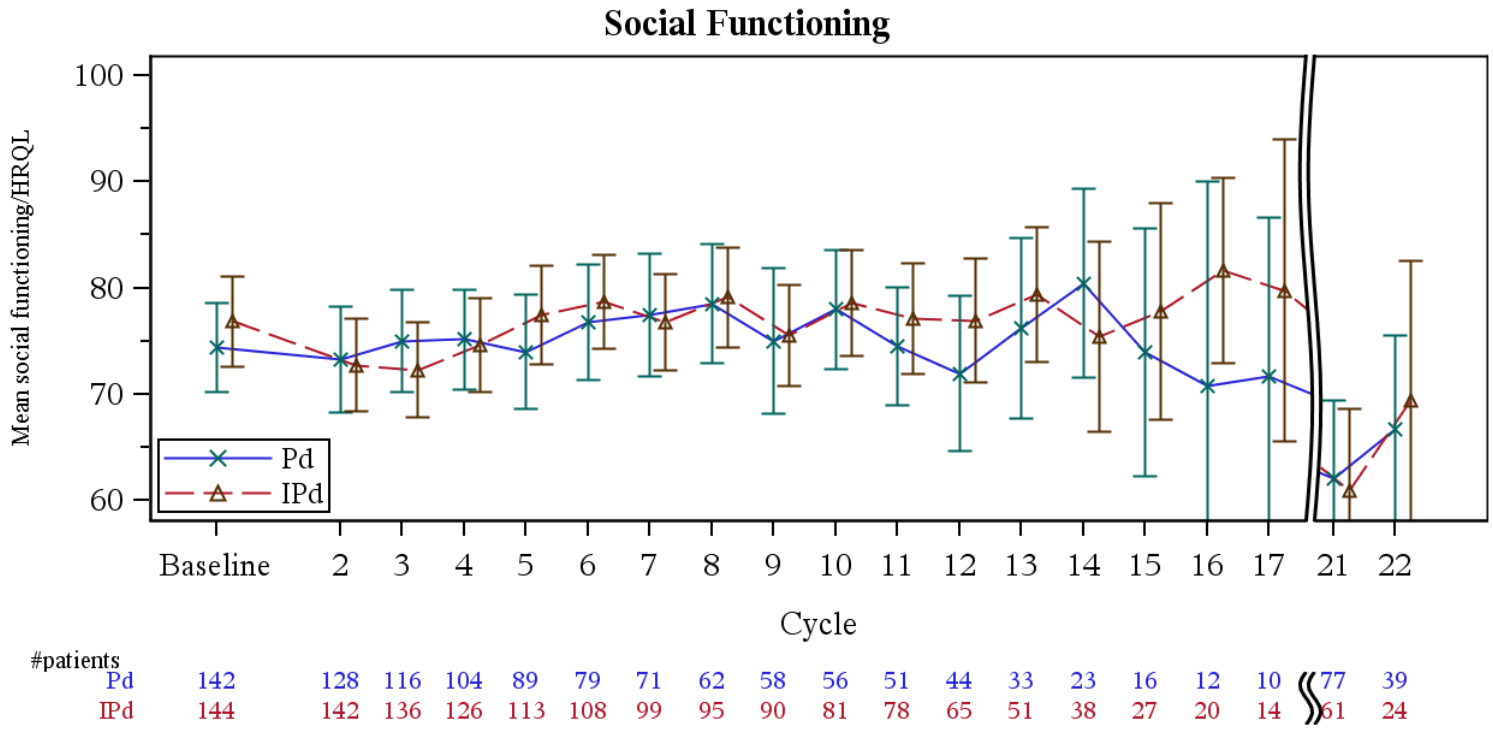
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Social functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-C30 - Mean and 95% CI for social functioning score over time (LOCF) - ITT population



A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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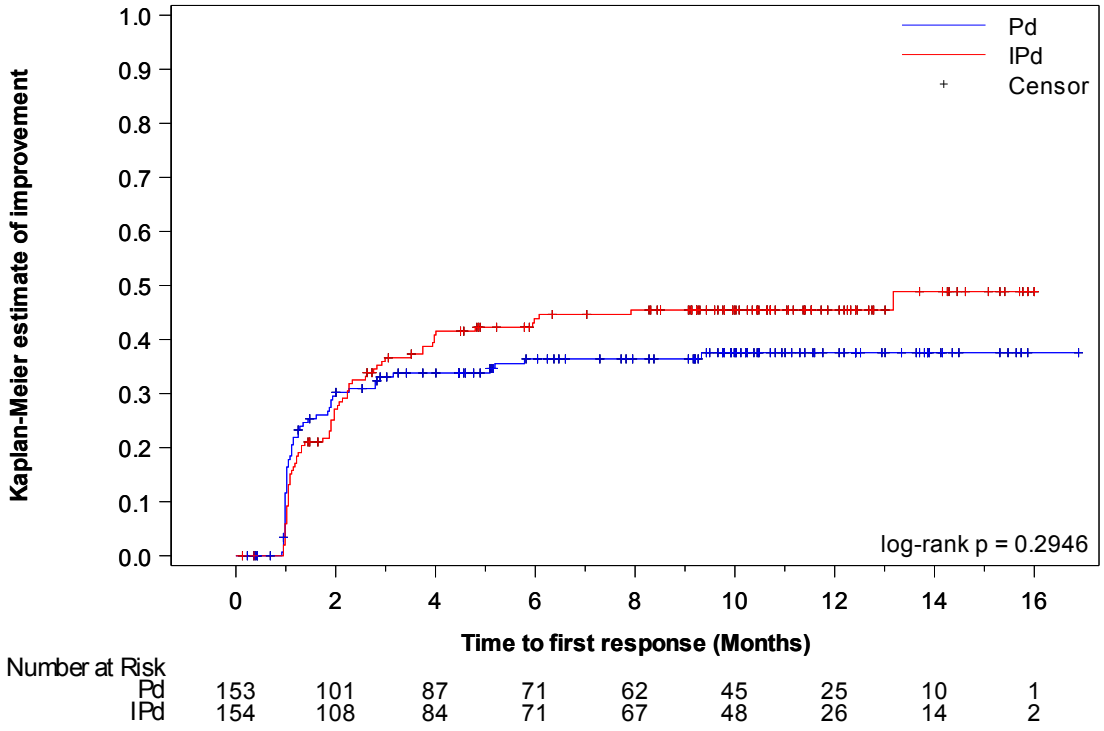
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Social functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-C30 - Time to first improvement by 15 pt in social functioning (LOCF) - ITT population

First improvement 15 points Social functioning (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	53 (34.6)	68 (44.2)
Number (%) of patients censored	100 (65.4)	86 (55.8)
Kaplan-Meier estimates of social functioning in months		
25% quantile (95% CI)	1.45 (1.051 to 2.793)	1.91 (1.216 to 2.267)
Median (95% CI)	NC (NC to NC)	NC (4.797 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2946
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.21 (0.85 to 1.74)
P-value	-	0.2954
Probability (95% CI)[c]		
2 Months	0.30 (0.223 to 0.371)	0.27 (0.203 to 0.344)
4 Months	0.34 (0.262 to 0.415)	0.41 (0.329 to 0.486)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_imp15l_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Social functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-C30 - Time to first improvement by 15 pt in social functioning - Kaplan-Meier curve (LOCF) - ITT population



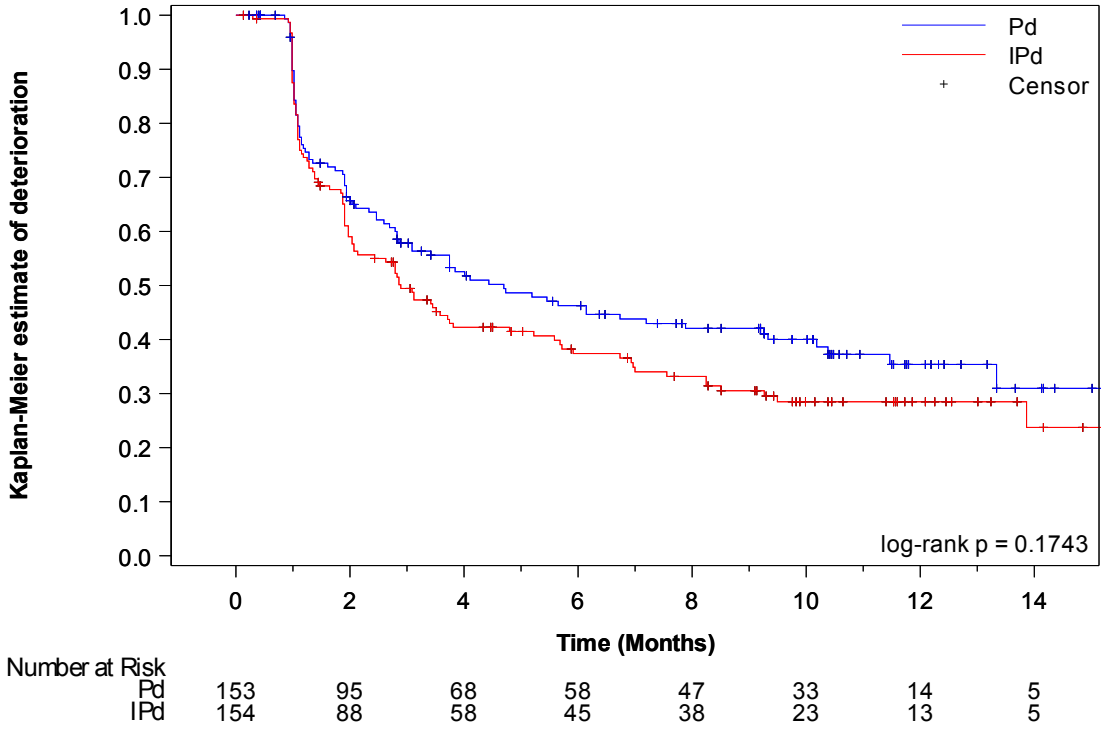
A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_imp15l_de_i_f_x.rtf (08APR2021 15:31)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Social functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-C30 - Time to first deterioration by 15 pt in social functioning (LOCF) - ITT population

First deterioration 15 points Social functioning (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	87 (56.9)	103 (66.9)
Number (%) of patients censored	66 (43.1)	51 (33.1)
Kaplan-Meier estimates of social functioning in months		
25% quantile (95% CI)	1.22 (1.051 to 1.938)	1.15 (1.051 to 1.643)
Median (95% CI)	4.70 (2.858 to 9.265)	2.89 (2.037 to 4.797)
75% quantile (95% CI)	NC (13.339 to NC)	13.86 (8.246 to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1743
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.22 (0.91 to 1.63)
P-value	-	0.1755
Probability (95% CI)[c]		
2 Months	0.66 (0.581 to 0.734)	0.59 (0.507 to 0.664)
4 Months	0.53 (0.440 to 0.604)	0.42 (0.342 to 0.501)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_det15l_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Social functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-C30 - Time to first deterioration by 15 pt in social functioning - Kaplan-Meier curve (LOCF) - ITT population



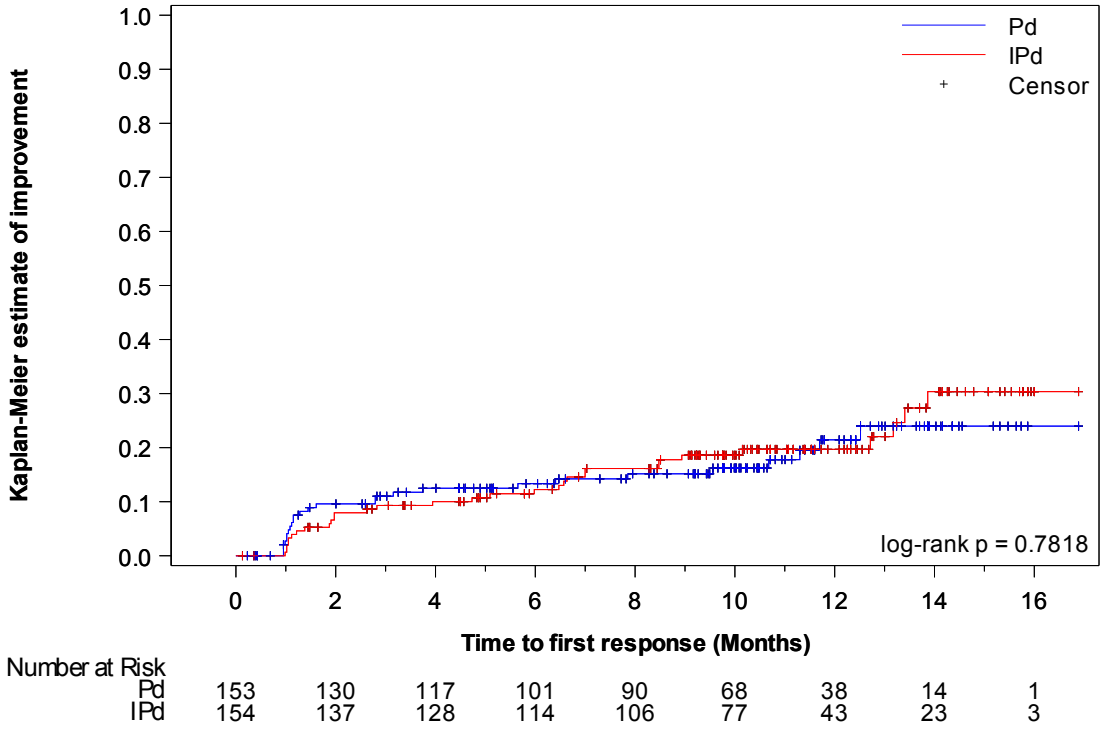
A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_det15l_de_i_f_x.rtf (08APR2021 15:31)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Social functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in social functioning (LOCF) - ITT population

First permanent improvement 15 points Social functioning (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	26 (17.0)	31 (20.1)
Number (%) of patients censored	127 (83.0)	123 (79.9)
Kaplan-Meier estimates of social functioning in months		
25% quantile (95% CI)	NC (10.678 to NC)	13.40 (8.476 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.7818
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.08 (0.64 to 1.81)
P-value	-	0.7823
Probability (95% CI)[c]		
2 Months	0.10 (0.055 to 0.150)	0.08 (0.043 to 0.130)
4 Months	0.12 (0.077 to 0.185)	0.10 (0.059 to 0.154)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_imp15pl_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Social functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-C30 - Time until permanent improvement by 15 pt in social functioning - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Social functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in social functioning (LOCF) - ITT population

First permanent deterioration 15 points Social functioning (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	52 (34.0)	46 (29.9)
Number (%) of patients censored	101 (66.0)	108 (70.1)
Kaplan-Meier estimates of social functioning in months		
25% quantile (95% CI)	4.11 (2.464 to 6.735)	8.11 (4.862 to 10.678)
Median (95% CI)	NC (NC to NC)	NC (14.817 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2107
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.78 (0.52 to 1.16)
P-value	-	0.2119
Probability (95% CI)[c]		
2 Months	0.84 (0.773 to 0.892)	0.89 (0.833 to 0.934)
4 Months	0.76 (0.677 to 0.818)	0.83 (0.762 to 0.884)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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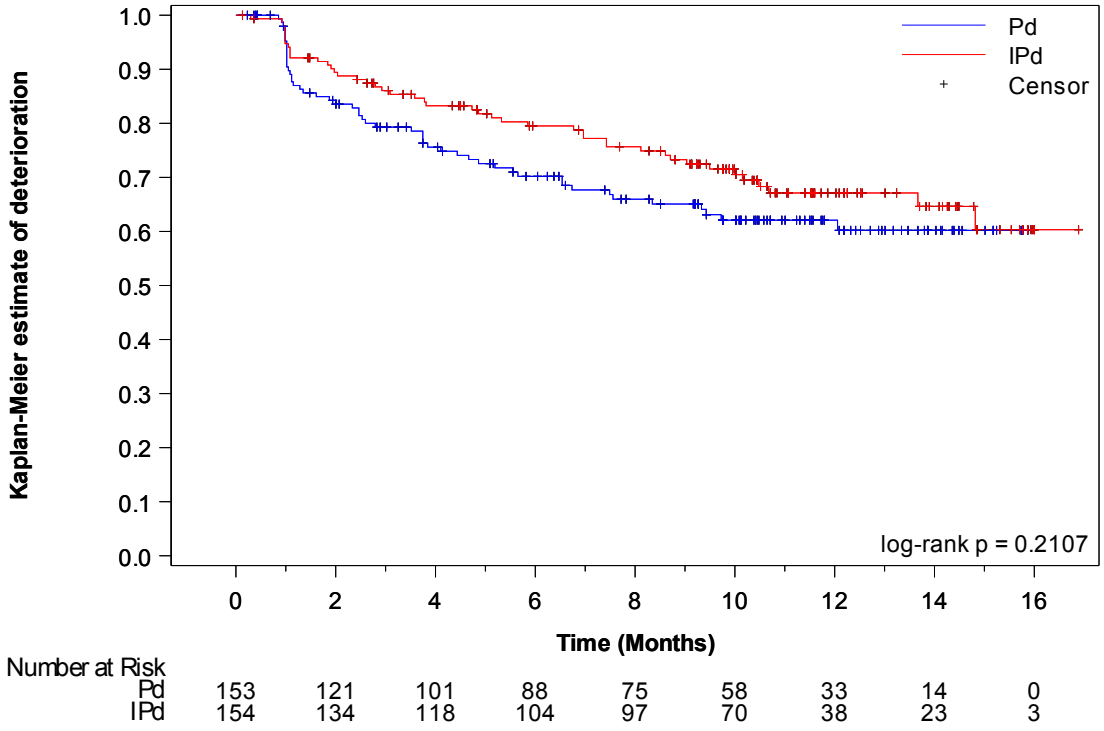
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Social functioning
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-C30 - Time until permanent deterioration by 15 pt in social functioning - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_det15pl_de_i_f_x.rtf (08APR2021 15:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (38.6)	23 (42.6)	16 (29.6)	26 (38.2)	10 (34.5)	19 (59.4)	0.3944
Number (%) of patients censored	43 (61.4)	31 (57.4)	38 (70.4)	42 (61.8)	19 (65.5)	13 (40.6)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	1.03 (0.986 to 1.938)	1.91 (1.084 to 2.760)	1.91 (1.150 to NC)	2.83 (1.314 to 4.797)	2.27 (1.018 to NC)	1.17 (0.986 to 1.971)	
Median (95% CI)	NC (2.793 to NC)	NC (2.760 to NC)	NC (NC to NC)	NC (5.979 to NC)	NC (2.793 to NC)	2.63 (1.248 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.918 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9014		0.4695		0.1046	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.55 to 1.68)		1.26 (0.67 to 2.34)		1.87 (0.87 to 4.02)	
P-value	-	0.9016		0.4704		0.1103	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (52.9)	35 (64.8)	29 (53.7)	51 (75.0)	21 (72.4)	17 (53.1)	0.0043
Number (%) of patients censored	33 (47.1)	19 (35.2)	25 (46.3)	17 (25.0)	8 (27.6)	15 (46.9)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	1.94 (1.051 to 3.745)	1.12 (0.986 to 2.037)	1.22 (1.018 to 2.103)	1.08 (1.018 to 1.347)	1.02 (0.986 to 1.117)	1.91 (1.084 to 3.515)	
Median (95% CI)	7.89 (3.844 to 13.339)	3.09 (2.037 to 8.509)	4.01 (2.103 to NC)	2.14 (1.380 to 3.450)	1.94 (1.018 to 3.417)	5.22 (1.906 to NC)	
75% quantile (95% CI)	NC (13.339 to NC)	13.86 (6.932 to NC)	NC (11.466 to NC)	8.25 (3.581 to NC)	4.44 (2.464 to NC)	NC (5.717 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1222		0.0350		0.0173	
Hazard ratio (95% CI) vs Pd	-	1.44 (0.90 to 2.29)		1.63 (1.03 to 2.57)		0.47 (0.24 to 0.89)	
P-value	-	0.1242		0.0368		0.0200	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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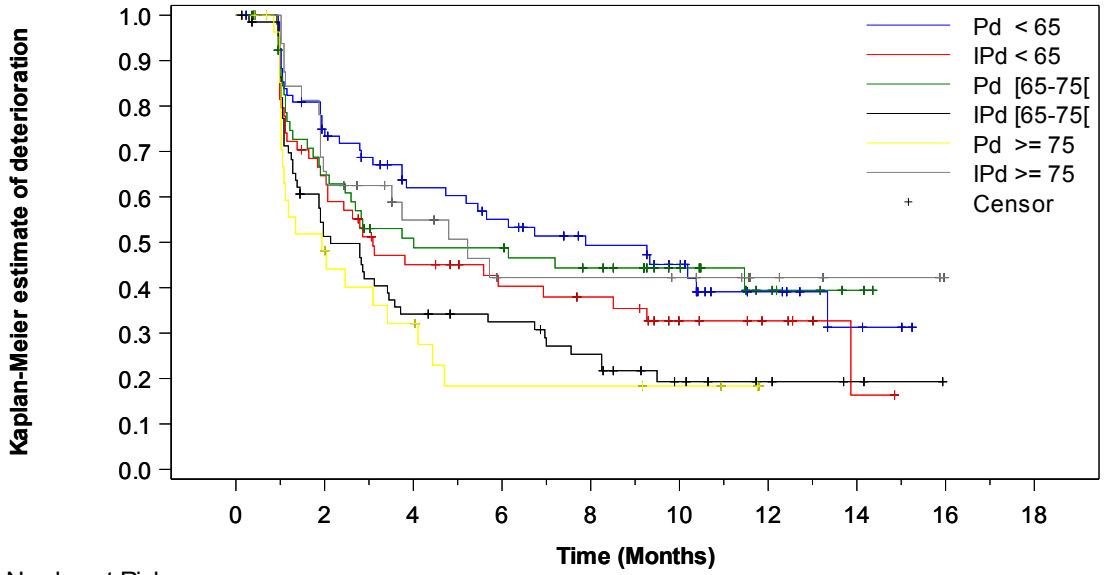
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to age (IRT) (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd < 65	70	43	31	24	8	2	0
IPd < 65	54	26	17	14	5	0	0
Pd [65-75[	54	26	23	17	6	0	0
IPd [65-75[	68	27	19	10	4	1	0
Pd >= 75	29	10	4	4	0	0	0
IPd >= 75	32	18	9	9	4	2	0

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_detl_age_de_i_f_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (24.3)	10 (18.5)	6 (11.1)	10 (14.7)	3 (10.3)	11 (34.4)	0.1537
Number (%) of patients censored	53 (75.7)	44 (81.5)	48 (88.9)	58 (85.3)	26 (89.7)	21 (65.6)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	11.30 (3.745 to NC)	NC (5.092 to NC)	NC (9.561 to NC)	13.86 (12.715 to NC)	NC (1.281 to NC)	4.73 (1.117 to 13.405)	
Median (95% CI)	NC (12.517 to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.864 to NC)	NC (NC to NC)	13.40 (6.637 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.405 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3908		0.7694		0.0625	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.33 to 1.55)		1.16 (0.42 to 3.21)		3.16 (0.88 to 11.32)	
P-value	-	0.3930		0.7696		0.0777	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_imppl_age_de_i_t_x.rtf (08APR2021 14:40)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.7 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (31.4)	21 (38.9)	16 (29.6)	20 (29.4)	14 (48.3)	5 (15.6)	0.0141
Number (%) of patients censored	48 (68.6)	33 (61.1)	38 (70.4)	48 (70.6)	15 (51.7)	27 (84.4)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	5.65 (2.793 to 12.057)	3.81 (1.840 to 8.608)	6.54 (1.610 to NC)	9.03 (5.848 to NC)	1.12 (0.986 to 3.745)	13.67 (5.125 to NC)	
Median (95% CI)	NC (12.057 to NC)	14.82 (7.425 to NC)	NC (NC to NC)	NC (NC to NC)	4.86 (1.347 to NC)	NC (13.667 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.667 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4870		0.6868		0.0025	
Hazard ratio (95% CI) vs Pd	-	1.24 (0.68 to 2.25)		0.87 (0.45 to 1.69)		0.23 (0.08 to 0.65)	
P-value	-	0.4878		0.6870		0.0054	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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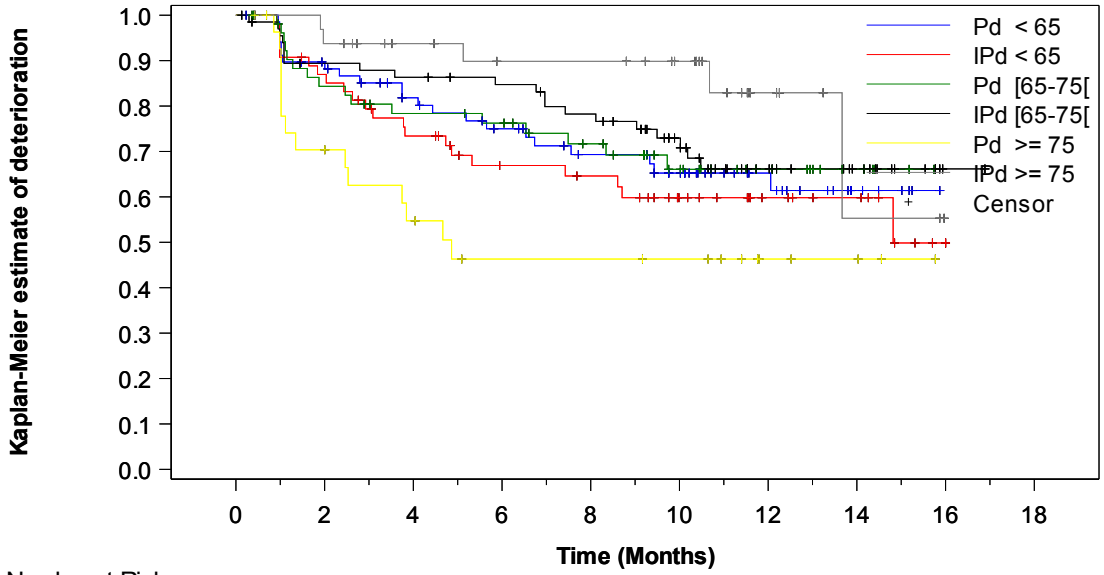
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.8 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to age (IRT) (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd < 65	70	54	42	35	17	4	0
IPd < 65	54	41	29	25	12	4	0
Pd [65-75[	54	40	36	27	12	2	0
IPd [65-75[	68	57	53	44	19	6	0
Pd >= 75	29	16	10	10	4	1	0
IPd >= 75	32	27	22	20	7	2	0

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_detpl_age_de_i_f_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	30 (29.7)	44 (43.1)	23 (44.2)	24 (46.2)	0.2339
Number (%) of patients censored	71 (70.3)	58 (56.9)	29 (55.8)	28 (53.8)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.84 (1.117 to NC)	1.91 (1.216 to 2.825)	1.15 (0.986 to 2.004)	1.91 (1.051 to 2.234)	
Median (95% CI)	NC (NC to NC)	NC (3.975 to NC)	NC (1.938 to NC)	NC (2.234 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1374		0.7238	
Hazard ratio (95% CI) vs Pd	-	1.42 (0.89 to 2.26)		0.90 (0.51 to 1.60)	
P-value	-	0.1394		0.7232	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_impl_plne_de_i_t_x.rtf (08APR2021 14:40)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	54 (53.5)	69 (67.6)	33 (63.5)	34 (65.4)	0.1786
Number (%) of patients censored	47 (46.5)	33 (32.4)	19 (36.5)	18 (34.6)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.87 (1.084 to 2.595)	1.38 (1.051 to 1.906)	1.05 (0.986 to 1.741)	1.10 (1.018 to 1.281)	
Median (95% CI)	5.65 (3.088 to 13.339)	2.86 (1.971 to 5.684)	3.09 (1.741 to 7.885)	2.89 (1.281 to 5.914)	
75% quantile (95% CI)	NC (13.339 to NC)	NC (6.998 to NC)	11.47 (7.195 to NC)	13.86 (5.914 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0466		0.7546	
Hazard ratio (95% CI) vs Pd	-	1.43 (1.00 to 2.05)		0.93 (0.57 to 1.50)	
P-value	-	0.0479		0.7545	
Hazard ratio inverted (95% CI) vs IPd		-		1.08 (0.67 to 1.75)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (15.8)	21 (20.6)	10 (19.2)	10 (19.2)	0.5504
Number (%) of patients censored	85 (84.2)	81 (79.4)	42 (80.8)	42 (80.8)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (9.561 to NC)	13.17 (6.998 to NC)	12.52 (1.610 to NC)	13.40 (5.092 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5676		0.7775	
Hazard ratio (95% CI) vs Pd	-	1.21 (0.63 to 2.32)		0.88 (0.37 to 2.12)	
P-value	-	0.5682		0.7771	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (32.7)	29 (28.4)	19 (36.5)	17 (32.7)	0.8455
Number (%) of patients censored	68 (67.3)	73 (71.6)	33 (63.5)	35 (67.3)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	5.19 (2.595 to 9.331)	8.61 (4.862 to NC)	2.53 (1.018 to 8.345)	7.43 (3.581 to 13.667)	
Median (95% CI)	NC (12.057 to NC)	NC (14.817 to NC)	NC (5.552 to NC)	NC (10.678 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3400		0.3515	
Hazard ratio (95% CI) vs Pd	-	0.78 (0.48 to 1.29)		0.73 (0.38 to 1.41)	
P-value	-	0.3403		0.3534	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (31.4)	42 (47.2)	31 (37.3)	26 (40.0)	0.2137
Number (%) of patients censored	48 (68.6)	47 (52.8)	52 (62.7)	39 (60.0)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	2.79 (1.117 to NC)	1.91 (1.084 to 2.924)	1.12 (1.018 to 1.906)	1.91 (1.084 to 2.760)	
Median (95% CI)	NC (NC to NC)	13.17 (3.745 to NC)	NC (5.782 to NC)	NC (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1099		0.8368	
Hazard ratio (95% CI) vs Pd	-	1.52 (0.91 to 2.54)		0.95 (0.56 to 1.59)	
P-value	-	0.1125		0.8371	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (60.0)	56 (62.9)	45 (54.2)	47 (72.3)	0.4091
Number (%) of patients censored	28 (40.0)	33 (37.1)	38 (45.8)	18 (27.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.12 (1.018 to 2.464)	1.13 (1.051 to 1.906)	1.22 (1.018 to 1.938)	1.13 (0.986 to 1.873)	
Median (95% CI)	5.19 (2.793 to 10.185)	2.89 (2.070 to 6.965)	4.11 (2.333 to 13.339)	2.78 (1.873 to 5.585)	
75% quantile (95% CI)	NC (10.185 to NC)	NC (7.556 to NC)	NC (13.339 to NC)	9.26 (5.717 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5880		0.0908	
Hazard ratio (95% CI) vs Pd	-	1.12 (0.75 to 1.67)		1.42 (0.94 to 2.14)	
P-value	-	0.5882		0.0924	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_detl_sex_de_i_t_x.rtf (08APR2021 14:39)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (11.4)	18 (20.2)	18 (21.7)	13 (20.0)	0.1561
Number (%) of patients censored	62 (88.6)	71 (79.8)	65 (78.3)	52 (80.0)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (11.302 to NC)	13.17 (6.998 to NC)	11.70 (1.610 to NC)	NC (6.472 to NC)	
Median (95% CI)	NC (NC to NC)	NC (13.405 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1933		0.5442	
Hazard ratio (95% CI) vs Pd	-	1.73 (0.75 to 3.97)		0.80 (0.39 to 1.64)	
P-value	-	0.1990		0.5450	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (32.9)	23 (25.8)	29 (34.9)	23 (35.4)	0.6016
Number (%) of patients censored	47 (67.1)	66 (74.2)	54 (65.1)	42 (64.6)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	5.19 (1.281 to 9.725)	10.02 (4.731 to NC)	3.84 (1.610 to 8.345)	6.77 (1.840 to 13.667)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.331 to NC)	NC (13.667 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2435		0.6101	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.40 to 1.27)		0.87 (0.50 to 1.50)	
P-value	-	0.2458		0.6104	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_detpl_sex_de_i_t_x.rtf (08APR2021 14:40)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (34.1)	51 (43.2)	9 (47.4)	14 (58.3)	0.9446
Number (%) of patients censored	83 (65.9)	67 (56.8)	10 (52.6)	10 (41.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.61 (1.051 to 2.891)	1.97 (1.183 to 2.760)	1.12 (0.986 to 9.331)	1.68 (0.986 to 2.333)	
Median (95% CI)	NC (NC to NC)	NC (5.947 to NC)	9.33 (1.117 to NC)	2.99 (1.971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.331 to NC)	NC (3.745 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4345		0.7515	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.78 to 1.76)		1.15 (0.49 to 2.65)	
P-value	-	0.4362		0.7517	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	75 (59.5)	81 (68.6)	8 (42.1)	16 (66.7)	0.2076
Number (%) of patients censored	51 (40.5)	37 (31.4)	11 (57.9)	8 (33.3)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.22 (1.018 to 1.906)	1.15 (1.018 to 1.478)	3.75 (1.018 to 11.466)	1.51 (0.986 to 2.037)	
Median (95% CI)	3.84 (2.694 to 6.735)	2.89 (1.906 to 3.811)	11.47 (3.745 to NC)	3.52 (1.906 to 8.509)	
75% quantile (95% CI)	NC (10.382 to NC)	13.86 (6.998 to NC)	NC (11.466 to NC)	8.51 (5.684 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3039		0.0755	
Hazard ratio (95% CI) vs Pd	-	1.18 (0.86 to 1.61)		2.14 (0.91 to 5.04)	
P-value	-	0.3038		0.0822	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (15.9)	27 (22.9)	5 (26.3)	2 (8.3)	0.0635
Number (%) of patients censored	106 (84.1)	91 (77.1)	14 (73.7)	22 (91.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (10.678 to NC)	13.17 (6.998 to NC)	7.85 (0.986 to NC)	NC (1.380 to NC)	
Median (95% CI)	NC (NC to NC)	NC (13.864 to NC)	NC (7.852 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3406		0.1141	
Hazard ratio (95% CI) vs Pd	-	1.32 (0.74 to 2.36)		0.29 (0.06 to 1.49)	
P-value	-	0.3422		0.1381	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (35.7)	34 (28.8)	5 (26.3)	9 (37.5)	0.1971
Number (%) of patients censored	81 (64.3)	84 (71.2)	14 (73.7)	15 (62.5)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	3.75 (2.333 to 6.538)	8.61 (3.811 to 14.817)	8.34 (1.018 to NC)	7.43 (2.037 to 13.667)	
Median (95% CI)	NC (12.057 to NC)	NC (14.817 to NC)	NC (8.345 to NC)	13.67 (7.425 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.667 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0948		0.5561	
Hazard ratio (95% CI) vs Pd	-	0.69 (0.44 to 1.07)		1.39 (0.46 to 4.21)	
P-value	-	0.0968		0.5578	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	3 (75.0)	48 (35.8)	56 (43.1)	0.6840
Number (%) of patients censored	2 (66.7)	1 (25.0)	86 (64.2)	74 (56.9)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	1.17 (1.018 to 2.595)	1.25 (1.018 to 2.793)	2.04 (1.314 to 2.760)	
Median (95% CI)	NC (1.281 to NC)	1.95 (1.018 to NC)	NC (NC to NC)	NC (5.947 to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7345		0.6062	
Hazard ratio (95% CI) vs Pd	-	1.48 (0.15 to 14.39)		1.11 (0.75 to 1.63)	
P-value	-	0.7362		0.6072	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	3 (75.0)	77 (57.5)	91 (70.0)	0.9797
Number (%) of patients censored	3 (100.0)	1 (25.0)	57 (42.5)	39 (30.0)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (NC to NC)	2.78 (2.136 to 5.585)	1.35 (1.051 to 2.037)	1.12 (1.018 to 1.380)	
Median (95% CI)	NC (NC to NC)	4.50 (2.136 to NC)	4.70 (3.088 to 9.331)	2.83 (1.906 to 3.745)	
75% quantile (95% CI)	NC (NC to NC)	NC (2.136 to NC)	NC (13.339 to NC)	13.86 (6.965 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1973		0.0422	
Hazard ratio (95% CI) vs Pd	-			1.37 (1.01 to 1.86)	
P-value	-	0.9984		0.0430	
Hazard ratio inverted (95% CI) vs IPd		-		0.73 (0.54 to 0.99)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	1 (25.0)	24 (17.9)	25 (19.2)	0.3694
Number (%) of patients censored	2 (66.7)	3 (75.0)	110 (82.1)	105 (80.8)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (6.998 to NC)	12.52 (10.678 to NC)	13.40 (10.152 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (6.998 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (6.998 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4504		0.9229	
Hazard ratio (95% CI) vs Pd	-	0.35 (0.02 to 5.89)		0.97 (0.56 to 1.70)	
P-value	-	0.4689		0.9229	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	45 (33.6)	42 (32.3)	0.9999
Number (%) of patients censored	3 (100.0)	4 (100.0)	89 (66.4)	88 (67.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	4.44 (2.464 to 7.491)	7.43 (3.811 to 10.480)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.667 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.4781	
Hazard ratio (95% CI) vs Pd	-			0.86 (0.56 to 1.31)	
P-value	-			0.4780	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	23 (30.3)	20 (36.4)	6 (30.0)	16 (57.1)	2 (40.0)	4 (57.1)	6 (40.0)	11 (52.4)	16 (43.2)	17 (39.5)	0.6401
Number (%) of patients censored	53 (69.7)	35 (63.6)	14 (70.0)	12 (42.9)	3 (60.0)	3 (42.9)	9 (60.0)	10 (47.6)	21 (56.8)	26 (60.5)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	2.27 (1.018 to NC)	2.27 (1.183 to 5.979)	1.05 (0.986 to NC)	1.07 (0.986 to 2.070)	1.91 (1.117 to NC)	1.25 (1.018 to 6.078)	1.15 (0.986 to NC)	2.23 (0.986 to 2.990)	1.25 (0.986 to 1.938)	1.91 (1.051 to 3.745)	
Median (95% CI)	NC (NC to NC)	NC (5.979 to NC)	NC (1.051 to NC)	3.40 (1.873 to NC)	NC (1.117 to NC)	6.08 (1.018 to NC)	NC (1.117 to NC)	4.80 (2.234 to NC)	NC (1.610 to NC)	NC (2.267 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.175 to NC)	NC (NC to NC)	NC (7.918 to NC)	NC (1.117 to NC)	NC (2.628 to NC)	NC (NC to NC)	NC (4.797 to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.7578		0.1502		0.6671		0.6015		0.5590	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.60 to 2.00)		1.97 (0.77 to 5.04)		1.45 (0.26 to 7.93)		1.30 (0.48 to 3.54)		0.82 (0.41 to 1.62)	
P-value	-	0.7579		0.1579		0.6689		0.6025		0.5597	
Improvement probability (95% CI)[b]											
2 Months	0.240 (0.148 to 0.344)	0.223 (0.123 to 0.341)	0.263 (0.096 to 0.468)	0.393 (0.217 to 0.565)	0.400 (0.052 to 0.753)	0.286 (0.041 to 0.612)	0.333 (0.122 to 0.564)	0.193 (0.060 to 0.382)	0.392 (0.235 to 0.547)	0.288 (0.161 to 0.428)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_impl_greg_de_i_t_x.rtf (08APR2021 14:40)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	37 (48.7)	29 (52.7)	16 (80.0)	19 (67.9)	2 (40.0)	7 (100.0)	8 (53.3)	15 (71.4)	24 (64.9)	33 (76.7)	0.2133
Number (%) of patients censored	39 (51.3)	26 (47.3)	4 (20.0)	9 (32.1)	3 (60.0)	0 (0.0)	7 (46.7)	6 (28.6)	13 (35.1)	10 (23.3)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	1.28 (1.084 to 2.464)	1.45 (1.018 to 2.070)	0.99 (0.953 to 1.216)	1.07 (0.986 to 1.906)	2.60 (0.986 to NC)	0.95 (0.920 to 2.136)	2.00 (1.018 to 5.651)	1.12 (0.986 to 2.037)	1.48 (0.986 to 2.037)	1.18 (1.018 to 1.873)	
Median (95% CI)	6.74 (2.793 to NC)	5.72 (2.070 to NC)	1.91 (0.986 to 6.144)	2.35 (1.084 to 6.965)	NC (0.986 to NC)	2.14 (0.920 to 3.450)	11.47 (1.051 to 11.466)	2.83 (1.117 to 8.246)	3.75 (1.906 to 7.885)	2.86 (1.380 to 3.811)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (13.339 to NC)	NC (NC to NC)	7.20 (1.906 to NC)	NC (3.121 to NC)	NC (0.986 to NC)	3.45 (1.084 to 3.515)	11.47 (NC to NC)	8.51 (2.825 to NC)	NC (3.844 to NC)	8.25 (3.581 to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.7587		0.4961		0.0626		0.1865		0.4816	
Hazard ratio (95% CI) vs Pd	-	1.08 (0.66 to 1.76)		0.79 (0.41 to 1.55)		4.11 (0.83 to 20.38)		1.78 (0.75 to 4.24)		1.21 (0.71 to 2.04)	
P-value	-	0.7574		0.4971		0.0834		0.1923		0.4823	
Deterioration probability (95% CI)[b]											

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	11 (14.5)	12 (21.8)	1 (5.0)	6 (21.4)	1 (20.0)	3 (42.9)	3 (20.0)	0 (0.0)	10 (27.0)	10 (23.3)	0.4940
Number (%) of patients censored	65 (85.5)	43 (78.2)	19 (95.0)	22 (78.6)	4 (80.0)	4 (57.1)	12 (80.0)	21 (100.0)	27 (73.0)	33 (76.7)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (3.154 to NC)	13.17 (5.979 to NC)	NC (6.407 to NC)	NC (1.018 to NC)	NC (1.117 to NC)	4.73 (2.628 to NC)	NC (1.150 to NC)	NC (NC to NC)	11.30 (1.610 to 12.517)	13.40 (5.092 to NC)	
Median (95% CI)	NC (NC to NC)	NC (13.175 to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.117 to NC)	NC (2.628 to NC)	NC (7.852 to NC)	NC (NC to NC)	NC (11.302 to NC)	NC (13.405 to NC)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.117 to NC)	NC (6.998 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.3915		0.1400		0.5240		0.0408		0.3749	
Hazard ratio (95% CI) vs Pd	-	1.43 (0.63 to 3.24)		4.31 (0.52 to 35.84)		2.06 (0.21 to 19.83)				0.67 (0.28 to 1.63)	
P-value	-	0.3940		0.1762		0.5328		0.9972		0.3779	
Improvement probability (95% CI)[b]											

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	22 (28.9)	16 (29.1)	10 (50.0)	7 (25.0)	2 (40.0)	1 (14.3)	5 (33.3)	9 (42.9)	13 (35.1)	13 (30.2)	0.5077
Number (%) of patients censored	54 (71.1)	39 (70.9)	10 (50.0)	21 (75.0)	3 (60.0)	6 (85.7)	10 (66.7)	12 (57.1)	24 (64.9)	30 (69.8)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	5.55 (2.333 to NC)	5.85 (1.643 to NC)	1.02 (0.953 to 9.331)	10.68 (1.084 to NC)	9.72 (2.595 to NC)	NC (0.920 to NC)	7.56 (1.018 to NC)	6.97 (2.037 to 10.480)	2.53 (1.018 to NC)	8.61 (3.581 to NC)	
Median (95% CI)	NC (12.057 to NC)	NC (14.817 to NC)	9.43 (1.018 to NC)	NC (10.678 to NC)	9.72 (2.595 to NC)	NC (0.920 to NC)	NC (5.191 to NC)	13.67 (6.965 to NC)	NC (3.745 to NC)	NC (10.185 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.429 to NC)	NC (NC to NC)	NC (2.595 to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.667 to NC)	NC (NC to NC)	NC (NC to NC)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.8260		0.0860		0.4651		0.6941		0.2955	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.49 to 1.77)		0.44 (0.17 to 1.15)		0.42 (0.04 to 4.65)		1.25 (0.41 to 3.78)		0.66 (0.31 to 1.44)	
P-value	-	0.8269		0.0949		0.4788		0.6947		0.2988	
Deterioration probability (95% CI)[b]											
2 Months	0.860 (0.755 to 0.922)	0.834 (0.705 to 0.910)	0.737 (0.479 to 0.881)	0.893 (0.704 to 0.964)	1.000 (1.000 to 1.000)	0.857 (0.334 to 0.979)	0.933 (0.613 to 0.990)	1.000 (1.000 to 1.000)	0.805 (0.633 to 0.902)	0.929 (0.795 to 0.976)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (34.0)	30 (39.0)	20 (35.7)	38 (49.4)	0.4055
Number (%) of patients censored	64 (66.0)	47 (61.0)	36 (64.3)	39 (50.6)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.87 (1.051 to 2.891)	2.04 (1.216 to 4.008)	1.15 (0.986 to 9.331)	1.91 (1.051 to 2.234)	
Median (95% CI)	NC (NC to NC)	NC (5.979 to NC)	NC (9.331 to NC)	7.92 (2.595 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9129		0.2114	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.63 to 1.69)		1.41 (0.82 to 2.43)	
P-value	-	0.9128		0.2136	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (49.5)	47 (61.0)	39 (69.6)	56 (72.7)	0.5812
Number (%) of patients censored	49 (50.5)	30 (39.0)	17 (30.4)	21 (27.3)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.28 (1.084 to 2.333)	1.12 (1.018 to 1.643)	1.12 (1.018 to 1.938)	1.23 (1.018 to 1.906)	
Median (95% CI)	7.89 (2.793 to NC)	3.42 (1.971 to 7.556)	3.75 (1.938 to 5.651)	2.83 (1.906 to 5.585)	
75% quantile (95% CI)	NC (13.339 to NC)	NC (9.265 to NC)	11.47 (5.454 to NC)	8.25 (5.914 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2200		0.5653	
Hazard ratio (95% CI) vs Pd	-	1.29 (0.86 to 1.92)		1.13 (0.75 to 1.70)	
P-value	-	0.2212		0.5656	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (16.5)	18 (23.4)	10 (17.9)	13 (16.9)	0.4852
Number (%) of patients censored	81 (83.5)	59 (76.6)	46 (82.1)	64 (83.1)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (5.651 to NC)	13.17 (6.571 to NC)	11.70 (7.852 to NC)	13.86 (10.152 to NC)	
Median (95% CI)	NC (NC to NC)	NC (13.405 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4702		0.7614	
Hazard ratio (95% CI) vs Pd	-	1.28 (0.65 to 2.51)		0.88 (0.39 to 2.01)	
P-value	-	0.4713		0.7616	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_imppl_rreg_de_i_t_x.rtf (08APR2021 14:40)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (30.9)	24 (31.2)	22 (39.3)	22 (28.6)	0.3955
Number (%) of patients censored	67 (69.1)	53 (68.8)	34 (60.7)	55 (71.4)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	4.11 (2.333 to 12.057)	5.85 (1.971 to 14.817)	4.44 (1.347 to 8.345)	8.61 (4.862 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (7.556 to NC)	NC (13.667 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7163		0.1219	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.53 to 1.55)		0.63 (0.35 to 1.14)	
P-value	-	0.7175		0.1253	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_detpl_rreg_de_i_t_x.rtf (08APR2021 14:40)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (32.8)	60 (43.5)	8 (50.0)	8 (50.0)	0.7129
Number (%) of patients censored	92 (67.2)	78 (56.5)	8 (50.0)	8 (50.0)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.61 (1.051 to 5.092)	1.97 (1.314 to 2.595)	1.15 (0.953 to 2.793)	1.05 (0.986 to 2.628)	
Median (95% CI)	NC (NC to NC)	NC (4.797 to NC)	2.89 (0.986 to NC)	13.17 (1.018 to 13.175)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.891 to NC)	13.17 (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2743		0.9204	
Hazard ratio (95% CI) vs Pd	-	1.24 (0.84 to 1.83)		1.05 (0.39 to 2.81)	
P-value	-	0.2752		0.9204	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	78 (56.9)	94 (68.1)	9 (56.3)	9 (56.3)	0.8091
Number (%) of patients censored	59 (43.1)	44 (31.9)	7 (43.8)	7 (43.8)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.28 (1.051 to 1.938)	1.18 (1.084 to 1.643)	1.05 (0.986 to 2.793)	0.99 (0.296 to 2.136)	
Median (95% CI)	4.73 (2.858 to 9.331)	2.86 (2.037 to 3.811)	3.75 (1.018 to NC)	5.22 (0.986 to NC)	
75% quantile (95% CI)	NC (13.339 to NC)	13.86 (7.556 to NC)	NC (3.745 to NC)	9.26 (5.224 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1265		0.7935	
Hazard ratio (95% CI) vs Pd	-	1.26 (0.94 to 1.71)		1.13 (0.45 to 2.86)	
P-value	-	0.1281		0.7931	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (16.1)	26 (18.8)	4 (25.0)	5 (31.3)	0.9613
Number (%) of patients censored	115 (83.9)	112 (81.2)	12 (75.0)	11 (68.8)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (10.678 to NC)	13.86 (8.936 to NC)	2.79 (0.953 to NC)	7.00 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.281 to NC)	13.17 (2.628 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.175 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8259		0.8242	
Hazard ratio (95% CI) vs Pd	-	1.07 (0.60 to 1.88)		1.16 (0.31 to 4.34)	
P-value	-	0.8263		0.8244	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (32.1)	44 (31.9)	8 (50.0)	2 (12.5)	0.0582
Number (%) of patients censored	93 (67.9)	94 (68.1)	8 (50.0)	14 (87.5)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	4.86 (2.464 to 9.331)	7.43 (3.811 to 10.185)	2.53 (0.986 to 3.745)	14.82 (0.296 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	8.34 (1.347 to NC)	14.82 (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.745 to NC)	NC (14.817 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5707		0.0118	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.58 to 1.35)		0.11 (0.01 to 0.88)	
P-value	-	0.5700		0.0379	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (43.1)	25 (39.1)	16 (28.6)	25 (47.2)	13 (30.2)	16 (47.1)	0.1821
Number (%) of patients censored	29 (56.9)	39 (60.9)	40 (71.4)	28 (52.8)	30 (69.8)	18 (52.9)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	1.05 (0.986 to 2.793)	2.60 (1.906 to 4.797)	2.27 (1.150 to NC)	1.97 (1.216 to 2.825)	1.45 (0.986 to NC)	1.05 (0.986 to 1.906)	
Median (95% CI)	NC (1.873 to NC)	NC (5.979 to NC)	NC (NC to NC)	13.17 (2.825 to NC)	NC (5.092 to NC)	NC (1.117 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.175 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4986		0.1106		0.2406	
Hazard ratio (95% CI) vs Pd	-	0.82 (0.46 to 1.46)		1.66 (0.88 to 3.11)		1.55 (0.74 to 3.21)	
P-value	-	0.4993		0.1144		0.2443	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (56.9)	45 (70.3)	33 (58.9)	35 (66.0)	24 (55.8)	20 (58.8)	0.3640
Number (%) of patients censored	22 (43.1)	19 (29.7)	23 (41.1)	18 (34.0)	19 (44.2)	14 (41.2)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	1.87 (1.084 to 2.825)	1.08 (0.986 to 1.873)	1.02 (0.986 to 1.150)	1.12 (1.051 to 1.906)	1.94 (1.084 to 2.464)	1.38 (0.986 to 1.906)	
Median (95% CI)	6.74 (2.793 to NC)	2.83 (1.873 to 5.684)	3.75 (1.117 to 6.144)	3.42 (1.906 to 6.965)	3.75 (2.037 to 9.331)	3.71 (1.840 to 9.495)	
75% quantile (95% CI)	NC (NC to NC)	NC (5.914 to NC)	NC (6.144 to NC)	13.86 (5.717 to NC)	10.38 (7.195 to NC)	NC (6.932 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0675		0.9721		0.8380	
Hazard ratio (95% CI) vs Pd	-	1.54 (0.97 to 2.46)		1.01 (0.62 to 1.63)		1.06 (0.59 to 1.93)	
P-value	-	0.0696		0.9721		0.8375	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (25.5)	11 (17.2)	6 (10.7)	12 (22.6)	6 (14.0)	8 (23.5)	0.1545
Number (%) of patients censored	38 (74.5)	53 (82.8)	50 (89.3)	41 (77.4)	37 (86.0)	26 (76.5)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	11.70 (1.150 to NC)	13.86 (8.936 to NC)	NC (10.678 to NC)	13.17 (4.731 to NC)	NC (2.793 to NC)	13.40 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.175 to NC)	NC (11.302 to NC)	NC (13.405 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2696		0.1466		0.3989	
Hazard ratio (95% CI) vs Pd	-	0.64 (0.29 to 1.43)		2.04 (0.76 to 5.43)		1.57 (0.54 to 4.54)	
P-value	-	0.2736		0.1552		0.4029	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (33.3)	20 (31.3)	21 (37.5)	14 (26.4)	13 (30.2)	10 (29.4)	0.4762
Number (%) of patients censored	34 (66.7)	44 (68.8)	35 (62.5)	39 (73.6)	30 (69.8)	24 (70.6)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	6.54 (2.793 to NC)	7.43 (2.628 to NC)	1.15 (1.018 to 9.429)	8.71 (2.924 to NC)	3.84 (1.281 to 12.057)	8.61 (1.840 to 14.817)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.491 to NC)	NC (NC to NC)	NC (4.665 to NC)	14.82 (13.667 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9246		0.1196		0.5558	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.51 to 1.85)		0.59 (0.30 to 1.16)		0.78 (0.34 to 1.79)	
P-value	-	0.9245		0.1240		0.5568	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (45.2)	16 (41.0)	32 (32.7)	45 (45.5)	7 (29.2)	7 (43.8)	0.3160
Number (%) of patients censored	17 (54.8)	23 (59.0)	66 (67.3)	54 (54.5)	17 (70.8)	9 (56.3)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	1.02 (0.986 to 2.793)	2.92 (1.084 to 4.797)	1.91 (1.150 to 9.331)	1.87 (1.084 to 2.267)	1.45 (0.953 to NC)	1.12 (0.986 to 2.760)	
Median (95% CI)	NC (1.084 to NC)	NC (3.745 to NC)	NC (NC to NC)	13.17 (3.943 to NC)	NC (1.446 to NC)	NC (1.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.760 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4619		0.1424		0.5336	
Hazard ratio (95% CI) vs Pd	-	0.76 (0.37 to 1.57)		1.40 (0.89 to 2.21)		1.39 (0.49 to 3.97)	
P-value	-	0.4632		0.1443		0.5355	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (54.8)	25 (64.1)	61 (62.2)	70 (70.7)	9 (37.5)	8 (50.0)	0.9276
Number (%) of patients censored	14 (45.2)	14 (35.9)	37 (37.8)	29 (29.3)	15 (62.5)	8 (50.0)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	1.87 (1.084 to 3.745)	1.38 (0.986 to 2.037)	1.05 (1.018 to 1.741)	1.08 (1.018 to 1.380)	1.94 (1.084 to 2.825)	1.84 (0.986 to 9.265)	
Median (95% CI)	7.89 (2.595 to NC)	3.12 (1.873 to NC)	4.01 (2.464 to 7.195)	2.79 (1.906 to 3.713)	NC (1.938 to NC)	9.26 (1.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (8.246 to NC)	13.34 (10.382 to NC)	13.86 (5.585 to NC)	NC (NC to NC)	NC (6.932 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3585		0.2515		0.8637	
Hazard ratio (95% CI) vs Pd	-	1.33 (0.72 to 2.47)		1.22 (0.87 to 1.73)		1.09 (0.41 to 2.89)	
P-value	-	0.3601		0.2524		0.8632	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (32.3)	8 (20.5)	11 (11.2)	21 (21.2)	5 (20.8)	2 (12.5)	0.0807
Number (%) of patients censored	21 (67.7)	31 (79.5)	87 (88.8)	78 (78.8)	19 (79.2)	14 (87.5)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	7.85 (1.051 to NC)	13.86 (6.998 to NC)	NC (11.302 to NC)	13.17 (6.637 to NC)	3.75 (0.953 to NC)	NC (1.018 to NC)	
Median (95% CI)	NC (11.696 to NC)	NC (13.864 to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.745 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2252		0.0997		0.4549	
Hazard ratio (95% CI) vs Pd	-	0.57 (0.22 to 1.44)		1.83 (0.88 to 3.79)		0.54 (0.10 to 2.79)	
P-value	-	0.2314		0.1049		0.4622	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (32.3)	10 (25.6)	35 (35.7)	29 (29.3)	7 (29.2)	7 (43.8)	0.5585
Number (%) of patients censored	21 (67.7)	29 (74.4)	63 (64.3)	70 (70.7)	17 (70.8)	9 (56.3)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	6.74 (2.595 to NC)	10.48 (1.643 to NC)	3.75 (1.051 to 7.491)	8.71 (4.862 to 13.667)	3.84 (1.117 to 12.057)	1.97 (0.986 to 8.608)	
Median (95% CI)	NC (8.345 to NC)	NC (NC to NC)	NC (9.725 to NC)	NC (13.667 to NC)	12.06 (3.844 to NC)	8.61 (1.840 to 14.817)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.057 to NC)	14.82 (8.608 to 14.817)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6456		0.1723		0.5573	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (43.5)	4 (28.6)	31 (32.6)	58 (49.2)	0.1355
Number (%) of patients censored	13 (56.5)	10 (71.4)	64 (67.4)	60 (50.8)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.28 (0.953 to 2.891)	1.31 (1.018 to NC)	1.84 (1.018 to 9.331)	1.91 (1.084 to 2.267)	
Median (95% CI)	5.78 (1.281 to NC)	NC (1.150 to NC)	NC (NC to NC)	13.17 (3.745 to NC)	
75% quantile (95% CI)	NC (5.782 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3346		0.0854	
Hazard ratio (95% CI) vs Pd	-	0.57 (0.18 to 1.82)		1.46 (0.95 to 2.26)	
P-value	-	0.3412		0.0873	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (47.8)	8 (57.1)	55 (57.9)	87 (73.7)	0.9956
Number (%) of patients censored	12 (52.2)	6 (42.9)	40 (42.1)	31 (26.3)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.15 (0.953 to 2.825)	0.99 (0.296 to 2.070)	1.28 (1.051 to 2.037)	1.12 (1.051 to 1.478)	
Median (95% CI)	4.01 (1.150 to NC)	2.07 (0.953 to NC)	6.14 (3.088 to 10.382)	2.79 (1.906 to 3.515)	
75% quantile (95% CI)	NC (4.008 to NC)	5.91 (2.070 to NC)	NC (11.466 to NC)	9.26 (5.717 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4874		0.0175	
Hazard ratio (95% CI) vs Pd	-	1.38 (0.55 to 3.44)		1.50 (1.07 to 2.11)	
P-value	-	0.4892		0.0183	
Hazard ratio inverted (95% CI) vs IPd		-		0.66 (0.47 to 0.93)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (26.1)	1 (7.1)	12 (12.6)	28 (23.7)	0.0916
Number (%) of patients censored	17 (73.9)	13 (92.9)	83 (87.4)	90 (76.3)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	3.75 (0.953 to NC)	NC (8.476 to NC)	NC (11.302 to NC)	13.17 (6.637 to NC)	
Median (95% CI)	NC (3.745 to NC)	NC (8.476 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1685		0.0963	
Hazard ratio (95% CI) vs Pd	-	0.25 (0.03 to 2.10)		1.76 (0.90 to 3.46)	
P-value	-	0.2024		0.1009	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (30.4)	5 (35.7)	33 (34.7)	40 (33.9)	0.4217
Number (%) of patients censored	16 (69.6)	9 (64.3)	62 (65.3)	78 (66.1)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	3.75 (0.953 to NC)	1.05 (0.296 to NC)	3.84 (1.610 to 8.345)	7.43 (4.731 to 10.185)	
Median (95% CI)	12.06 (3.745 to NC)	NC (0.986 to NC)	NC (NC to NC)	NC (13.667 to NC)	
75% quantile (95% CI)	NC (12.057 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5405		0.4805	
Hazard ratio (95% CI) vs Pd	-	1.43 (0.45 to 4.54)		0.85 (0.53 to 1.34)	
P-value	-	0.5426		0.4810	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (36.1)	7 (29.2)	26 (33.3)	53 (51.5)	0.1713
Number (%) of patients censored	23 (63.9)	17 (70.8)	52 (66.7)	50 (48.5)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.28 (0.986 to 5.782)	2.27 (1.018 to NC)	1.12 (1.018 to 9.331)	1.87 (1.051 to 2.234)	
Median (95% CI)	NC (1.610 to NC)	NC (2.267 to NC)	NC (NC to NC)	6.08 (2.990 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4598		0.0977	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.28 to 1.78)		1.48 (0.93 to 2.37)	
P-value	-	0.4621		0.0999	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (52.8)	17 (70.8)	44 (56.4)	76 (73.8)	0.7232
Number (%) of patients censored	17 (47.2)	7 (29.2)	34 (43.6)	27 (26.2)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.15 (1.051 to 2.793)	1.02 (0.296 to 1.281)	1.61 (1.051 to 2.694)	1.12 (1.051 to 1.873)	
Median (95% CI)	4.44 (1.347 to NC)	1.97 (1.018 to 5.717)	7.89 (3.417 to 11.466)	2.79 (1.906 to 3.515)	
75% quantile (95% CI)	NC (4.731 to NC)	5.91 (2.070 to NC)	NC (13.339 to NC)	9.49 (5.585 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1067		0.0156	
Hazard ratio (95% CI) vs Pd	-	1.71 (0.88 to 3.29)		1.58 (1.09 to 2.30)	
P-value	-	0.1108		0.0165	
Hazard ratio inverted (95% CI) vs IPd		-		0.63 (0.44 to 0.92)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (22.2)	3 (12.5)	10 (12.8)	25 (24.3)	0.1082
Number (%) of patients censored	28 (77.8)	21 (87.5)	68 (87.2)	78 (75.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	9.56 (1.281 to NC)	NC (6.637 to NC)	NC (11.302 to NC)	12.71 (6.571 to NC)	
Median (95% CI)	NC (9.561 to NC)	NC (8.476 to NC)	NC (NC to NC)	NC (13.864 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2687		0.1113	
Hazard ratio (95% CI) vs Pd	-	0.48 (0.13 to 1.81)		1.80 (0.86 to 3.75)	
P-value	-	0.2793		0.1167	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (33.3)	10 (41.7)	26 (33.3)	34 (33.0)	0.4254
Number (%) of patients censored	24 (66.7)	14 (58.3)	52 (66.7)	69 (67.0)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	3.75 (1.051 to 12.057)	1.97 (0.296 to 6.965)	4.86 (2.004 to 9.725)	8.11 (4.731 to 10.678)	
Median (95% CI)	NC (3.844 to NC)	10.02 (3.778 to NC)	NC (NC to NC)	NC (13.667 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.021 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5180		0.5707	
Hazard ratio (95% CI) vs Pd	-	1.32 (0.57 to 3.07)		0.86 (0.52 to 1.44)	
P-value	-	0.5194		0.5710	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (36.7)	34 (41.0)	20 (31.7)	34 (47.9)	0.6164
Number (%) of patients censored	57 (63.3)	49 (59.0)	43 (68.3)	37 (52.1)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.87 (1.051 to 3.154)	1.91 (1.084 to 2.924)	1.28 (1.018 to NC)	1.97 (1.117 to 2.628)	
Median (95% CI)	NC (9.331 to NC)	NC (4.008 to NC)	NC (NC to NC)	13.17 (2.990 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7034		0.3228	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.68 to 1.77)		1.32 (0.76 to 2.30)	
P-value	-	0.7033		0.3243	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	47 (52.2)	51 (61.4)	40 (63.5)	52 (73.2)	0.7559
Number (%) of patients censored	43 (47.8)	32 (38.6)	23 (36.5)	19 (26.8)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.61 (1.051 to 2.004)	1.28 (1.051 to 2.037)	1.15 (1.018 to 2.037)	1.08 (1.018 to 1.478)	
Median (95% CI)	9.26 (2.825 to NC)	3.12 (2.431 to 8.509)	3.42 (2.037 to 5.651)	2.04 (1.873 to 3.745)	
75% quantile (95% CI)	NC (13.339 to NC)	NC (9.265 to NC)	10.38 (5.651 to NC)	7.00 (5.224 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2343		0.4207	
Hazard ratio (95% CI) vs Pd	-	1.27 (0.85 to 1.89)		1.18 (0.78 to 1.79)	
P-value	-	0.2354		0.4212	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (18.9)	11 (13.3)	9 (14.3)	20 (28.2)	0.1077
Number (%) of patients censored	73 (81.1)	72 (86.7)	54 (85.7)	51 (71.8)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (6.407 to NC)	NC (12.715 to NC)	12.52 (9.561 to NC)	8.94 (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.517 to NC)	NC (13.864 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2902		0.2241	
Hazard ratio (95% CI) vs Pd	-	0.67 (0.31 to 1.42)		1.63 (0.74 to 3.59)	
P-value	-	0.2935		0.2286	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (33.3)	26 (31.3)	22 (34.9)	20 (28.2)	0.4403
Number (%) of patients censored	60 (66.7)	57 (68.7)	41 (65.1)	51 (71.8)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	4.44 (2.004 to 9.429)	7.43 (2.793 to 14.817)	3.84 (1.150 to 7.556)	9.49 (4.862 to NC)	
Median (95% CI)	NC (12.057 to NC)	NC (14.817 to NC)	NC (7.491 to NC)	NC (13.667 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6523		0.1540	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.52 to 1.50)		0.65 (0.35 to 1.18)	
P-value	-	0.6531		0.1573	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	2 (100.0)	51 (33.8)	66 (43.4)	0.6073
Number (%) of patients censored	0 (0.0)	0 (0.0)	100 (66.2)	86 (56.6)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.08 (1.084 to 1.938)	1.08 (1.084 to 5.947)	1.45 (1.051 to 2.891)	1.97 (1.216 to 2.333)	
Median (95% CI)	1.51 (1.084 to 1.938)	3.52 (1.084 to 5.947)	NC (NC to NC)	NC (4.797 to NC)	
75% quantile (95% CI)	1.94 (1.084 to 1.938)	5.95 (1.084 to 5.947)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5637		0.2930	
Hazard ratio (95% CI) vs Pd	-	0.50 (0.05 to 5.51)		1.22 (0.84 to 1.75)	
P-value	-	0.5715		0.2938	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (100.0)	87 (57.6)	101 (66.4)	0.9762
Number (%) of patients censored	2 (100.0)	0 (0.0)	64 (42.4)	51 (33.6)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (NC to NC)	1.12 (1.117 to 2.037)	1.22 (1.051 to 1.906)	1.15 (1.051 to 1.643)	
Median (95% CI)	NC (NC to NC)	1.58 (1.117 to 2.037)	4.44 (2.825 to 7.885)	3.09 (2.070 to 4.797)	
75% quantile (95% CI)	NC (NC to NC)	2.04 (1.117 to 2.037)	NC (13.339 to NC)	13.86 (8.246 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.1966	
Hazard ratio (95% CI) vs Pd	-			1.21 (0.91 to 1.61)	
P-value	-	0.9991		0.1977	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	0 (0.0)	24 (15.9)	31 (20.4)	0.9807
Number (%) of patients censored	0 (0.0)	2 (100.0)	127 (84.1)	121 (79.6)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.08 (1.084 to 5.651)	NC (NC to NC)	NC (11.302 to NC)	13.40 (8.476 to NC)	
Median (95% CI)	3.37 (1.084 to 5.651)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	5.65 (1.084 to 5.651)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.5576	
Hazard ratio (95% CI) vs Pd	-			1.17 (0.69 to 2.00)	
P-value	-	0.9991		0.5580	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (100.0)	52 (34.4)	44 (28.9)	0.9824
Number (%) of patients censored	2 (100.0)	0 (0.0)	99 (65.6)	108 (71.1)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (NC to NC)	2.04 (2.037 to 8.706)	4.11 (2.464 to 6.735)	8.61 (4.862 to 13.667)	
Median (95% CI)	NC (NC to NC)	5.37 (2.037 to 8.706)	NC (NC to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	8.71 (2.037 to 8.706)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.1262	
Hazard ratio (95% CI) vs Pd	-			0.73 (0.49 to 1.09)	
P-value	-	0.9991		0.1278	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (36.6)	49 (47.1)	11 (26.8)	12 (36.4)	0.6529
Number (%) of patients censored	64 (63.4)	55 (52.9)	30 (73.2)	21 (63.6)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.28 (1.018 to 2.891)	1.91 (1.084 to 2.234)	1.91 (1.117 to NC)	3.94 (1.084 to NC)	
Median (95% CI)	NC (9.331 to NC)	13.17 (2.924 to NC)	NC (NC to NC)	NC (3.975 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3640		0.5534	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.79 to 1.87)		1.28 (0.56 to 2.90)	
P-value	-	0.3648		0.5544	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_impl_semm_de_i_t_x.rtf (08APR2021 14:40)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	64 (63.4)	69 (66.3)	17 (41.5)	23 (69.7)	0.1912
Number (%) of patients censored	37 (36.6)	35 (33.7)	24 (58.5)	10 (30.3)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.12 (1.018 to 1.938)	1.15 (1.018 to 1.873)	1.74 (1.018 to 3.745)	1.12 (0.986 to 1.380)	
Median (95% CI)	3.75 (2.595 to 6.144)	3.09 (2.070 to 5.684)	NC (2.037 to NC)	2.04 (1.248 to 6.735)	
75% quantile (95% CI)	13.34 (10.185 to NC)	13.86 (8.246 to NC)	NC (NC to NC)	NC (3.121 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7809		0.0337	
Hazard ratio (95% CI) vs Pd	-	1.05 (0.75 to 1.48)		1.95 (1.04 to 3.66)	
P-value	-	0.7810		0.0371	
Hazard ratio inverted (95% CI) vs IPd		-		0.51 (0.27 to 0.96)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (17.8)	20 (19.2)	5 (12.2)	6 (18.2)	0.8802
Number (%) of patients censored	83 (82.2)	84 (80.8)	36 (87.8)	27 (81.8)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	12.52 (9.561 to NC)	13.17 (8.936 to NC)	NC (1.150 to NC)	NC (1.216 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8637		0.6133	
Hazard ratio (95% CI) vs Pd	-	0.95 (0.50 to 1.79)		1.36 (0.41 to 4.45)	
P-value	-	0.8635		0.6146	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (36.6)	28 (26.9)	12 (29.3)	12 (36.4)	0.4223
Number (%) of patients censored	64 (63.4)	76 (73.1)	29 (70.7)	21 (63.6)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	3.75 (1.347 to 7.491)	10.02 (4.731 to NC)	5.55 (1.610 to NC)	6.77 (1.084 to 14.817)	
Median (95% CI)	NC (9.725 to NC)	NC (NC to NC)	NC (9.331 to NC)	14.82 (8.115 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0720		0.8672	
Hazard ratio (95% CI) vs Pd	-	0.64 (0.39 to 1.04)		1.07 (0.48 to 2.39)	
P-value	-	0.0744		0.8672	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (36.0)	47 (46.1)	16 (30.8)	20 (39.2)	0.9314
Number (%) of patients censored	64 (64.0)	55 (53.9)	36 (69.2)	31 (60.8)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.35 (1.018 to 2.891)	1.91 (1.084 to 2.234)	1.91 (1.018 to NC)	2.76 (1.117 to 5.979)	
Median (95% CI)	NC (9.331 to NC)	13.17 (2.924 to NC)	NC (NC to NC)	NC (5.979 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3730		0.6444	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.79 to 1.88)		1.17 (0.60 to 2.25)	
P-value	-	0.3738		0.6447	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_impl_dghc_de_i_t_x.rtf (08APR2021 14:40)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	63 (63.0)	68 (66.7)	23 (44.2)	35 (68.6)	0.0752
Number (%) of patients censored	37 (37.0)	34 (33.3)	29 (55.8)	16 (31.4)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.12 (1.018 to 1.938)	1.22 (1.018 to 1.873)	1.74 (1.051 to 3.088)	1.08 (1.018 to 1.643)	
Median (95% CI)	3.75 (2.464 to 6.144)	3.09 (2.070 to 5.684)	9.33 (3.088 to NC)	2.79 (1.380 to 4.797)	
75% quantile (95% CI)	13.34 (10.185 to NC)	13.86 (6.998 to NC)	NC (NC to NC)	NC (4.797 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7444		0.0224	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.75 to 1.49)		1.83 (1.08 to 3.11)	
P-value	-	0.7446		0.0245	
Hazard ratio inverted (95% CI) vs IPd		-		0.55 (0.32 to 0.92)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (17.0)	19 (18.6)	8 (15.4)	11 (21.6)	0.6357
Number (%) of patients censored	83 (83.0)	83 (81.4)	44 (84.6)	40 (78.4)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	12.52 (10.678 to NC)	13.17 (8.936 to NC)	NC (1.150 to NC)	13.40 (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.405 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9177		0.5911	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.50 to 1.86)		1.28 (0.52 to 3.19)	
P-value	-	0.9176		0.5921	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (37.0)	27 (26.5)	15 (28.8)	19 (37.3)	0.1431
Number (%) of patients censored	63 (63.0)	75 (73.5)	37 (71.2)	32 (62.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	3.75 (1.347 to 7.491)	10.02 (3.811 to NC)	4.67 (1.610 to NC)	6.97 (1.971 to 10.678)	
Median (95% CI)	NC (9.429 to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.495 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0578		0.7328	
Hazard ratio (95% CI) vs Pd	-	0.62 (0.38 to 1.02)		1.13 (0.57 to 2.22)	
P-value	-	0.0601		0.7329	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (20.0)	6 (42.9)	51 (35.7)	62 (44.3)	0.6564
Number (%) of patients censored	8 (80.0)	8 (57.1)	92 (64.3)	78 (55.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (0.953 to NC)	1.91 (1.084 to NC)	1.45 (1.084 to 2.793)	1.97 (1.183 to 2.267)	
Median (95% CI)	NC (0.953 to NC)	NC (1.906 to NC)	NC (NC to NC)	13.17 (3.975 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5018		0.3615	
Hazard ratio (95% CI) vs Pd	-	1.72 (0.35 to 8.53)		1.19 (0.82 to 1.72)	
P-value	-	0.5070		0.3621	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (60.0)	12 (85.7)	81 (56.6)	91 (65.0)	0.6951
Number (%) of patients censored	4 (40.0)	2 (14.3)	62 (43.4)	49 (35.0)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.28 (0.920 to 2.333)	1.08 (0.986 to 1.840)	1.22 (1.051 to 1.938)	1.18 (1.051 to 1.873)	
Median (95% CI)	2.33 (0.920 to NC)	3.76 (0.986 to 6.735)	4.73 (3.088 to 9.331)	2.89 (2.037 to 3.811)	
75% quantile (95% CI)	3.75 (1.741 to NC)	6.83 (1.840 to NC)	NC (13.339 to NC)	NC (8.509 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8867		0.1522	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.34 to 2.56)		1.24 (0.92 to 1.68)	
P-value	-	0.8867		0.1524	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (20.0)	1 (7.1)	24 (16.8)	30 (21.4)	0.1535
Number (%) of patients censored	8 (80.0)	13 (92.9)	119 (83.2)	110 (78.6)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (0.953 to NC)	NC (5.092 to NC)	NC (10.678 to NC)	13.17 (8.476 to NC)	
Median (95% CI)	NC (0.953 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2196		0.5133	
Hazard ratio (95% CI) vs Pd	-	0.25 (0.02 to 2.77)		1.20 (0.70 to 2.05)	
P-value	-	0.2555		0.5138	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_imppl_mri_de_i_t_x.rtf (08APR2021 14:40)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (50.0)	6 (42.9)	47 (32.9)	40 (28.6)	0.2301
Number (%) of patients censored	5 (50.0)	8 (57.1)	96 (67.1)	100 (71.4)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.28 (0.920 to 3.745)	8.61 (1.084 to 9.495)	4.86 (2.530 to 8.345)	8.11 (4.731 to 13.667)	
Median (95% CI)	3.75 (0.920 to NC)	9.49 (7.425 to NC)	NC (NC to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (2.333 to NC)	NC (9.495 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0260		0.2747	
Hazard ratio (95% CI) vs Pd	-	0.19 (0.04 to 0.97)		0.79 (0.52 to 1.21)	
P-value	-	0.0461		0.2759	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_detpl_mri_de_i_t_x.rtf (08APR2021 14:40)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (39.6)	39 (44.8)	14 (28.6)	26 (47.3)	0.2431
Number (%) of patients censored	58 (60.4)	48 (55.2)	35 (71.4)	29 (52.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.25 (1.018 to 2.004)	2.23 (1.216 to 2.924)	1.91 (1.018 to NC)	1.31 (1.051 to 2.136)	
Median (95% CI)	NC (5.782 to NC)	13.17 (3.943 to NC)	NC (NC to NC)	NC (2.136 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9184		0.1510	
Hazard ratio (95% CI) vs Pd	-	1.02 (0.65 to 1.60)		1.60 (0.84 to 3.07)	
P-value	-	0.9184		0.1548	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_impl_crcl_de_i_t_x.rtf (08APR2021 14:40)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (52.1)	60 (69.0)	33 (67.3)	37 (67.3)	0.0829
Number (%) of patients censored	46 (47.9)	27 (31.0)	16 (32.7)	18 (32.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.28 (1.018 to 2.825)	1.12 (1.018 to 1.873)	1.35 (1.018 to 2.004)	1.28 (1.018 to 1.906)	
Median (95% CI)	9.33 (3.745 to NC)	2.86 (1.906 to 5.684)	2.79 (1.906 to 5.454)	3.42 (1.906 to 6.932)	
75% quantile (95% CI)	NC (13.339 to NC)	13.86 (6.965 to NC)	7.89 (4.698 to NC)	NC (5.585 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0342		0.6406	
Hazard ratio (95% CI) vs Pd	-	1.50 (1.03 to 2.18)		0.89 (0.56 to 1.43)	
P-value	-	0.0354		0.6408	
Hazard ratio inverted (95% CI) vs IPd		-		1.12 (0.70 to 1.79)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_detl_crcl_de_i_t_x.rtf (08APR2021 14:39)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (20.8)	15 (17.2)	5 (10.2)	14 (25.5)	0.0533
Number (%) of patients censored	76 (79.2)	72 (82.8)	44 (89.8)	41 (74.5)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	11.70 (5.651 to NC)	13.17 (8.936 to NC)	NC (10.678 to NC)	13.40 (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.405 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3322		0.0870	
Hazard ratio (95% CI) vs Pd	-	0.72 (0.37 to 1.40)		2.38 (0.86 to 6.61)	
P-value	-	0.3344		0.0970	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_imppl_crcl_de_i_t_x.rtf (08APR2021 14:40)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (31.3)	28 (32.2)	20 (40.8)	15 (27.3)	0.1372
Number (%) of patients censored	66 (68.8)	59 (67.8)	29 (59.2)	40 (72.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	5.55 (2.333 to 12.057)	6.97 (3.581 to 10.480)	2.79 (1.347 to 6.538)	10.68 (3.778 to 14.817)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.435 to NC)	14.82 (13.667 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8953		0.0254	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.58 to 1.62)		0.47 (0.23 to 0.92)	
P-value	-	0.8954		0.0290	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	2 (100.0)	52 (34.4)	66 (43.4)	0.6773
Number (%) of patients censored	1 (50.0)	0 (0.0)	99 (65.6)	86 (56.6)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	1.91 (1.906 to 3.975)	1.61 (1.051 to 2.793)	1.97 (1.216 to 2.333)	
Median (95% CI)	NC (1.281 to NC)	2.94 (1.906 to 3.975)	NC (NC to NC)	NC (5.947 to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	3.98 (1.906 to 3.975)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6949		0.3509	
Hazard ratio (95% CI) vs Pd	-	1.62 (0.14 to 18.31)		1.19 (0.83 to 1.71)	
P-value	-	0.6975		0.3515	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	86 (57.0)	102 (67.1)	0.8910
Number (%) of patients censored	1 (50.0)	1 (50.0)	65 (43.0)	50 (32.9)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	2.10 (2.103 to NC)	0.99 (0.986 to NC)	1.22 (1.051 to 1.906)	1.15 (1.051 to 1.643)	
Median (95% CI)	NC (2.103 to NC)	NC (0.986 to NC)	4.70 (2.858 to 9.265)	2.89 (2.037 to 4.797)	
75% quantile (95% CI)	NC (2.103 to NC)	NC (0.986 to NC)	NC (13.339 to NC)	13.86 (8.246 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.1244	
Hazard ratio (95% CI) vs Pd	-	1.41 (0.08 to 23.57)		1.25 (0.94 to 1.67)	
P-value	-	0.8092		0.1256	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_detl_prmab_de_i_t_x.rtf (08APR2021 14:39)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	25 (16.6)	30 (19.7)	0.6175
Number (%) of patients censored	1 (50.0)	1 (50.0)	126 (83.4)	122 (80.3)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	5.09 (5.092 to NC)	NC (10.678 to NC)	13.40 (8.936 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.7546	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		1.09 (0.64 to 1.85)	
P-value	-	0.8092		0.7553	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	52 (34.4)	46 (30.3)	0.9998
Number (%) of patients censored	2 (100.0)	2 (100.0)	99 (65.6)	106 (69.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	4.11 (2.464 to 6.735)	8.11 (4.862 to 10.678)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.2057	
Hazard ratio (95% CI) vs Pd	-			0.77 (0.52 to 1.15)	
P-value	-			0.2069	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (33.9)	55 (46.6)	14 (36.8)	13 (36.1)	0.5156
Number (%) of patients censored	76 (66.1)	63 (53.4)	24 (63.2)	23 (63.9)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.61 (1.018 to 2.891)	1.91 (1.216 to 2.267)	1.28 (1.018 to 9.331)	1.87 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	13.17 (3.975 to NC)	NC (5.191 to NC)	NC (2.990 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2355		0.8863	
Hazard ratio (95% CI) vs Pd	-	1.28 (0.85 to 1.93)		0.95 (0.44 to 2.01)	
P-value	-	0.2367		0.8864	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	62 (53.9)	78 (66.1)	25 (65.8)	25 (69.4)	0.4556
Number (%) of patients censored	53 (46.1)	40 (33.9)	13 (34.2)	11 (30.6)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.35 (1.084 to 2.333)	1.08 (1.018 to 1.446)	1.12 (0.986 to 1.938)	1.43 (1.084 to 1.971)	
Median (95% CI)	5.45 (3.088 to 10.185)	3.12 (1.971 to 5.585)	2.86 (1.610 to 11.466)	2.14 (1.873 to 5.717)	
75% quantile (95% CI)	NC (NC to NC)	13.86 (6.998 to NC)	13.34 (4.731 to NC)	NC (3.121 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0948		0.8684	
Hazard ratio (95% CI) vs Pd	-	1.33 (0.95 to 1.85)		1.05 (0.60 to 1.83)	
P-value	-	0.0959		0.8684	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (18.3)	25 (21.2)	5 (13.2)	6 (16.7)	0.5880
Number (%) of patients censored	94 (81.7)	93 (78.8)	33 (86.8)	30 (83.3)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	12.52 (9.561 to NC)	13.17 (8.476 to NC)	NC (7.852 to NC)	NC (3.943 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9516		0.6028	
Hazard ratio (95% CI) vs Pd	-	0.98 (0.55 to 1.76)		1.37 (0.42 to 4.50)	
P-value	-	0.9516		0.6043	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_imppl_refr4_de_i_t_x.rtf (08APR2021 14:40)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (32.2)	32 (27.1)	15 (39.5)	14 (38.9)	0.3994
Number (%) of patients censored	78 (67.8)	86 (72.9)	23 (60.5)	22 (61.1)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	3.75 (1.873 to 7.556)	8.71 (5.125 to NC)	4.86 (1.610 to 9.725)	3.09 (1.084 to 10.185)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.538 to NC)	14.82 (8.115 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1529		0.9523	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.44 to 1.14)		1.02 (0.49 to 2.12)	
P-value	-	0.1549		0.9522	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (34.7)	63 (42.9)	3 (33.3)	5 (71.4)	0.3048
Number (%) of patients censored	94 (65.3)	84 (57.1)	6 (66.7)	2 (28.6)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.61 (1.084 to 2.793)	1.97 (1.216 to 2.595)	1.25 (0.986 to NC)	1.12 (1.018 to 1.971)	
Median (95% CI)	NC (NC to NC)	NC (5.947 to NC)	NC (0.986 to NC)	1.97 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.971 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4533		0.2805	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.80 to 1.67)		2.16 (0.51 to 9.11)	
P-value	-	0.4537		0.2922	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	82 (56.9)	99 (67.3)	5 (55.6)	4 (57.1)	0.9244
Number (%) of patients censored	62 (43.1)	48 (32.7)	4 (44.4)	3 (42.9)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.22 (1.051 to 1.906)	1.15 (1.051 to 1.840)	2.83 (0.986 to 6.144)	0.99 (0.986 to 3.088)	
Median (95% CI)	4.44 (2.825 to 9.265)	2.86 (2.037 to 4.797)	6.14 (0.986 to NC)	3.09 (0.986 to NC)	
75% quantile (95% CI)	NC (13.339 to NC)	13.86 (7.556 to NC)	NC (3.088 to NC)	NC (1.446 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1498		0.8416	
Hazard ratio (95% CI) vs Pd	-	1.24 (0.92 to 1.66)		1.14 (0.31 to 4.27)	
P-value	-	0.1505		0.8417	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (16.7)	29 (19.7)	2 (22.2)	2 (28.6)	0.5340
Number (%) of patients censored	120 (83.3)	118 (80.3)	7 (77.8)	5 (71.4)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (9.561 to NC)	13.40 (8.936 to NC)	11.70 (10.678 to NC)	1.97 (1.117 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.678 to NC)	NC (1.117 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.696 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8859		0.2467	
Hazard ratio (95% CI) vs Pd	-	1.04 (0.61 to 1.79)		3.89 (0.33 to 45.38)	
P-value	-	0.8861		0.2782	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (34.7)	42 (28.6)	2 (22.2)	4 (57.1)	0.0753
Number (%) of patients censored	94 (65.3)	105 (71.4)	7 (77.8)	3 (42.9)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	3.84 (2.333 to 6.538)	8.61 (4.862 to 13.667)	NC (0.986 to NC)	3.09 (0.986 to 10.480)	
Median (95% CI)	NC (12.057 to NC)	NC (14.817 to NC)	NC (0.986 to NC)	9.03 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	10.48 (9.035 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0893		0.0814	
Hazard ratio (95% CI) vs Pd	-	0.70 (0.46 to 1.06)		4.21 (0.74 to 23.93)	
P-value	-	0.0910		0.1051	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (35.2)	39 (41.9)	22 (33.8)	29 (47.5)	0.8152
Number (%) of patients censored	57 (64.8)	54 (58.1)	43 (66.2)	32 (52.5)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.35 (1.018 to 5.191)	2.14 (1.183 to 2.924)	1.87 (1.018 to 5.092)	1.91 (1.051 to 2.595)	
Median (95% CI)	NC (NC to NC)	NC (3.943 to NC)	NC (5.092 to NC)	13.17 (2.628 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5355		0.4141	
Hazard ratio (95% CI) vs Pd	-	1.16 (0.72 to 1.86)		1.26 (0.72 to 2.19)	
P-value	-	0.5359		0.4151	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	54 (61.4)	59 (63.4)	33 (50.8)	44 (72.1)	0.1403
Number (%) of patients censored	34 (38.6)	34 (36.6)	32 (49.2)	17 (27.9)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.28 (1.051 to 1.938)	1.64 (1.117 to 1.971)	1.22 (1.018 to 2.825)	1.02 (0.986 to 1.084)	
Median (95% CI)	4.44 (2.333 to 7.885)	3.12 (2.070 to 6.932)	5.65 (2.825 to NC)	2.79 (1.117 to 3.811)	
75% quantile (95% CI)	13.34 (10.382 to NC)	NC (8.246 to NC)	NC (NC to NC)	13.86 (3.811 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7648		0.0479	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.73 to 1.53)		1.57 (1.00 to 2.48)	
P-value	-	0.7650		0.0498	
Hazard ratio inverted (95% CI) vs IPd		-		0.64 (0.40 to 1.00)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (19.3)	16 (17.2)	9 (13.8)	15 (24.6)	0.2991
Number (%) of patients censored	71 (80.7)	77 (82.8)	56 (86.2)	46 (75.4)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	12.52 (6.407 to NC)	13.86 (8.936 to NC)	NC (10.678 to NC)	13.17 (5.092 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.405 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6335		0.3402	
Hazard ratio (95% CI) vs Pd	-	0.85 (0.43 to 1.68)		1.49 (0.65 to 3.41)	
P-value	-	0.6332		0.3434	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Social functioning
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (35.2)	24 (25.8)	21 (32.3)	22 (36.1)	0.3641
Number (%) of patients censored	57 (64.8)	69 (74.2)	44 (67.7)	39 (63.9)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	4.11 (1.873 to 6.735)	10.02 (4.862 to NC)	4.44 (1.347 to 9.725)	6.97 (3.581 to 10.678)	
Median (95% CI)	NC (12.057 to NC)	NC (14.817 to NC)	NC (9.429 to NC)	NC (10.480 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1189		0.8636	
Hazard ratio (95% CI) vs Pd	-	0.66 (0.38 to 1.12)		0.95 (0.52 to 1.73)	
P-value	-	0.1216		0.8635	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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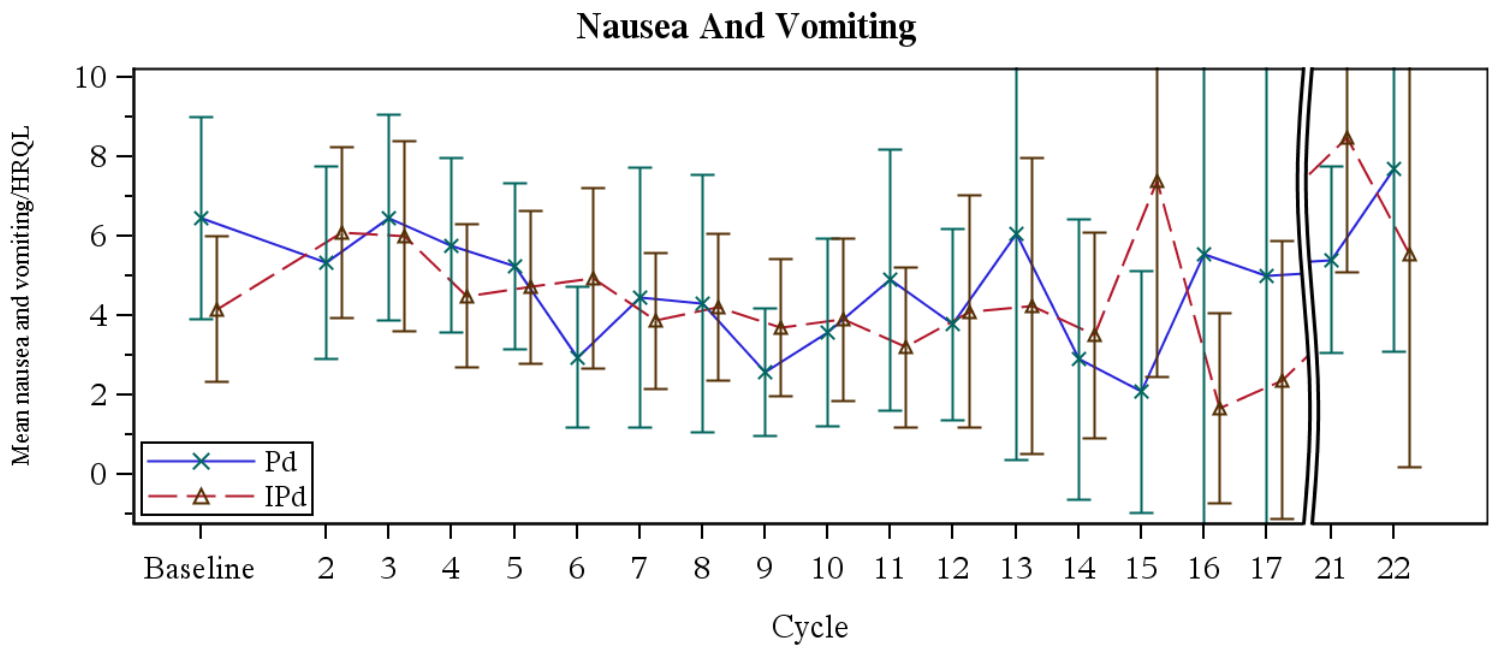
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Nausea and vomiting
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-C30 - Mean and 95% CI for nausea and vomiting score over time (LOCF) - ITT population



#patients																			
Pd	142	128	116	104	89	79	71	62	58	56	51	44	33	23	16	12	10	77	39
IPd	144	142	136	126	113	108	99	95	90	81	78	65	51	38	27	20	14	61	24

A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Nausea and vomiting
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-C30 - Time to first improvement by 15 pt in nausea and vomiting (LOCF) - ITT population

First improvement 15 points Nausea and vomiting (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	23 (15.0)	21 (13.6)
Number (%) of patients censored	130 (85.0)	133 (86.4)
Kaplan-Meier estimates of nausea and vomiting in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6682
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.88 (0.49 to 1.59)
P-value	-	0.6685
Probability (95% CI)[c]		
2 Months	0.12 (0.076 to 0.183)	0.11 (0.063 to 0.160)
4 Months	0.15 (0.100 to 0.216)	0.13 (0.079 to 0.184)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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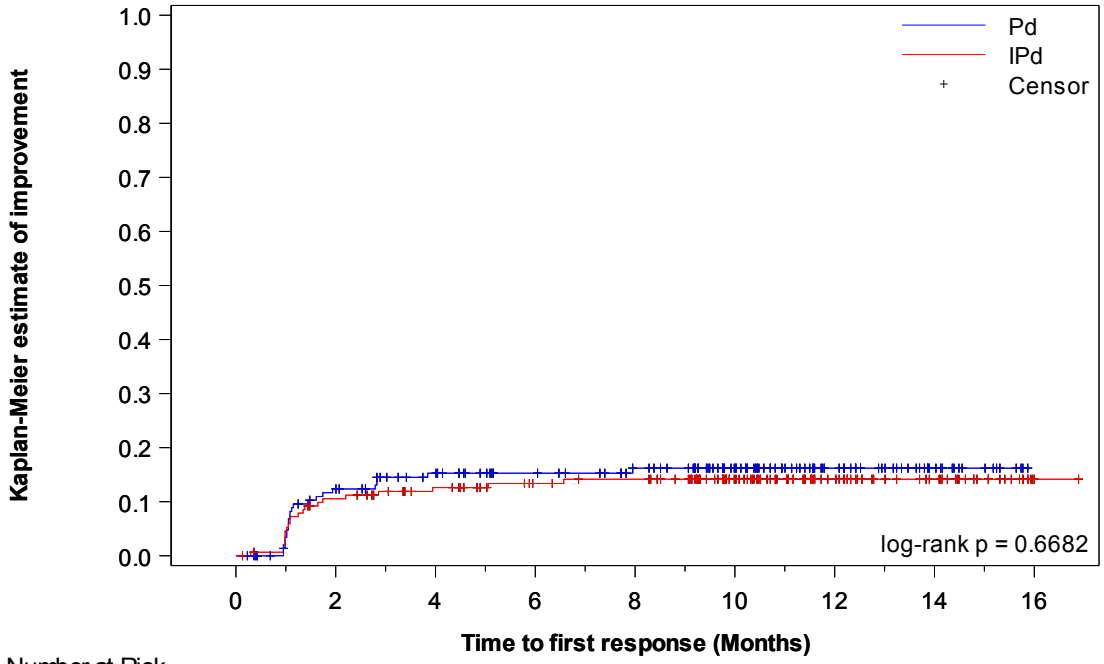
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Nausea and vomiting
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-C30 - Time to first improvement by 15 pt in nausea and vomiting - Kaplan-Meier curve (LOCF) - ITT population



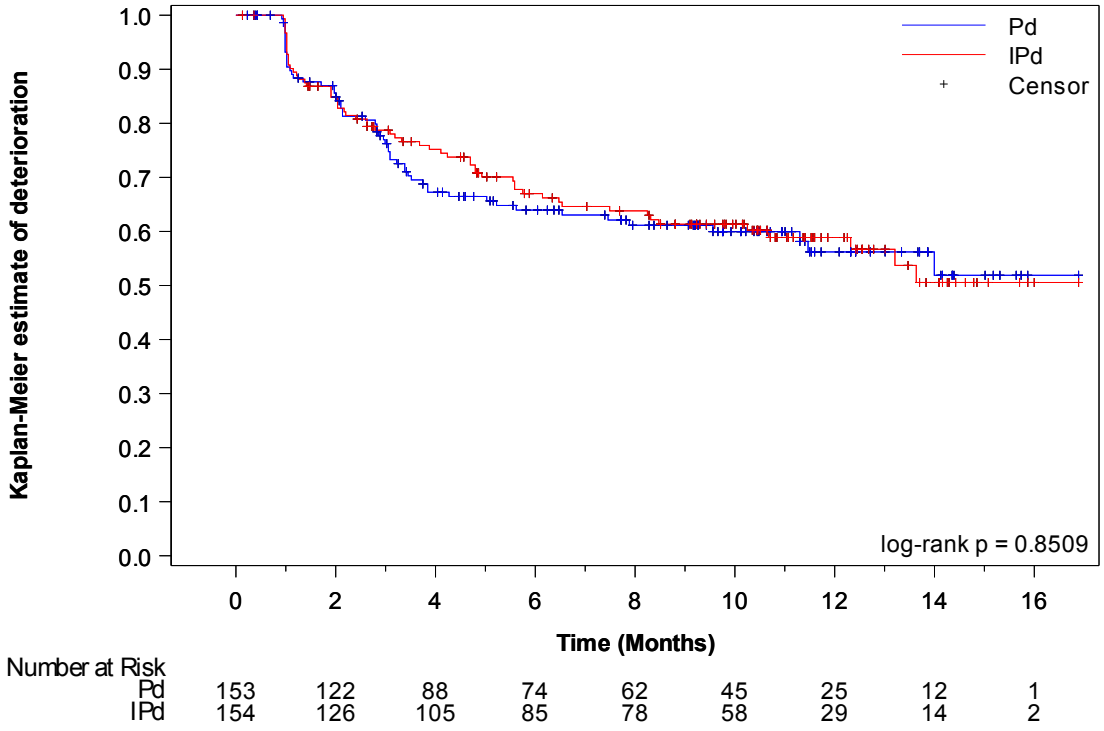
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_imp15l_de_i_f_x.rtf (08APR2021 15:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Nausea and vomiting
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-C30 - Time to first deterioration by 15 pt in nausea and vomiting (LOCF) - ITT population

First deterioration 15 points Nausea and vomiting (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	57 (37.3)	60 (39.0)
Number (%) of patients censored	96 (62.7)	94 (61.0)
Kaplan-Meier estimates of nausea and vomiting in months		
25% quantile (95% CI)	3.06 (2.136 to 3.844)	4.11 (2.201 to 5.585)
Median (95% CI)	NC (11.302 to NC)	NC (10.678 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8509
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.97 (0.67 to 1.39)
P-value	-	0.8508
Probability (95% CI)[c]		
2 Months	0.86 (0.787 to 0.903)	0.85 (0.780 to 0.896)
4 Months	0.67 (0.588 to 0.744)	0.75 (0.674 to 0.814)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_det15l_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Nausea and vomiting
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-C30 - Time to first deterioration by 15 pt in nausea and vomiting - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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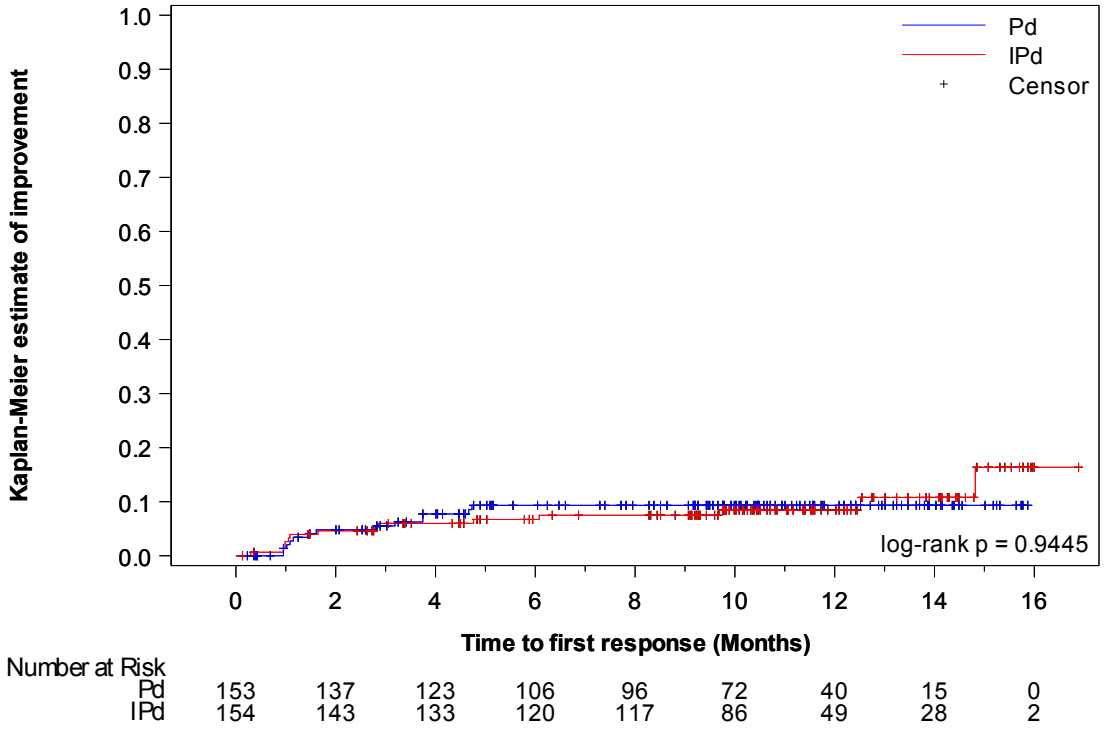
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Nausea and vomiting
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in nausea and vomiting (LOCF) - ITT population

First permanent improvement 15 points Nausea and vomiting (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	13 (8.5)	14 (9.1)
Number (%) of patients censored	140 (91.5)	140 (90.9)
Kaplan-Meier estimates of nausea and vomiting in months		
25% quantile (95% CI)	NC (NC to NC)	NC (14.817 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9445
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.97 (0.46 to 2.08)
P-value	-	0.9445
Probability (95% CI)[c]		
2 Months	0.05 (0.021 to 0.091)	0.05 (0.020 to 0.088)
4 Months	0.08 (0.041 to 0.129)	0.06 (0.029 to 0.106)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_imp15pl_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Nausea and vomiting
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-C30 - Time until permanent improvement by 15 pt in nausea and vomiting - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_imp15pl_de_i_f_x.rtf (08APR2021 15:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Nausea and vomiting
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in nausea and vomiting (LOCF) - ITT population

First permanent deterioration 15 points Nausea and vomiting (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	18 (11.8)	19 (12.3)
Number (%) of patients censored	135 (88.2)	135 (87.7)
Kaplan-Meier estimates of nausea and vomiting in months		
25% quantile (95% CI)	14.69 (13.339 to NC)	NC (12.747 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8109
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.92 (0.48 to 1.77)
P-value	-	0.8106
Probability (95% CI)[c]		
2 Months	0.97 (0.928 to 0.990)	0.97 (0.931 to 0.990)
4 Months	0.94 (0.879 to 0.966)	0.94 (0.886 to 0.968)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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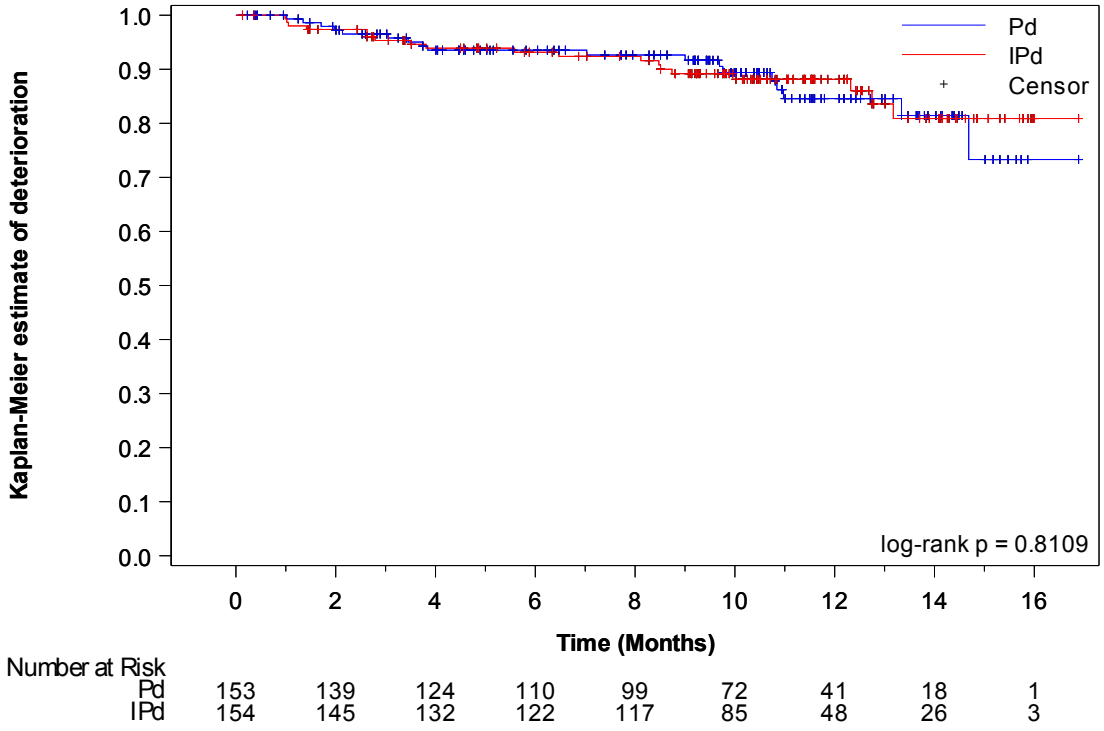
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.1 Nausea and vomiting
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-C30 - Time until permanent deterioration by 15 pt in nausea and vomiting - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_det15pl_de_i_f_x.rtf (08APR2021 15:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (20.0)	12 (22.2)	6 (11.1)	8 (11.8)	3 (10.3)	1 (3.1)	0.5016
Number (%) of patients censored	56 (80.0)	42 (77.8)	48 (88.9)	60 (88.2)	26 (89.7)	31 (96.9)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	NC (1.446 to NC)	NC (1.380 to NC)	NC (7.951 to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8216		0.9575		0.2199	
Hazard ratio (95% CI) vs Pd	-	1.09 (0.51 to 2.36)		1.03 (0.36 to 2.97)		0.27 (0.03 to 2.57)	
P-value	-	0.8208		0.9576		0.2534	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (34.3)	16 (29.6)	21 (38.9)	33 (48.5)	12 (41.4)	11 (34.4)	0.3350
Number (%) of patients censored	46 (65.7)	38 (70.4)	33 (61.1)	35 (51.5)	17 (58.6)	21 (65.6)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	2.83 (1.084 to 7.885)	8.48 (2.037 to NC)	3.22 (2.595 to 5.224)	2.79 (1.150 to 4.928)	3.06 (1.018 to 9.561)	4.80 (1.051 to 12.320)	
Median (95% CI)	NC (11.302 to NC)	NC (13.207 to NC)	NC (4.271 to NC)	10.68 (5.552 to NC)	14.00 (3.384 to NC)	12.32 (5.585 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.996 to NC)	NC (12.320 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3741		0.4332		0.3961	
Hazard ratio (95% CI) vs Pd	-	0.75 (0.40 to 1.41)		1.24 (0.72 to 2.15)		0.70 (0.31 to 1.60)	
P-value	-	0.3757		0.4341		0.3985	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (14.3)	9 (16.7)	2 (3.7)	4 (5.9)	1 (3.4)	1 (3.1)	0.9289
Number (%) of patients censored	60 (85.7)	45 (83.3)	52 (96.3)	64 (94.1)	28 (96.6)	31 (96.9)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	NC (4.731 to NC)	14.82 (2.858 to NC)	NC (NC to NC)	NC (12.517 to NC)	NC (3.745 to NC)	NC (6.078 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8044		0.6446		0.8587	
Hazard ratio (95% CI) vs Pd	-	1.12 (0.45 to 2.76)		1.49 (0.27 to 8.14)		0.78 (0.05 to 12.51)	
P-value	-	0.8045		0.6468		0.8590	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (12.9)	6 (11.1)	4 (7.4)	10 (14.7)	5 (17.2)	3 (9.4)	0.2744
Number (%) of patients censored	61 (87.1)	48 (88.9)	50 (92.6)	58 (85.3)	24 (82.8)	29 (90.6)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	14.69 (10.743 to NC)	NC (8.509 to NC)	NC (10.842 to NC)	NC (10.021 to NC)	10.97 (1.971 to NC)	NC (12.320 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.973 to NC)	NC (12.320 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7186		0.3089		0.2143	
Hazard ratio (95% CI) vs Pd	-	0.83 (0.29 to 2.33)		1.81 (0.57 to 5.77)		0.41 (0.10 to 1.74)	
P-value	-	0.7190		0.3162		0.2288	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_detpl_age_de_i_t_x.rtf (08APR2021 14:43)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (14.9)	14 (13.7)	8 (15.4)	7 (13.5)	0.8545
Number (%) of patients censored	86 (85.1)	88 (86.3)	44 (84.6)	45 (86.5)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.938 to NC)	NC (5.060 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7824		0.6527	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.44 to 1.87)		0.79 (0.29 to 2.19)	
P-value	-	0.7825		0.6530	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_impl_plne_de_i_t_x.rtf (08APR2021 14:43)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (33.7)	43 (42.2)	23 (44.2)	17 (32.7)	0.0756
Number (%) of patients censored	67 (66.3)	59 (57.8)	29 (55.8)	35 (67.3)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	3.09 (2.136 to 6.538)	3.68 (1.906 to 6.472)	3.06 (1.018 to 3.515)	4.70 (2.037 to NC)	
Median (95% CI)	NC (11.302 to NC)	13.21 (8.312 to NC)	11.47 (3.450 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.996 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3897		0.1243	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.78 to 1.91)		0.61 (0.33 to 1.15)	
P-value	-	0.3904		0.1280	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (10.9)	9 (8.8)	2 (3.8)	5 (9.6)	0.2144
Number (%) of patients censored	90 (89.1)	93 (91.2)	50 (96.2)	47 (90.4)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4676		0.3022	
Hazard ratio (95% CI) vs Pd	-	0.72 (0.30 to 1.75)		2.32 (0.45 to 11.96)	
P-value	-	0.4692		0.3162	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (9.9)	14 (13.7)	8 (15.4)	5 (9.6)	0.1786
Number (%) of patients censored	91 (90.1)	88 (86.3)	44 (84.6)	47 (90.4)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	14.69 (13.339 to NC)	NC (12.320 to NC)	10.97 (9.692 to NC)	NC (12.747 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (10.973 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5166		0.2185	
Hazard ratio (95% CI) vs Pd	-	1.31 (0.58 to 2.95)		0.50 (0.16 to 1.54)	
P-value	-	0.5179		0.2275	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (12.9)	11 (12.4)	14 (16.9)	10 (15.4)	0.9236
Number (%) of patients censored	61 (87.1)	78 (87.6)	69 (83.1)	55 (84.6)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.825 to NC)	NC (1.380 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8612		0.7423	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.38 to 2.23)		0.87 (0.39 to 1.97)	
P-value	-	0.8606		0.7425	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (30.0)	34 (38.2)	36 (43.4)	26 (40.0)	0.2377
Number (%) of patients censored	49 (70.0)	55 (61.8)	47 (56.6)	39 (60.0)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	5.03 (2.037 to 11.466)	4.70 (2.628 to 7.491)	2.96 (1.971 to 3.384)	2.40 (1.150 to 6.472)	
Median (95% CI)	NC (11.466 to NC)	NC (10.251 to NC)	14.00 (3.515 to NC)	13.63 (6.472 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.996 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4353		0.4123	
Hazard ratio (95% CI) vs Pd	-	1.24 (0.72 to 2.14)		0.81 (0.49 to 1.34)	
P-value	-	0.4362		0.4131	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (7.1)	7 (7.9)	8 (9.6)	7 (10.8)	0.9616
Number (%) of patients censored	65 (92.9)	82 (92.1)	75 (90.4)	58 (89.2)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (12.517 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9476		0.9193	
Hazard ratio (95% CI) vs Pd	-	1.04 (0.33 to 3.28)		1.05 (0.38 to 2.91)	
P-value	-	0.9477		0.9192	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (8.6)	10 (11.2)	12 (14.5)	9 (13.8)	0.5340
Number (%) of patients censored	64 (91.4)	79 (88.8)	71 (85.5)	56 (86.2)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (10.842 to NC)	NC (12.320 to NC)	13.34 (10.743 to NC)	NC (8.739 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6483		0.6224	
Hazard ratio (95% CI) vs Pd	-	1.27 (0.46 to 3.48)		0.80 (0.34 to 1.91)	
P-value	-	0.6490		0.6231	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (15.9)	18 (15.3)	3 (15.8)	1 (4.2)	0.2827
Number (%) of patients censored	106 (84.1)	100 (84.7)	16 (84.2)	23 (95.8)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (7.951 to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (1.248 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7556		0.1828	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.48 to 1.71)		0.24 (0.03 to 2.33)	
P-value	-	0.7560		0.2198	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (39.7)	50 (42.4)	6 (31.6)	7 (29.2)	0.9170
Number (%) of patients censored	76 (60.3)	68 (57.6)	13 (68.4)	17 (70.8)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	2.99 (2.103 to 3.515)	3.68 (2.037 to 5.585)	3.22 (0.986 to NC)	3.88 (1.018 to NC)	
Median (95% CI)	14.00 (7.458 to NC)	13.21 (8.312 to NC)	11.47 (3.220 to NC)	NC (6.144 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.466 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7962		0.8307	
Hazard ratio (95% CI) vs Pd	-	0.95 (0.64 to 1.41)		0.89 (0.30 to 2.66)	
P-value	-	0.7962		0.8308	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (9.5)	11 (9.3)	1 (5.3)	1 (4.2)	0.9342
Number (%) of patients censored	114 (90.5)	107 (90.7)	18 (94.7)	23 (95.8)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (1.150 to NC)	NC (6.078 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7407		0.8908	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.38 to 1.98)		0.82 (0.05 to 13.18)	
P-value	-	0.7409		0.8910	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (12.7)	18 (15.3)	1 (5.3)	0 (0.0)	0.9890
Number (%) of patients censored	110 (87.3)	100 (84.7)	18 (94.7)	24 (100.0)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	14.69 (10.973 to NC)	NC (12.320 to NC)	NC (1.708 to NC)	NC (NC to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8069		0.2712	
Hazard ratio (95% CI) vs Pd	-	1.09 (0.55 to 2.13)			
P-value	-	0.8072		0.9984	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_detpl_race_de_i_t_x.rtf (08APR2021 14:44)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (25.0)	22 (16.4)	16 (12.3)	0.9857
Number (%) of patients censored	3 (100.0)	3 (75.0)	112 (83.6)	114 (87.7)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (1.018 to NC)	NC (3.844 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.2755	
Hazard ratio (95% CI) vs Pd	-			0.70 (0.37 to 1.33)	
P-value	-	0.9985		0.2781	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_impl_ethn_de_i_t_x.rtf (08APR2021 14:43)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (25.0)	52 (38.8)	53 (40.8)	0.9867
Number (%) of patients censored	3 (100.0)	3 (75.0)	82 (61.2)	77 (59.2)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (10.678 to NC)	3.06 (2.103 to 3.844)	3.68 (2.168 to 5.585)	
Median (95% CI)	NC (NC to NC)	NC (10.678 to NC)	14.00 (9.561 to NC)	13.63 (10.251 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.678 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.8531	
Hazard ratio (95% CI) vs Pd	-			0.96 (0.66 to 1.41)	
P-value	-			0.8531	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_detl_ethn_de_i_t_x.rtf (08APR2021 14:43)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (25.0)	13 (9.7)	10 (7.7)	0.9899
Number (%) of patients censored	3 (100.0)	3 (75.0)	121 (90.3)	120 (92.3)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	12.52 (12.517 to NC)	NC (NC to NC)	NC (14.817 to NC)	
Median (95% CI)	NC (NC to NC)	NC (12.517 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.517 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.4127	
Hazard ratio (95% CI) vs Pd	-			0.71 (0.31 to 1.62)	
P-value	-			0.4150	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_imppl_ethn_de_i_t_x.rtf (08APR2021 14:44)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	17 (12.7)	17 (13.1)	1.0000
Number (%) of patients censored	3 (100.0)	4 (100.0)	117 (87.3)	113 (86.9)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	14.69 (10.973 to NC)	NC (12.747 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.8594	
Hazard ratio (95% CI) vs Pd	-			0.94 (0.48 to 1.84)	
P-value	-			0.8593	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	10 (13.2)	9 (16.4)	2 (10.0)	2 (7.1)	0 (0.0)	2 (28.6)	2 (13.3)	0 (0.0)	9 (24.3)	8 (18.6)	0.9543
Number (%) of patients censored	66 (86.8)	46 (83.6)	18 (90.0)	26 (92.9)	5 (100.0)	5 (71.4)	13 (86.7)	21 (100.0)	28 (75.7)	35 (81.4)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (7.951 to NC)	NC (1.643 to NC)	NC (1.051 to NC)	NC (1.084 to NC)	NC (NC to NC)	1.25 (1.018 to NC)	NC (1.117 to NC)	NC (NC to NC)	3.84 (1.446 to NC)	NC (1.741 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.6902		0.7043		0.2137		0.0886		0.4720	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.49 to 2.96)		0.69 (0.10 to 4.87)						0.71 (0.27 to 1.83)	
P-value	-	0.6906		0.7059		0.9978		0.9977		0.4743	
Improvement probability (95% CI)[b]											
2 Months	0.112 (0.052 to 0.198)	0.129 (0.057 to 0.233)	0.053 (0.004 to 0.214)	0.071 (0.013 to 0.204)		0.286 (0.041 to 0.612)	0.133 (0.022 to 0.346)		0.197 (0.087 to 0.340)	0.120 (0.044 to 0.237)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_impl_greg_de_i_t_x.rtf (08APR2021 14:43)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	21 (27.6)	16 (29.1)	10 (50.0)	11 (39.3)	2 (40.0)	5 (71.4)	5 (33.3)	5 (23.8)	19 (51.4)	23 (53.5)	0.7825
Number (%) of patients censored	55 (72.4)	39 (70.9)	10 (50.0)	17 (60.7)	3 (60.0)	2 (28.6)	10 (66.7)	16 (76.2)	18 (48.6)	20 (46.5)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	5.03 (2.957 to NC)	5.59 (1.216 to NC)	1.12 (0.953 to 3.515)	2.79 (0.986 to 13.634)	2.79 (2.595 to NC)	2.63 (1.150 to 4.698)	3.22 (0.986 to 11.466)	6.14 (1.018 to NC)	2.04 (0.986 to 3.450)	2.63 (1.084 to 5.552)	
Median (95% CI)	NC (NC to NC)	NC (12.320 to NC)	14.00 (1.117 to NC)	13.63 (4.238 to NC)	NC (2.595 to NC)	4.70 (1.150 to 10.678)	11.47 (2.103 to 11.466)	NC (6.144 to NC)	7.46 (3.055 to NC)	8.25 (4.698 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.996 to NC)	NC (13.634 to NC)	NC (2.595 to NC)	10.68 (3.318 to 10.678)	11.47 (NC to NC)	NC (NC to NC)	NC (7.885 to NC)	NC (13.207 to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.9982		0.4918		0.4354		0.4653		0.4519	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.52 to 1.92)		0.74 (0.31 to 1.76)		1.90 (0.37 to 9.85)		0.63 (0.18 to 2.22)		0.79 (0.43 to 1.46)	
P-value	-	0.9982		0.4934		0.4431		0.4691		0.4529	
Deterioration probability (95% CI)[b]											

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	6 (7.9)	6 (10.9)	1 (5.0)	2 (7.1)	0 (0.0)	2 (28.6)	1 (6.7)	0 (0.0)	5 (13.5)	4 (9.3)	0.9098
Number (%) of patients censored	70 (92.1)	49 (89.1)	19 (95.0)	26 (92.9)	5 (100.0)	5 (71.4)	14 (93.3)	21 (100.0)	32 (86.5)	39 (90.7)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.731 to NC)	NC (4.764 to NC)	NC (NC to NC)	12.52 (6.078 to NC)	NC (1.150 to NC)	NC (NC to NC)	NC (3.745 to NC)	NC (14.817 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	12.52 (6.078 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.517 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.5960		0.8143		0.3613		0.2367		0.3552	
Hazard ratio (95% CI) vs Pd	-	1.36 (0.44 to 4.21)		1.33 (0.12 to 14.69)						0.54 (0.14 to 2.05)	
P-value	-	0.5974		0.8149		0.9984		0.9984		0.3622	
Improvement probability (95% CI)[b]											
2 Months	0.042 (0.011 to 0.107)	0.092 (0.034 to 0.187)		0.036 (0.003 to 0.154)			0.067 (0.004 to 0.260)		0.084 (0.022 to 0.202)	0.024 (0.002 to 0.108)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	6 (7.9)	9 (16.4)	3 (15.0)	4 (14.3)	1 (20.0)	1 (14.3)	0 (0.0)	0 (0.0)	8 (21.6)	5 (11.6)	0.3101
Number (%) of patients censored	70 (92.1)	46 (83.6)	17 (85.0)	24 (85.7)	4 (80.0)	6 (85.7)	15 (100.0)	21 (100.0)	29 (78.4)	38 (88.4)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (13.339 to NC)	13.17 (8.509 to NC)	NC (3.450 to NC)	12.75 (2.793 to NC)	NC (9.002 to NC)	NC (2.628 to NC)	NC (NC to NC)	NC (NC to NC)	10.74 (2.136 to NC)	NC (10.021 to NC)	
Median (95% CI)	NC (NC to NC)	NC (13.175 to NC)	NC (10.973 to NC)	NC (12.747 to NC)	NC (9.002 to NC)	NC (2.628 to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.747 to NC)	NC (9.002 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.1150		0.8747		0.9055				0.1111	
Hazard ratio (95% CI) vs Pd	-	2.25 (0.80 to 6.37)		1.13 (0.25 to 5.11)		0.85 (0.05 to 13.65)				0.41 (0.13 to 1.27)	
P-value	-	0.1249		0.8748		0.9056				0.1226	
Deterioration probability (95% CI)[b]											

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (12.4)	15 (19.5)	11 (19.6)	6 (7.8)	0.0290
Number (%) of patients censored	85 (87.6)	62 (80.5)	45 (80.4)	71 (92.2)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (2.858 to NC)	NC (1.610 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2774		0.0491	
Hazard ratio (95% CI) vs Pd	-	1.52 (0.71 to 3.24)		0.38 (0.14 to 1.03)	
P-value	-	0.2808		0.0582	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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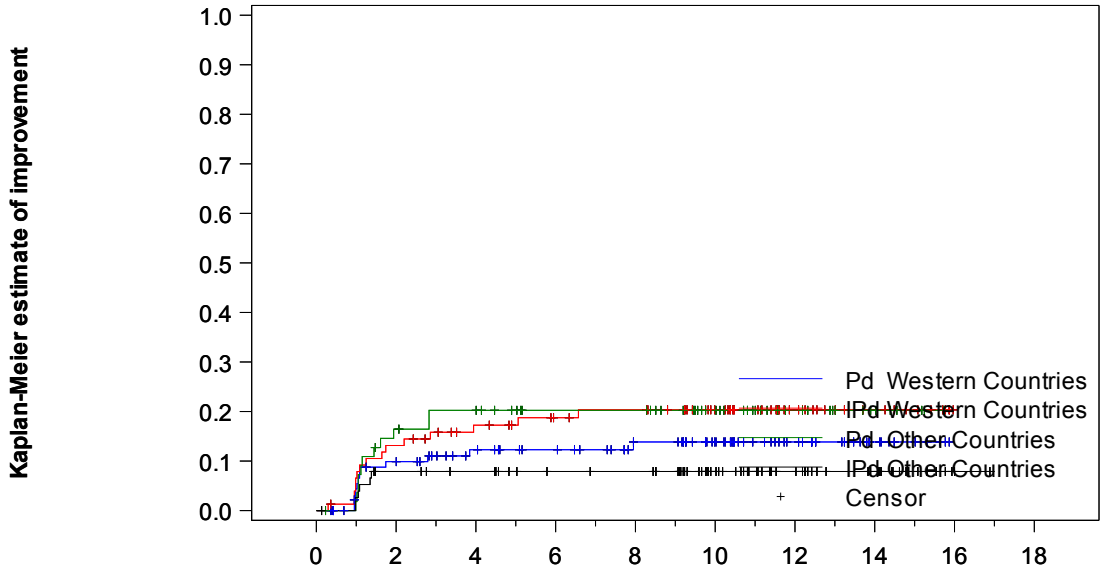
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to regulatory region (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd Western Countries	97	75	64	54	25	5	0
IPd Western Countries	77	62	52	47	19	7	0
Pd Other Countries	56	42	35	31	13	3	0
IPd Other Countries	77	66	59	55	25	7	0

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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (34.0)	30 (39.0)	24 (42.9)	30 (39.0)	0.4457
Number (%) of patients censored	64 (66.0)	47 (61.0)	32 (57.1)	47 (61.0)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	3.38 (2.793 to 5.618)	4.70 (1.380 to 5.749)	2.10 (1.117 to 4.271)	3.88 (2.037 to 8.246)	
Median (95% CI)	NC (9.561 to NC)	NC (8.476 to NC)	11.47 (3.515 to NC)	13.63 (8.312 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.996 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8374		0.4369	
Hazard ratio (95% CI) vs Pd	-	1.05 (0.64 to 1.73)		0.81 (0.47 to 1.38)	
P-value	-	0.8371		0.4377	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (6.2)	10 (13.0)	7 (12.5)	4 (5.2)	0.0446
Number (%) of patients censored	91 (93.8)	67 (87.0)	49 (87.5)	73 (94.8)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (12.517 to NC)	NC (4.731 to NC)	NC (14.817 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1685		0.1050	
Hazard ratio (95% CI) vs Pd	-	2.01 (0.73 to 5.52)		0.37 (0.11 to 1.29)	
P-value	-	0.1772		0.1189	
Improvement probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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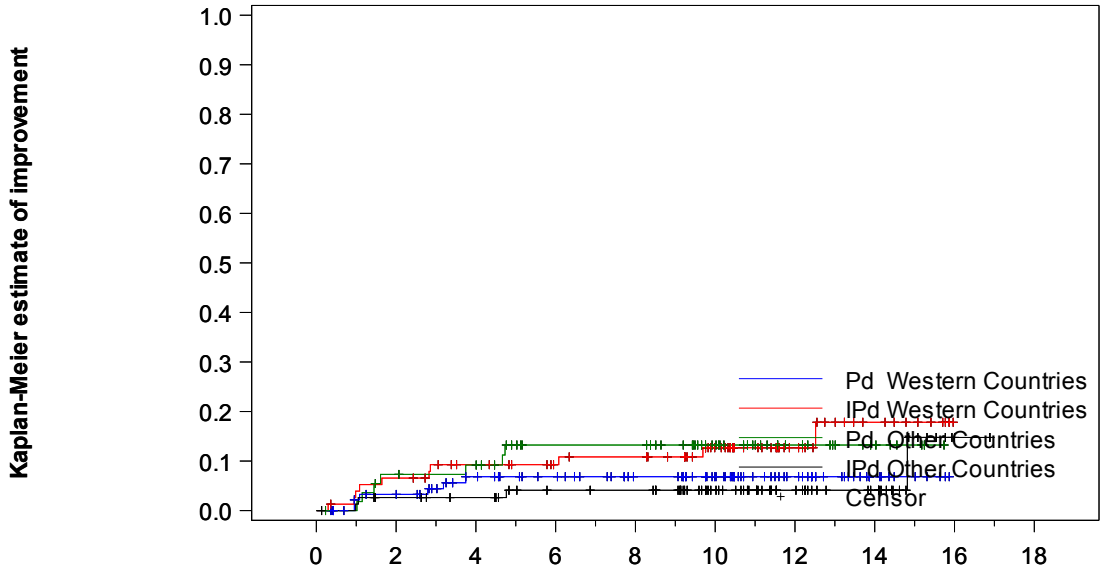
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.7 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to regulatory region (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd Western Countries	97	81	68	58	27	5	0
IPd Western Countries	77	67	58	53	21	7	0
Pd Other Countries	56	49	38	34	13	3	0
IPd Other Countries	77	70	62	58	28	7	0

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.8 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (11.3)	12 (15.6)	7 (12.5)	7 (9.1)	0.3424
Number (%) of patients censored	86 (88.7)	65 (84.4)	49 (87.5)	70 (90.9)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (13.339 to NC)	13.17 (10.021 to NC)	14.69 (10.743 to NC)	NC (12.747 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5327		0.4288	
Hazard ratio (95% CI) vs Pd	-	1.30 (0.57 to 2.94)		0.66 (0.23 to 1.88)	
P-value	-	0.5338		0.4322	
Deterioration probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (12.4)	19 (13.8)	6 (37.5)	2 (12.5)	0.1422
Number (%) of patients censored	120 (87.6)	119 (86.2)	10 (62.5)	14 (87.5)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	1.08 (0.953 to NC)	NC (0.296 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8527		0.1413	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.55 to 2.05)		0.32 (0.06 to 1.59)	
P-value	-	0.8529		0.1631	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	52 (38.0)	54 (39.1)	5 (31.3)	6 (37.5)	0.5497
Number (%) of patients censored	85 (62.0)	84 (60.9)	11 (68.8)	10 (62.5)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	3.06 (2.136 to 3.844)	4.24 (2.201 to 5.749)	1.35 (0.986 to NC)	1.91 (0.986 to 10.678)	
Median (95% CI)	NC (9.561 to NC)	NC (12.320 to NC)	NC (1.084 to NC)	10.68 (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.678 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6770		0.7531	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.63 to 1.35)		1.21 (0.37 to 3.98)	
P-value	-	0.6765		0.7534	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (5.1)	12 (8.7)	6 (37.5)	2 (12.5)	0.0418
Number (%) of patients censored	130 (94.9)	126 (91.3)	10 (62.5)	14 (87.5)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (14.817 to NC)	2.79 (0.953 to NC)	12.52 (0.296 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.084 to NC)	NC (12.517 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.665 to NC)	NC (12.517 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3224		0.0416	
Hazard ratio (95% CI) vs Pd	-	1.60 (0.63 to 4.06)		0.15 (0.02 to 1.24)	
P-value	-	0.3268		0.0778	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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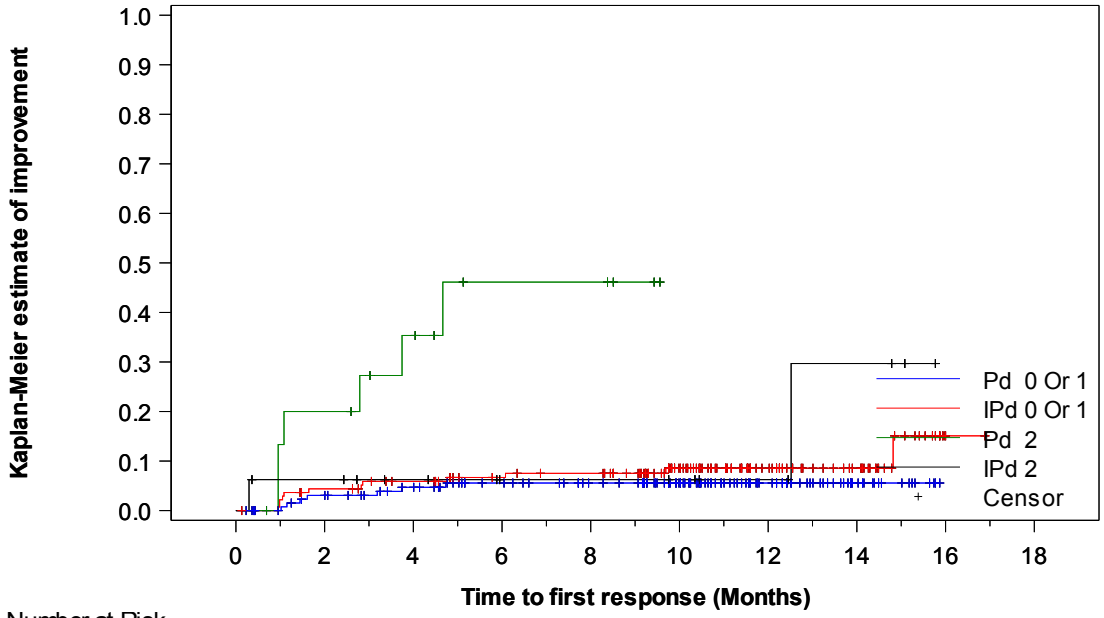
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to baseline ECOG PS (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd 0 Or 1	137	120	102	90	40	8	0
IPd 0 Or 1	138	125	112	103	44	12	0
Pd 2	16	10	4	2	0	0	0
IPd 2	16	12	8	8	5	2	0

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_imppl_ecog_de_i_f_x.rtf (08APR2021 14:34)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.7 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (12.4)	16 (11.6)	1 (6.3)	3 (18.8)	0.2861
Number (%) of patients censored	120 (87.6)	122 (88.4)	15 (93.8)	13 (81.3)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	14.69 (10.973 to NC)	NC (12.747 to NC)	NC (1.347 to NC)	13.17 (2.628 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.515 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.175 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5916		0.2623	
Hazard ratio (95% CI) vs Pd	-	0.83 (0.42 to 1.64)		3.39 (0.35 to 32.67)	
P-value	-	0.5921		0.2915	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_detpl_ecog_de_i_t_x.rtf (08APR2021 14:43)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (15.7)	8 (12.5)	10 (17.9)	10 (18.9)	5 (11.6)	2 (5.9)	0.6669
Number (%) of patients censored	43 (84.3)	56 (87.5)	46 (82.1)	43 (81.1)	38 (88.4)	32 (94.1)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	NC (1.610 to NC)	NC (NC to NC)	NC (1.938 to NC)	NC (1.248 to NC)	NC (1.741 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6483		0.9376		0.2897	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.30 to 2.12)		1.04 (0.43 to 2.49)		0.42 (0.08 to 2.18)	
P-value	-	0.6490		0.9376		0.3044	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (39.2)	24 (37.5)	20 (35.7)	23 (43.4)	15 (34.9)	11 (32.4)	0.6060
Number (%) of patients censored	31 (60.8)	40 (62.5)	36 (64.3)	30 (56.6)	28 (65.1)	23 (67.6)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	3.84 (1.971 to 9.561)	4.70 (2.037 to 8.312)	3.09 (1.971 to 13.996)	3.19 (1.216 to 6.472)	2.83 (1.018 to 5.618)	3.09 (1.018 to NC)	
Median (95% CI)	NC (7.885 to NC)	NC (10.678 to NC)	NC (4.271 to NC)	12.32 (6.144 to NC)	11.30 (3.088 to NC)	NC (5.585 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.634 to NC)	NC (11.302 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9445		0.5934		0.4416	
Hazard ratio (95% CI) vs Pd	-	0.98 (0.54 to 1.77)		1.18 (0.65 to 2.14)		0.74 (0.34 to 1.61)	
P-value	-	0.9444		0.5942		0.4434	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (11.8)	6 (9.4)	4 (7.1)	7 (13.2)	3 (7.0)	1 (2.9)	0.4000
Number (%) of patients censored	45 (88.2)	58 (90.6)	52 (92.9)	46 (86.8)	40 (93.0)	33 (97.1)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	NC (NC to NC)	NC (12.517 to NC)	NC (NC to NC)	14.82 (14.817 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6941		0.3976		0.3611	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.26 to 2.47)		1.70 (0.49 to 5.84)		0.36 (0.04 to 3.50)	
P-value	-	0.6947		0.4029		0.3813	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (7.8)	3 (4.7)	7 (12.5)	11 (20.8)	6 (14.0)	5 (14.7)	0.5186
Number (%) of patients censored	47 (92.2)	61 (95.3)	49 (87.5)	42 (79.2)	37 (86.0)	29 (85.3)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (9.758 to NC)	12.32 (8.476 to NC)	13.34 (9.692 to NC)	12.75 (5.585 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.175 to NC)	NC (10.842 to NC)	NC (12.747 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.339 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5395		0.3626		0.6813	
Hazard ratio (95% CI) vs Pd	-	0.63 (0.14 to 2.81)		1.55 (0.60 to 4.00)		0.78 (0.24 to 2.57)	
P-value	-	0.5431		0.3664		0.6824	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (16.1)	6 (15.4)	15 (15.3)	13 (13.1)	3 (12.5)	2 (12.5)	0.9760
Number (%) of patients censored	26 (83.9)	33 (84.6)	83 (84.7)	86 (86.9)	21 (87.5)	14 (87.5)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	NC (1.117 to NC)	NC (1.347 to NC)	NC (3.844 to NC)	NC (NC to NC)	NC (1.084 to NC)	NC (1.380 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.951 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9403		0.6168		0.8124	
Hazard ratio (95% CI) vs Pd	-	0.96 (0.29 to 3.13)		0.83 (0.39 to 1.74)		0.81 (0.13 to 4.84)	
P-value	-	0.9401		0.6176		0.8128	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (41.9)	13 (33.3)	37 (37.8)	43 (43.4)	7 (29.2)	4 (25.0)	0.3183
Number (%) of patients censored	18 (58.1)	26 (66.7)	61 (62.2)	56 (56.6)	17 (70.8)	12 (75.0)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	2.60 (0.986 to 7.885)	8.25 (3.680 to NC)	3.09 (2.136 to 4.271)	2.63 (1.380 to 4.797)	2.14 (0.986 to 5.618)	5.59 (1.018 to NC)	
Median (95% CI)	NC (5.027 to NC)	NC (10.678 to NC)	14.00 (11.302 to NC)	13.63 (6.144 to NC)	5.62 (2.136 to NC)	NC (2.037 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.618 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3595		0.4634		0.3607	
Hazard ratio (95% CI) vs Pd	-	0.70 (0.32 to 1.51)		1.18 (0.76 to 1.83)		0.56 (0.16 to 1.97)	
P-value	-	0.3620		0.4647		0.3665	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (12.9)	5 (12.8)	7 (7.1)	8 (8.1)	2 (8.3)	1 (6.3)	0.9117
Number (%) of patients censored	27 (87.1)	34 (87.2)	91 (92.9)	91 (91.9)	22 (91.7)	15 (93.8)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	NC (2.793 to NC)	NC (9.692 to NC)	NC (NC to NC)	NC (14.817 to NC)	NC (1.084 to NC)	NC (2.858 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9389		0.9141		0.6773	
Hazard ratio (95% CI) vs Pd	-	0.95 (0.25 to 3.54)		1.06 (0.38 to 2.93)		0.60 (0.05 to 6.69)	
P-value	-	0.9387		0.9142		0.6806	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (6.5)	1 (2.6)	13 (13.3)	15 (15.2)	3 (12.5)	3 (18.8)	0.7478
Number (%) of patients censored	29 (93.5)	38 (97.4)	85 (86.7)	84 (84.8)	21 (87.5)	13 (81.3)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	14.69 (14.686 to NC)	NC (NC to NC)	NC (10.842 to NC)	13.17 (12.320 to NC)	9.69 (1.347 to NC)	NC (1.051 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.692 to NC)	NC (5.585 to NC)	
75% quantile (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3669		0.8504		0.9060	
Hazard ratio (95% CI) vs Pd	-	0.35 (0.03 to 3.87)		1.07 (0.51 to 2.26)		1.10 (0.22 to 5.53)	
P-value	-	0.3883		0.8507		0.9059	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (13.0)	2 (14.3)	17 (17.9)	17 (14.4)	0.6635
Number (%) of patients censored	20 (87.0)	12 (85.7)	78 (82.1)	101 (85.6)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (1.051 to NC)	NC (0.296 to NC)	NC (2.825 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8837		0.4099	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.19 to 6.85)		0.75 (0.39 to 1.48)	
P-value	-	0.8838		0.4115	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (26.1)	5 (35.7)	35 (36.8)	43 (36.4)	0.4843
Number (%) of patients censored	17 (73.9)	9 (64.3)	60 (63.2)	75 (63.6)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	3.45 (0.986 to NC)	4.70 (1.018 to NC)	2.96 (1.971 to 7.458)	4.24 (2.398 to 6.472)	
Median (95% CI)	NC (3.450 to NC)	8.48 (1.906 to NC)	NC (11.302 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (8.476 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5857		0.6543	
Hazard ratio (95% CI) vs Pd	-	1.39 (0.42 to 4.59)		0.90 (0.58 to 1.41)	
P-value	-	0.5873		0.6545	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (8.7)	2 (14.3)	10 (10.5)	10 (8.5)	0.4539
Number (%) of patients censored	21 (91.3)	12 (85.7)	85 (89.5)	108 (91.5)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (1.446 to NC)	NC (0.296 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5985		0.5187	
Hazard ratio (95% CI) vs Pd	-	1.68 (0.24 to 11.96)		0.75 (0.31 to 1.80)	
P-value	-	0.6026		0.5202	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	3 (21.4)	11 (11.6)	14 (11.9)	0.9858
Number (%) of patients censored	23 (100.0)	11 (78.6)	84 (88.4)	104 (88.1)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	8.48 (1.018 to NC)	NC (13.339 to NC)	NC (12.747 to NC)	
Median (95% CI)	NC (NC to NC)	NC (8.476 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0249		0.8459	
Hazard ratio (95% CI) vs Pd	-			0.92 (0.42 to 2.04)	
P-value	-	0.9973		0.8450	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (16.7)	4 (16.7)	13 (16.7)	14 (13.6)	0.7655
Number (%) of patients censored	30 (83.3)	20 (83.3)	65 (83.3)	89 (86.4)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (1.150 to NC)	NC (0.296 to NC)	NC (2.825 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9497		0.4958	
Hazard ratio (95% CI) vs Pd	-	0.96 (0.27 to 3.41)		0.77 (0.36 to 1.64)	
P-value	-	0.9499		0.4971	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (25.0)	10 (41.7)	30 (38.5)	37 (35.9)	0.0990
Number (%) of patients censored	27 (75.0)	14 (58.3)	48 (61.5)	66 (64.1)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	3.84 (1.347 to NC)	2.20 (1.018 to 5.585)	2.83 (1.708 to 7.458)	4.70 (2.628 to 7.491)	
Median (95% CI)	NC (9.561 to NC)	8.48 (2.201 to NC)	14.00 (11.302 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (8.476 to NC)	NC (13.996 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1847		0.4067	
Hazard ratio (95% CI) vs Pd	-	1.83 (0.74 to 4.51)		0.82 (0.50 to 1.32)	
P-value	-	0.1913		0.4075	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (13.9)	3 (12.5)	7 (9.0)	8 (7.8)	0.9299
Number (%) of patients censored	31 (86.1)	21 (87.5)	71 (91.0)	95 (92.2)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (1.446 to NC)	NC (0.296 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8594		0.6808	
Hazard ratio (95% CI) vs Pd	-	0.88 (0.21 to 3.68)		0.81 (0.29 to 2.23)	
P-value	-	0.8595		0.6813	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (5.6)	5 (20.8)	9 (11.5)	12 (11.7)	0.1006
Number (%) of patients censored	34 (94.4)	19 (79.2)	69 (88.5)	91 (88.3)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (3.844 to NC)	10.02 (1.018 to NC)	NC (10.743 to NC)	NC (12.747 to NC)	
Median (95% CI)	NC (NC to NC)	NC (10.021 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0890		0.8303	
Hazard ratio (95% CI) vs Pd	-	3.77 (0.73 to 19.48)		0.91 (0.38 to 2.16)	
P-value	-	0.1133		0.8303	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (22.2)	11 (13.3)	3 (4.8)	10 (14.1)	0.0318
Number (%) of patients censored	70 (77.8)	72 (86.7)	60 (95.2)	61 (85.9)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (1.446 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1204		0.0931	
Hazard ratio (95% CI) vs Pd	-	0.56 (0.27 to 1.17)		2.87 (0.79 to 10.44)	
P-value	-	0.1256		0.1088	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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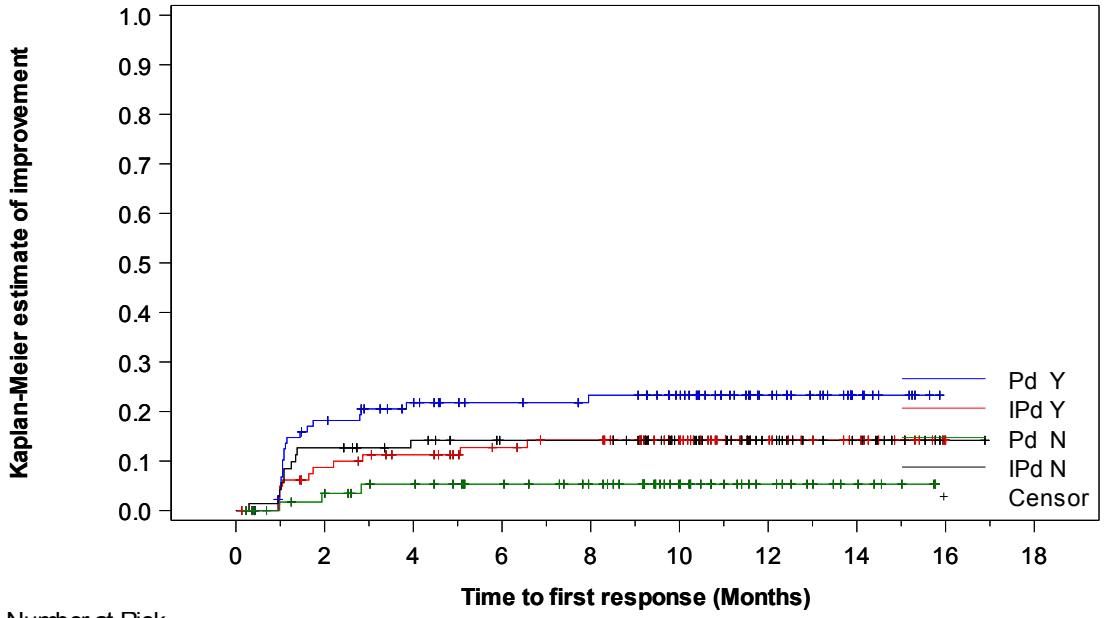
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to previous autologous stem-cell (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd Y	90	66	55	51	25	5	0
IPd Y	83	69	59	52	21	8	0
Pd N	63	51	44	34	13	3	0
IPd N	71	59	52	50	23	6	0

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_impl_auto_de_i_f_x.rtf (08APR2021 14:36)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (36.7)	33 (39.8)	24 (38.1)	27 (38.0)	0.5640
Number (%) of patients censored	57 (63.3)	50 (60.2)	39 (61.9)	44 (62.0)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	3.06 (2.136 to 4.271)	3.19 (2.037 to 6.472)	3.22 (1.347 to 6.538)	4.24 (1.906 to 8.312)	
Median (95% CI)	NC (7.458 to NC)	13.63 (8.246 to NC)	14.00 (6.538 to NC)	NC (10.251 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.996 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8399		0.5201	
Hazard ratio (95% CI) vs Pd	-	1.05 (0.65 to 1.70)		0.83 (0.48 to 1.45)	
P-value	-	0.8398		0.5207	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (13.3)	8 (9.6)	1 (1.6)	6 (8.5)	0.1036
Number (%) of patients censored	78 (86.7)	75 (90.4)	62 (98.4)	65 (91.5)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.517 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4680		0.1430	
Hazard ratio (95% CI) vs Pd	-	0.72 (0.29 to 1.76)		4.29 (0.51 to 35.86)	
P-value	-	0.4700		0.1787	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.7 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (14.4)	11 (13.3)	5 (7.9)	8 (11.3)	0.8035
Number (%) of patients censored	77 (85.6)	72 (86.7)	58 (92.1)	63 (88.7)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	14.69 (10.743 to NC)	NC (10.021 to NC)	NC (10.842 to NC)	NC (12.320 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8147		0.9028	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.41 to 2.03)		1.07 (0.35 to 3.29)	
P-value	-	0.8152		0.9028	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_detpl_auto_de_i_t_x.rtf (08APR2021 14:43)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	22 (14.6)	21 (13.8)	0.9890
Number (%) of patients censored	1 (50.0)	2 (100.0)	129 (85.4)	131 (86.2)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	1.08 (1.084 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (1.084 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.084 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.7512	
Hazard ratio (95% CI) vs Pd	-			0.91 (0.50 to 1.65)	
P-value	-	0.9990		0.7512	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_impl_allt_de_i_t_x.rtf (08APR2021 14:43)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (100.0)	57 (37.7)	58 (38.2)	0.9767
Number (%) of patients censored	2 (100.0)	0 (0.0)	94 (62.3)	94 (61.8)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	2.04 (2.037 to 3.187)	3.06 (2.136 to 3.844)	4.24 (2.201 to 5.749)	
Median (95% CI)	NC (NC to NC)	2.61 (2.037 to 3.187)	NC (11.302 to NC)	NC (12.320 to NC)	
75% quantile (95% CI)	NC (NC to NC)	3.19 (2.037 to 3.187)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.6337	
Hazard ratio (95% CI) vs Pd	-			0.91 (0.63 to 1.32)	
P-value	-	0.9991		0.6333	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	12 (7.9)	14 (9.2)	0.9886
Number (%) of patients censored	1 (50.0)	2 (100.0)	139 (92.1)	138 (90.8)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	3.19 (3.187 to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
Median (95% CI)	NC (3.187 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (3.187 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.8599	
Hazard ratio (95% CI) vs Pd	-			1.07 (0.50 to 2.32)	
P-value	-	0.9990		0.8602	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	18 (11.9)	19 (12.5)	1.0000
Number (%) of patients censored	2 (100.0)	2 (100.0)	133 (88.1)	133 (87.5)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	14.69 (10.973 to NC)	NC (12.747 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.8602	
Hazard ratio (95% CI) vs Pd	-			0.94 (0.49 to 1.80)	
P-value	-			0.8600	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (14.9)	13 (12.5)	5 (12.2)	4 (12.1)	0.9528
Number (%) of patients censored	86 (85.1)	91 (87.5)	36 (87.8)	29 (87.9)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (7.951 to NC)	NC (NC to NC)	NC (2.825 to NC)	NC (1.347 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5483		0.9904	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.38 to 1.67)		0.99 (0.27 to 3.70)	
P-value	-	0.5490		0.9904	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (40.6)	40 (38.5)	13 (31.7)	15 (45.5)	0.5249
Number (%) of patients censored	60 (59.4)	64 (61.5)	28 (68.3)	18 (54.5)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	2.99 (2.103 to 3.844)	4.70 (2.201 to 6.538)	3.22 (1.150 to NC)	2.17 (1.051 to 5.585)	
Median (95% CI)	14.00 (7.458 to NC)	NC (10.251 to NC)	NC (3.745 to NC)	13.21 (3.318 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.207 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4399		0.3651	
Hazard ratio (95% CI) vs Pd	-	0.84 (0.54 to 1.30)		1.41 (0.67 to 2.96)	
P-value	-	0.4404		0.3674	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (7.9)	10 (9.6)	3 (7.3)	2 (6.1)	0.7835
Number (%) of patients censored	93 (92.1)	94 (90.4)	38 (92.7)	31 (93.9)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8358		0.8179	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.43 to 2.80)		0.81 (0.14 to 4.85)	
P-value	-	0.8365		0.8182	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (15.8)	11 (10.6)	2 (4.9)	6 (18.2)	0.1256
Number (%) of patients censored	85 (84.2)	93 (89.4)	39 (95.1)	27 (81.8)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	13.34 (10.743 to NC)	NC (12.747 to NC)	NC (NC to NC)	12.32 (5.585 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.320 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1403		0.0971	
Hazard ratio (95% CI) vs Pd	-	0.56 (0.26 to 1.22)		3.56 (0.72 to 17.67)	
P-value	-	0.1454		0.1203	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_detpl_semm_de_i_t_x.rtf (08APR2021 14:44)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (15.0)	13 (12.7)	8 (15.4)	8 (15.7)	0.7497
Number (%) of patients censored	85 (85.0)	89 (87.3)	44 (84.6)	43 (84.3)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (7.951 to NC)	NC (NC to NC)	NC (1.741 to NC)	NC (1.643 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5659		0.9957	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.38 to 1.69)		1.00 (0.37 to 2.66)	
P-value	-	0.5666		0.9957	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_impl_dghc_de_i_t_x.rtf (08APR2021 14:43)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (41.0)	38 (37.3)	16 (30.8)	21 (41.2)	0.2222
Number (%) of patients censored	59 (59.0)	64 (62.7)	36 (69.2)	30 (58.8)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	2.99 (2.103 to 3.844)	4.70 (2.398 to 8.246)	3.22 (1.971 to NC)	3.32 (1.248 to 5.585)	
Median (95% CI)	14.00 (7.458 to NC)	NC (10.678 to NC)	NC (5.224 to NC)	13.21 (4.797 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3040		0.4141	
Hazard ratio (95% CI) vs Pd	-	0.79 (0.51 to 1.23)		1.31 (0.68 to 2.51)	
P-value	-	0.3051		0.4155	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (8.0)	10 (9.8)	5 (9.6)	4 (7.8)	0.6078
Number (%) of patients censored	92 (92.0)	92 (90.2)	47 (90.4)	47 (92.2)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8224		0.7138	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.44 to 2.82)		0.78 (0.21 to 2.91)	
P-value	-	0.8232		0.7145	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (16.0)	10 (9.8)	2 (3.8)	8 (15.7)	0.0226
Number (%) of patients censored	84 (84.0)	92 (90.2)	50 (96.2)	43 (84.3)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	13.34 (10.743 to NC)	NC (12.747 to NC)	NC (NC to NC)	NC (8.115 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0949		0.0582	
Hazard ratio (95% CI) vs Pd	-	0.52 (0.23 to 1.14)		3.99 (0.85 to 18.82)	
P-value	-	0.1010		0.0799	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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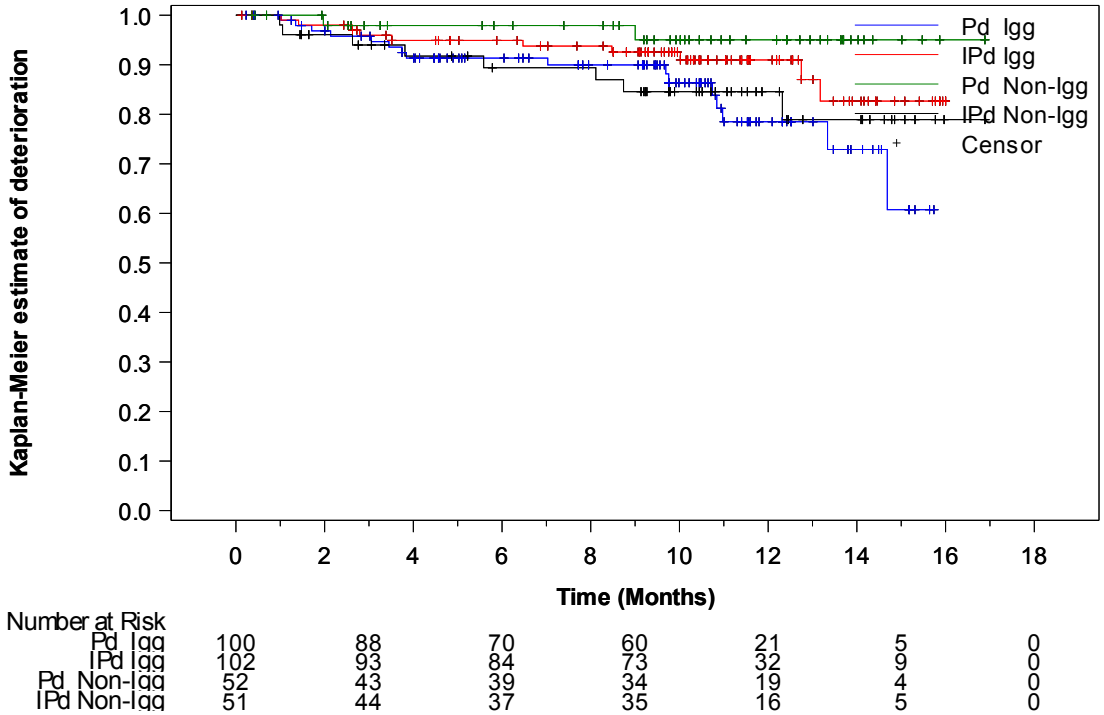
16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.7 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to MM type at initial diagnosis (LOCF) - Kaplan-Meier curve - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_detpl_dghc_de_i_f_x.rtf (08APR2021 14:37)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (20.0)	4 (28.6)	21 (14.7)	17 (12.1)	0.5924
Number (%) of patients censored	8 (80.0)	10 (71.4)	122 (85.3)	123 (87.9)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (0.986 to NC)	1.38 (0.986 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (0.986 to NC)	NC (1.084 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7147		0.4648	
Hazard ratio (95% CI) vs Pd	-	1.37 (0.25 to 7.49)		0.79 (0.42 to 1.49)	
P-value	-	0.7159		0.4659	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (30.0)	3 (21.4)	54 (37.8)	57 (40.7)	0.2944
Number (%) of patients censored	7 (70.0)	11 (78.6)	89 (62.2)	83 (59.3)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	3.06 (2.825 to NC)	10.25 (1.906 to NC)	3.06 (2.103 to 3.844)	3.68 (2.037 to 5.552)	
Median (95% CI)	NC (2.825 to NC)	NC (10.251 to NC)	NC (11.302 to NC)	13.63 (8.476 to NC)	
75% quantile (95% CI)	NC (3.384 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1780		0.9077	
Hazard ratio (95% CI) vs Pd	-	0.31 (0.05 to 1.87)		1.02 (0.70 to 1.48)	
P-value	-	0.2022		0.9077	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	3 (21.4)	12 (8.4)	11 (7.9)	0.6210
Number (%) of patients censored	9 (90.0)	11 (78.6)	131 (91.6)	129 (92.1)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (3.745 to NC)	14.82 (0.986 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (3.745 to NC)	NC (14.817 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8554		0.7786	
Hazard ratio (95% CI) vs Pd	-	1.25 (0.11 to 13.82)		0.89 (0.39 to 2.02)	
P-value	-	0.8557		0.7787	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	0 (0.0)	17 (11.9)	19 (13.6)	0.9853
Number (%) of patients censored	9 (90.0)	14 (100.0)	126 (88.1)	121 (86.4)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (3.055 to NC)	NC (NC to NC)	14.69 (13.339 to NC)	NC (12.747 to NC)	
Median (95% CI)	NC (3.055 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.8282	
Hazard ratio (95% CI) vs Pd	-			1.08 (0.56 to 2.07)	
P-value	-	0.9985		0.8284	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (15.6)	10 (11.5)	8 (16.3)	9 (16.4)	0.6767
Number (%) of patients censored	81 (84.4)	77 (88.5)	41 (83.7)	46 (83.6)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (3.844 to NC)	NC (NC to NC)	NC (1.741 to NC)	NC (2.858 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3912		0.8480	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.32 to 1.57)		0.91 (0.35 to 2.36)	
P-value	-	0.3936		0.8474	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (37.5)	34 (39.1)	20 (40.8)	23 (41.8)	0.8286
Number (%) of patients censored	60 (62.5)	53 (60.9)	29 (59.2)	32 (58.2)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	3.06 (1.971 to 5.027)	4.70 (2.398 to 6.538)	2.96 (1.971 to 3.844)	3.09 (1.380 to 5.585)	
Median (95% CI)	NC (11.302 to NC)	13.63 (10.678 to NC)	NC (3.450 to NC)	12.32 (5.585 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8636		0.6644	
Hazard ratio (95% CI) vs Pd	-	0.96 (0.60 to 1.53)		0.88 (0.48 to 1.60)	
P-value	-	0.8637		0.6647	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_detl_crcl_de_i_t_x.rtf (08APR2021 14:43)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (9.4)	6 (6.9)	4 (8.2)	6 (10.9)	0.5276
Number (%) of patients censored	87 (90.6)	81 (93.1)	45 (91.8)	49 (89.1)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	14.82 (14.817 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4782		0.9949	
Hazard ratio (95% CI) vs Pd	-	0.69 (0.25 to 1.94)		1.00 (0.27 to 3.74)	
P-value	-	0.4808		0.9949	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (9.4)	9 (10.3)	8 (16.3)	9 (16.4)	0.7463
Number (%) of patients censored	87 (90.6)	78 (89.7)	41 (83.7)	46 (83.6)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (13.339 to NC)	NC (12.747 to NC)	10.84 (3.844 to NC)	NC (8.115 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (10.842 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9743		0.7504	
Hazard ratio (95% CI) vs Pd	-	1.02 (0.40 to 2.56)		0.86 (0.33 to 2.22)	
P-value	-	0.9743		0.7506	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	23 (15.2)	20 (13.2)	0.9838
Number (%) of patients censored	2 (100.0)	1 (50.0)	128 (84.8)	132 (86.8)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	0.99 (0.986 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.5138	
Hazard ratio (95% CI) vs Pd	-			0.82 (0.45 to 1.49)	
P-value	-	0.9990		0.5147	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	56 (37.1)	59 (38.8)	0.6087
Number (%) of patients censored	1 (50.0)	1 (50.0)	95 (62.9)	93 (61.2)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	2.10 (2.103 to NC)	12.32 (NC to NC)	3.09 (2.136 to 3.844)	3.88 (2.168 to 5.585)	
Median (95% CI)	NC (2.103 to NC)	12.32 (NC to NC)	NC (11.302 to NC)	NC (10.678 to NC)	
75% quantile (95% CI)	NC (2.103 to NC)	12.32 (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.8536	
Hazard ratio (95% CI) vs Pd	-			0.97 (0.67 to 1.39)	
P-value	-	0.9990		0.8535	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	13 (8.6)	13 (8.6)	0.9912
Number (%) of patients censored	2 (100.0)	1 (50.0)	138 (91.4)	139 (91.4)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	0.99 (0.986 to NC)	NC (NC to NC)	NC (14.817 to NC)	
Median (95% CI)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.8180	
Hazard ratio (95% CI) vs Pd	-			0.91 (0.42 to 1.97)	
P-value	-	0.9990		0.8178	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	18 (11.9)	18 (11.8)	0.9873
Number (%) of patients censored	2 (100.0)	1 (50.0)	133 (88.1)	134 (88.2)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	12.32 (NC to NC)	14.69 (13.339 to NC)	NC (13.175 to NC)	
Median (95% CI)	NC (NC to NC)	12.32 (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	12.32 (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.7553	
Hazard ratio (95% CI) vs Pd	-			0.90 (0.47 to 1.73)	
P-value	-			0.7549	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (15.7)	13 (11.0)	5 (13.2)	8 (22.2)	0.1412
Number (%) of patients censored	97 (84.3)	105 (89.0)	33 (86.8)	28 (77.8)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (7.951 to NC)	NC (NC to NC)	NC (1.610 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2387		0.3122	
Hazard ratio (95% CI) vs Pd	-	0.65 (0.32 to 1.33)		1.77 (0.58 to 5.40)	
P-value	-	0.2423		0.3187	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (34.8)	45 (38.1)	17 (44.7)	15 (41.7)	0.7804
Number (%) of patients censored	75 (65.2)	73 (61.9)	21 (55.3)	21 (58.3)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	3.38 (2.595 to 5.618)	4.24 (2.398 to 6.144)	2.10 (0.986 to 4.271)	2.20 (1.051 to 8.246)	
Median (95% CI)	NC (11.302 to NC)	NC (12.320 to NC)	11.47 (2.990 to NC)	13.21 (4.698 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.207 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9610		0.7309	
Hazard ratio (95% CI) vs Pd	-	0.99 (0.65 to 1.52)		0.89 (0.44 to 1.77)	
P-value	-	0.9610		0.7314	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (8.7)	9 (7.6)	3 (7.9)	5 (13.9)	0.2967
Number (%) of patients censored	105 (91.3)	109 (92.4)	35 (92.1)	31 (86.1)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	12.52 (4.764 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.517 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5738		0.3537	
Hazard ratio (95% CI) vs Pd	-	0.77 (0.31 to 1.91)		1.95 (0.46 to 8.20)	
P-value	-	0.5749		0.3624	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (11.3)	15 (12.7)	5 (13.2)	4 (11.1)	0.9821
Number (%) of patients censored	102 (88.7)	103 (87.3)	33 (86.8)	32 (88.9)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (10.842 to NC)	NC (12.747 to NC)	14.69 (7.031 to NC)	NC (8.115 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.339 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9196		0.9928	
Hazard ratio (95% CI) vs Pd	-	0.96 (0.46 to 2.03)		0.99 (0.26 to 3.76)	
P-value	-	0.9195		0.9928	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (15.3)	19 (12.9)	1 (11.1)	2 (28.6)	0.2636
Number (%) of patients censored	122 (84.7)	128 (87.1)	8 (88.9)	5 (71.4)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.951 to NC)	1.05 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.951 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4664		0.3066	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.43 to 1.47)		3.29 (0.29 to 36.85)	
P-value	-	0.4672		0.3338	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	52 (36.1)	58 (39.5)	5 (55.6)	2 (28.6)	0.2976
Number (%) of patients censored	92 (63.9)	89 (60.5)	4 (44.4)	5 (71.4)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	3.22 (2.136 to 5.027)	4.11 (2.168 to 5.585)	2.14 (0.986 to 3.088)	3.09 (2.037 to NC)	
Median (95% CI)	NC (11.302 to NC)	NC (10.678 to NC)	3.09 (0.986 to NC)	NC (2.037 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.088 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9778		0.3111	
Hazard ratio (95% CI) vs Pd	-	1.01 (0.69 to 1.46)		0.44 (0.08 to 2.26)	
P-value	-	0.9778		0.3246	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_detl_refr1_de_i_t_x.rtf (08APR2021 14:43)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (9.0)	12 (8.2)	0 (0.0)	2 (28.6)	0.9882
Number (%) of patients censored	131 (91.0)	135 (91.8)	9 (100.0)	5 (71.4)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	2.83 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5958		0.0954	
Hazard ratio (95% CI) vs Pd	-	0.81 (0.37 to 1.78)			
P-value	-	0.5965		0.9977	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (10.4)	19 (12.9)	3 (33.3)	0 (0.0)	0.9854
Number (%) of patients censored	129 (89.6)	128 (87.1)	6 (66.7)	7 (100.0)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (13.339 to NC)	NC (12.747 to NC)	14.69 (3.450 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	14.69 (3.450 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7651		0.2600	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.56 to 2.18)			
P-value	-	0.7662		0.9978	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (15.9)	14 (15.1)	9 (13.8)	7 (11.5)	0.7198
Number (%) of patients censored	74 (84.1)	79 (84.9)	56 (86.2)	54 (88.5)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (2.825 to NC)	NC (6.571 to NC)	NC (3.844 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8672		0.5533	
Hazard ratio (95% CI) vs Pd	-	0.94 (0.45 to 1.97)		0.74 (0.28 to 1.99)	
P-value	-	0.8671		0.5547	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (37.5)	34 (36.6)	24 (36.9)	26 (42.6)	0.9548
Number (%) of patients censored	55 (62.5)	59 (63.4)	41 (63.1)	35 (57.4)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	3.45 (2.103 to 6.538)	4.70 (2.037 to 8.246)	2.83 (1.347 to 3.384)	3.68 (1.906 to 5.585)	
Median (95% CI)	NC (7.885 to NC)	NC (10.678 to NC)	NC (3.515 to NC)	13.63 (5.585 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7966		0.9352	
Hazard ratio (95% CI) vs Pd	-	0.94 (0.58 to 1.52)		0.98 (0.56 to 1.70)	
P-value	-	0.7964		0.9352	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (11.4)	8 (8.6)	3 (4.6)	6 (9.8)	0.2630
Number (%) of patients censored	78 (88.6)	85 (91.4)	62 (95.4)	55 (90.2)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (12.517 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4787		0.3383	
Hazard ratio (95% CI) vs Pd	-	0.72 (0.28 to 1.82)		1.94 (0.49 to 7.77)	
P-value	-	0.4808		0.3472	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.3.1 Nausea and vomiting
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (10.2)	12 (12.9)	9 (13.8)	7 (11.5)	0.3499
Number (%) of patients censored	79 (89.8)	81 (87.1)	56 (86.2)	54 (88.5)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (13.339 to NC)	NC (12.320 to NC)	14.69 (9.758 to NC)	NC (13.175 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6188		0.3839	
Hazard ratio (95% CI) vs Pd	-	1.24 (0.52 to 2.95)		0.65 (0.24 to 1.74)	
P-value	-	0.6195		0.3876	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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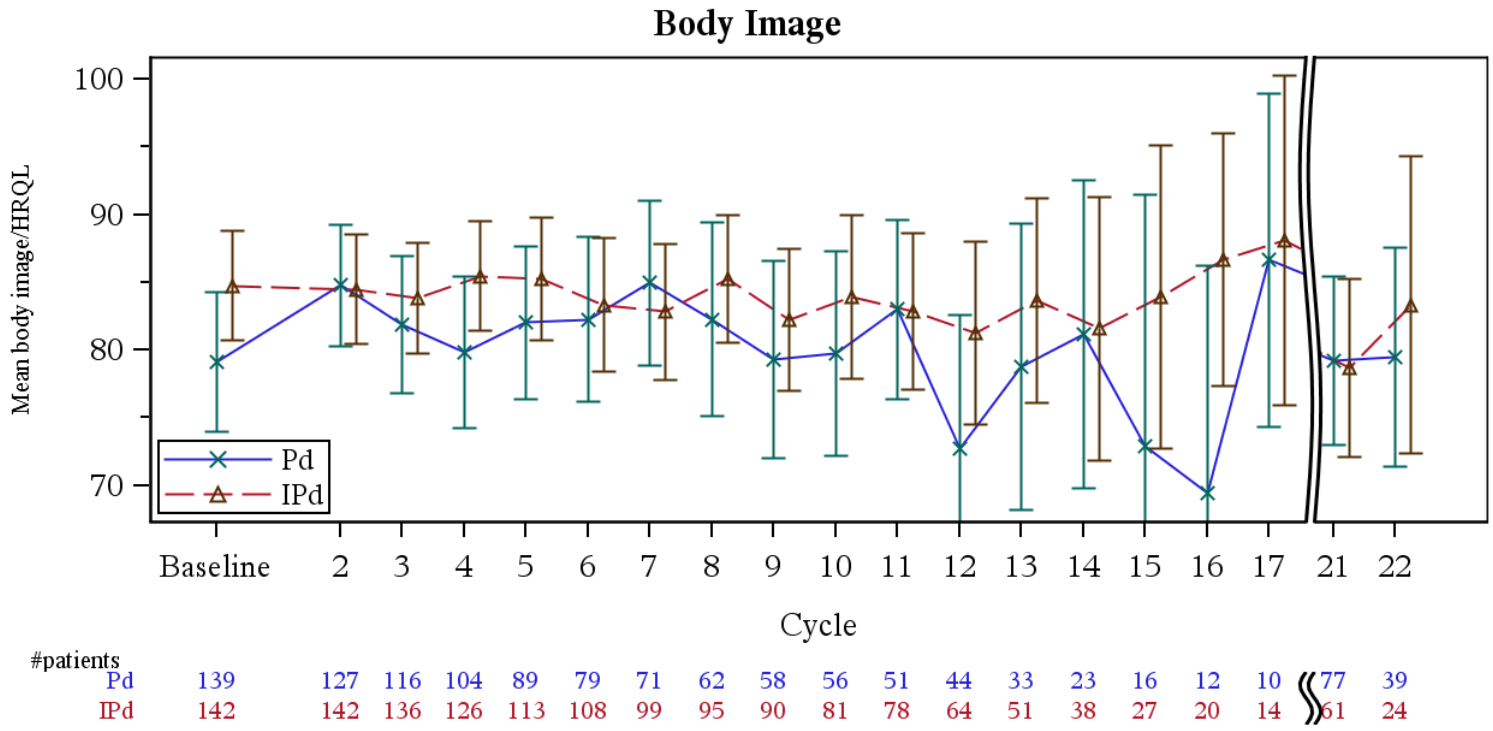
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Body image
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-MY20 - Mean and 95% CI for body image score over time - ITT population



A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Body image
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-MY20 - Time to first improvement by 15 pt in body image (LOCF) - ITT population

First improvement 15 points Body image (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	40 (26.1)	31 (20.1)
Number (%) of patients censored	113 (73.9)	123 (79.9)
Kaplan-Meier estimates of body image in months		
25% quantile (95% CI)	5.26 (1.150 to NC)	NC (3.285 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1266
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.70 (0.43 to 1.11)
P-value	-	0.1291
Probability (95% CI)[c]		
2 Months	0.21 (0.150 to 0.282)	0.17 (0.111 to 0.228)
4 Months	0.24 (0.175 to 0.313)	0.19 (0.128 to 0.251)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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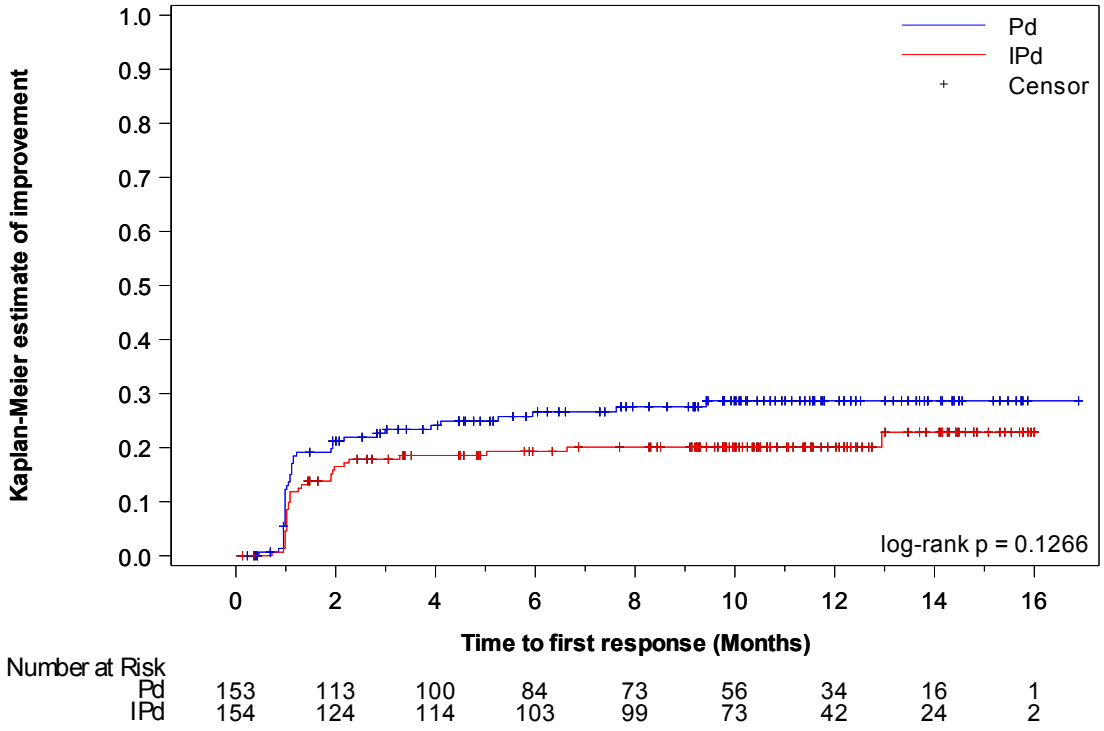
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Body image
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-MY20 - Time to first improvement by 15 pt in body image - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imp15l_de_i_f_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Body image
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-MY20 - Time to first deterioration by 15 pt in body image (LOCF) - ITT population

First deterioration 15 points Body image (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	60 (39.2)	67 (43.5)
Number (%) of patients censored	93 (60.8)	87 (56.5)
Kaplan-Meier estimates of body image in months		
25% quantile (95% CI)	3.15 (2.825 to 4.665)	2.20 (1.906 to 2.990)
Median (95% CI)	13.90 (7.458 to NC)	12.06 (8.246 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4566
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.14 (0.80 to 1.62)
P-value	-	0.4573
Probability (95% CI)[c]		
2 Months	0.89 (0.827 to 0.931)	0.80 (0.729 to 0.857)
4 Months	0.69 (0.609 to 0.763)	0.65 (0.569 to 0.722)

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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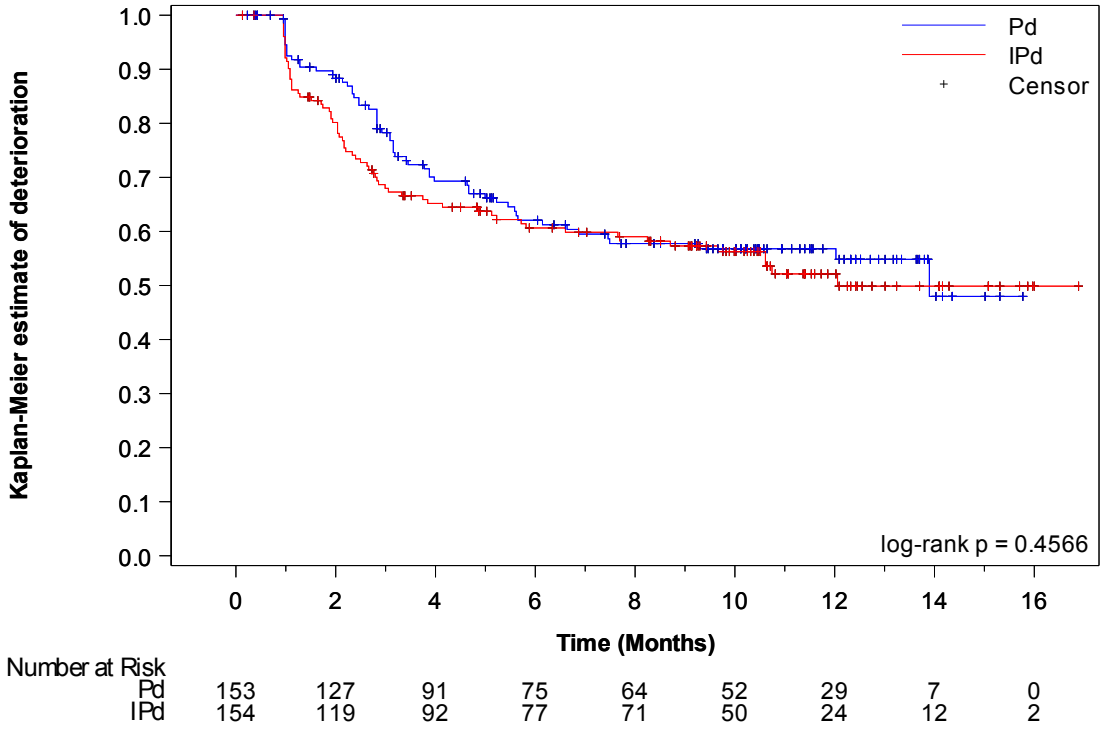
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Body image
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-MY20 - Time to first deterioration by 15 pt in body image - Kaplan-Meier curve (LOCF) - ITT population



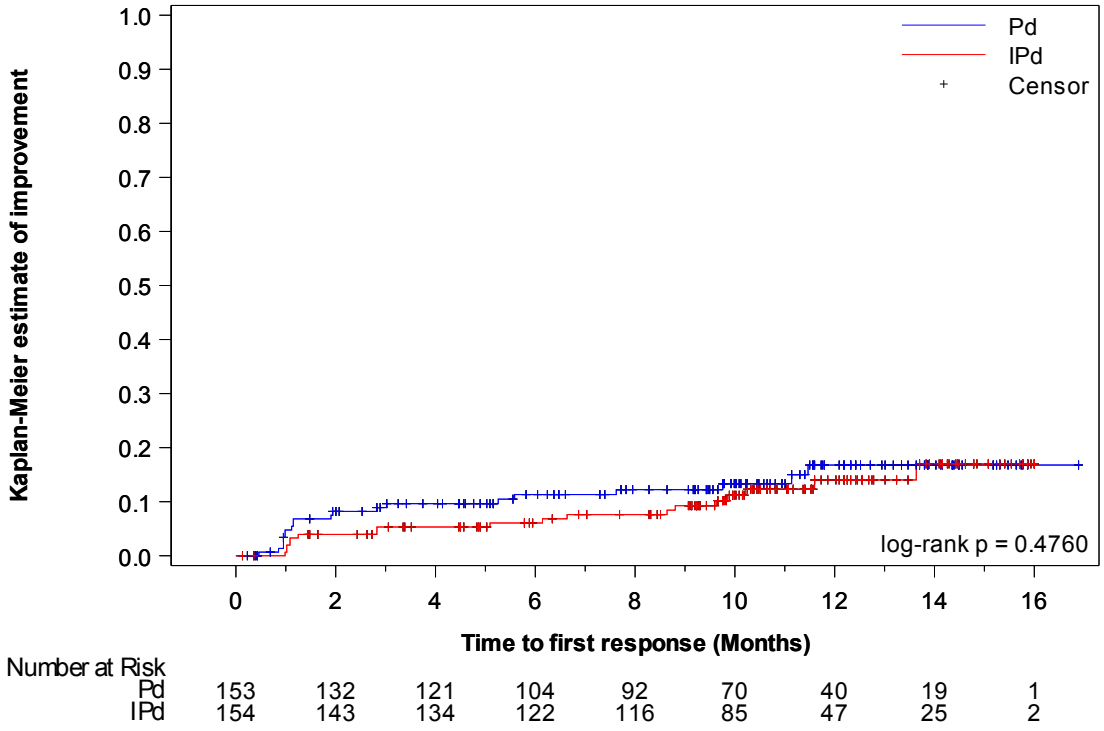
A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_det15l_de_i_f_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Body image
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-MY20 - Time until permanent improvement by 15 pt in body image (LOCF) - ITT population

First permanent improvement 15 points Body image (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	20 (13.1)	18 (11.7)
Number (%) of patients censored	133 (86.9)	136 (88.3)
Kaplan-Meier estimates of body image in months		
25% quantile (95% CI)	NC (11.466 to NC)	NC (13.634 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4760
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.79 (0.42 to 1.50)
P-value	-	0.4769
Probability (95% CI)[c]		
2 Months	0.08 (0.045 to 0.134)	0.04 (0.016 to 0.079)
4 Months	0.10 (0.055 to 0.151)	0.05 (0.025 to 0.097)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imp15pl_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Body image
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-MY20 - Time until permanent improvement by 15 pt in body image - Kaplan-Meier curve (LOCF) - ITT population



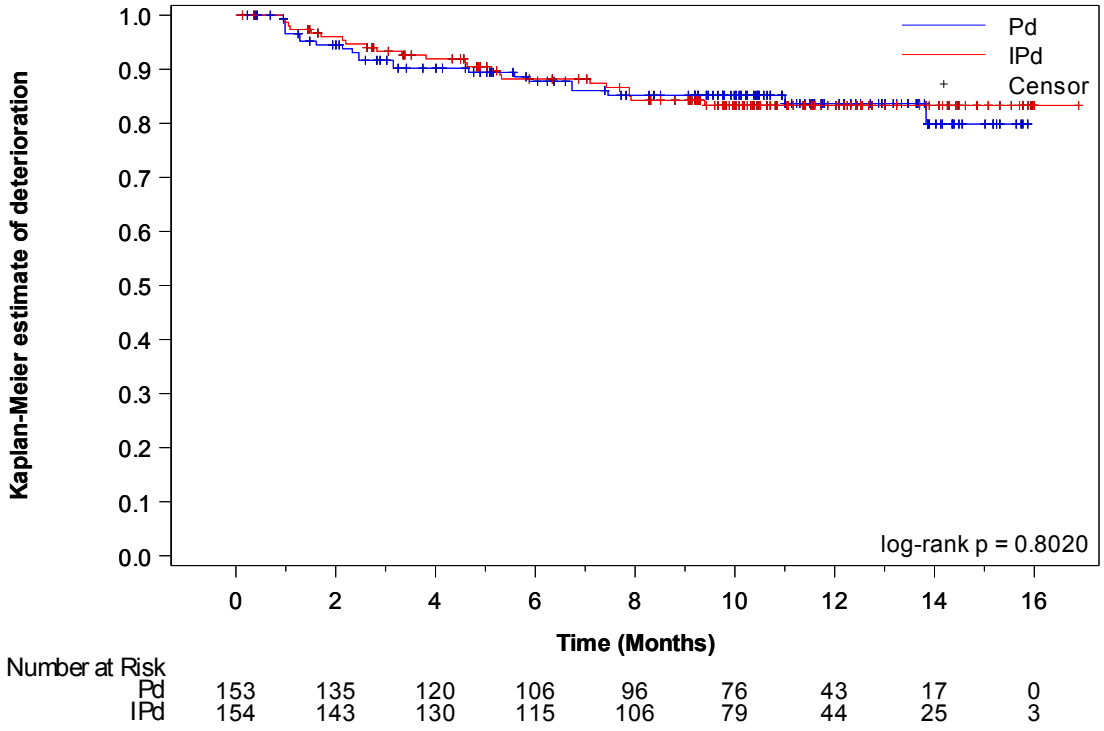
A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imp15pl_de_i_f_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Body image
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-MY20 - Time until permanent deterioration by 15 pt in body image (LOCF) - ITT population

First permanent deterioration 15 points Body image (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	22 (14.4)	23 (14.9)
Number (%) of patients censored	131 (85.6)	131 (85.1)
Kaplan-Meier estimates of body image in months		
25% quantile (95% CI)	NC (13.832 to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8020
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.93 (0.52 to 1.67)
P-value	-	0.8017
Probability (95% CI)[c]		
2 Months	0.95 (0.893 to 0.972)	0.96 (0.914 to 0.982)
4 Months	0.90 (0.840 to 0.941)	0.92 (0.862 to 0.953)

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_det15pl_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Body image
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-MY20 - Time until permanent deterioration by 15 pt in body image - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_det15pl_de_i_f_x.rtf (08APR2021 15:29)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (30.0)	9 (16.7)	12 (22.2)	13 (19.1)	7 (24.1)	9 (28.1)	0.4037
Number (%) of patients censored	49 (70.0)	45 (83.3)	42 (77.8)	55 (80.9)	22 (75.9)	23 (71.9)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	2.83 (0.986 to NC)	NC (1.906 to NC)	NC (1.051 to NC)	NC (1.446 to NC)	4.11 (0.986 to NC)	4.40 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0634		0.5698		0.8527	
Hazard ratio (95% CI) vs Pd	-	0.49 (0.22 to 1.06)		0.80 (0.36 to 1.75)		1.10 (0.41 to 2.95)	
P-value	-	0.0694		0.5706		0.8527	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_impl_age_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (40.0)	23 (42.6)	23 (42.6)	32 (47.1)	9 (31.0)	12 (37.5)	0.9879
Number (%) of patients censored	42 (60.0)	31 (57.4)	31 (57.4)	36 (52.9)	20 (69.0)	20 (62.5)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	3.15 (2.136 to 6.637)	2.14 (0.986 to 4.140)	3.15 (2.464 to 4.632)	2.50 (1.281 to 3.844)	3.98 (0.986 to NC)	2.25 (1.084 to NC)	
Median (95% CI)	13.90 (7.458 to NC)	NC (2.990 to NC)	NC (3.877 to NC)	10.61 (5.125 to NC)	NC (4.665 to NC)	NC (3.318 to NC)	
75% quantile (95% CI)	NC (13.897 to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.057 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7115		0.5471		0.8390	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.64 to 1.93)		1.18 (0.69 to 2.02)		1.09 (0.46 to 2.60)	
P-value	-	0.7117		0.5476		0.8391	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detl_age_de_i_t_x.rtf (08APR2021 14:57)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (15.7)	5 (9.3)	4 (7.4)	9 (13.2)	5 (17.2)	4 (12.5)	0.3186
Number (%) of patients censored	59 (84.3)	49 (90.7)	50 (92.6)	59 (86.8)	24 (82.8)	28 (87.5)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	NC (9.758 to NC)	NC (10.218 to NC)	NC (NC to NC)	NC (11.598 to NC)	NC (0.986 to NC)	NC (6.637 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2473		0.3878		0.4112	
Hazard ratio (95% CI) vs Pd	-	0.54 (0.19 to 1.56)		1.67 (0.51 to 5.43)		0.58 (0.16 to 2.16)	
P-value	-	0.2549		0.3931		0.4170	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imppl_age_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (14.3)	9 (16.7)	6 (11.1)	8 (11.8)	6 (20.7)	6 (18.8)	0.8383
Number (%) of patients censored	60 (85.7)	45 (83.3)	48 (88.9)	60 (88.2)	23 (79.3)	26 (81.3)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	NC (11.006 to NC)	NC (5.322 to NC)	NC (6.735 to NC)	NC (NC to NC)	5.88 (1.281 to NC)	NC (5.125 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.881 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7952		0.9736		0.5576	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.46 to 2.77)		1.02 (0.35 to 2.93)		0.71 (0.23 to 2.22)	
P-value	-	0.7953		0.9736		0.5594	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_age_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (25.7)	17 (16.7)	14 (26.9)	14 (26.9)	0.3346
Number (%) of patients censored	75 (74.3)	85 (83.3)	38 (73.1)	38 (73.1)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	5.26 (1.117 to NC)	NC (6.637 to NC)	4.11 (1.051 to NC)	2.17 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0797		0.8507	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.32 to 1.07)		0.93 (0.44 to 1.95)	
P-value	-	0.0833		0.8506	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	41 (40.6)	47 (46.1)	19 (36.5)	20 (38.5)	0.5294
Number (%) of patients censored	60 (59.4)	55 (53.9)	33 (63.5)	32 (61.5)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	3.88 (2.464 to 5.585)	2.17 (1.248 to 2.990)	2.92 (2.136 to 3.877)	2.79 (1.741 to 8.706)	
Median (95% CI)	13.90 (6.867 to NC)	10.61 (5.717 to NC)	NC (3.450 to NC)	NC (5.125 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3433		0.9661	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.81 to 1.86)		0.99 (0.53 to 1.85)	
P-value	-	0.3442		0.9661	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detl_plne_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	13 (12.9)	11 (10.8)	7 (13.5)	7 (13.5)	0.8234
Number (%) of patients censored	88 (87.1)	91 (89.2)	45 (86.5)	45 (86.5)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (11.138 to NC)	NC (13.634 to NC)	NC (9.758 to NC)	NC (8.805 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5022		0.7876	
Hazard ratio (95% CI) vs Pd	-	0.76 (0.34 to 1.70)		0.87 (0.30 to 2.47)	
P-value	-	0.5031		0.7878	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imppl_plne_de_i_t_x.rtf (08APR2021 14:59)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (16.8)	14 (13.7)	5 (9.6)	9 (17.3)	0.2725
Number (%) of patients censored	84 (83.2)	88 (86.3)	47 (90.4)	43 (82.7)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (7.458 to NC)	NC (NC to NC)	NC (6.735 to NC)	NC (7.097 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4746		0.4311	
Hazard ratio (95% CI) vs Pd	-	0.77 (0.38 to 1.57)		1.55 (0.52 to 4.61)	
P-value	-	0.4764		0.4348	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_plne_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (18.6)	19 (21.3)	27 (32.5)	12 (18.5)	0.1004
Number (%) of patients censored	57 (81.4)	70 (78.7)	56 (67.5)	53 (81.5)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (1.117 to NC)	12.94 (1.446 to NC)	1.94 (1.018 to 9.429)	NC (2.168 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7921		0.0301	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.54 to 2.23)		0.48 (0.24 to 0.95)	
P-value	-	0.7921		0.0340	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_impl_sex_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (40.0)	40 (44.9)	32 (38.6)	27 (41.5)	0.8005
Number (%) of patients censored	42 (60.0)	49 (55.1)	51 (61.4)	38 (58.5)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	3.15 (2.464 to 5.454)	2.50 (1.938 to 3.318)	3.42 (2.333 to 5.224)	1.79 (1.051 to 5.717)	
Median (95% CI)	NC (5.585 to NC)	12.06 (5.224 to NC)	13.90 (6.867 to NC)	NC (5.815 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.897 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4624		0.8173	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.74 to 1.94)		1.06 (0.64 to 1.78)	
P-value	-	0.4630		0.8167	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detl_sex_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (11.4)	12 (13.5)	12 (14.5)	6 (9.2)	0.2971
Number (%) of patients censored	62 (88.6)	77 (86.5)	71 (85.5)	59 (90.8)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.598 to NC)	NC (9.758 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8315		0.2192	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.45 to 2.70)		0.55 (0.20 to 1.46)	
P-value	-	0.8316		0.2263	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imppl_sex_de_i_t_x.rtf (08APR2021 14:59)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (12.9)	15 (16.9)	13 (15.7)	8 (12.3)	0.2743
Number (%) of patients censored	61 (87.1)	74 (83.1)	70 (84.3)	57 (87.7)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (13.832 to NC)	NC (7.097 to NC)	NC (6.735 to NC)	NC (9.396 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5132		0.3834	
Hazard ratio (95% CI) vs Pd	-	1.32 (0.58 to 3.01)		0.68 (0.28 to 1.64)	
P-value	-	0.5146		0.3864	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_sex_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (23.8)	22 (18.6)	8 (42.1)	8 (33.3)	0.9688
Number (%) of patients censored	96 (76.2)	96 (81.4)	11 (57.9)	16 (66.7)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	7.62 (1.906 to NC)	NC (5.027 to NC)	1.12 (0.986 to NC)	1.91 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.117 to NC)	NC (2.168 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2260		0.4430	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.41 to 1.24)		0.68 (0.26 to 1.82)	
P-value	-	0.2282		0.4458	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_impl_race_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	52 (41.3)	54 (45.8)	8 (42.1)	9 (37.5)	0.7495
Number (%) of patients censored	74 (58.7)	64 (54.2)	11 (57.9)	15 (62.5)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	3.09 (2.366 to 3.877)	2.17 (1.248 to 3.055)	4.67 (0.953 to NC)	2.83 (0.986 to NC)	
Median (95% CI)	13.90 (6.144 to NC)	12.06 (7.655 to NC)	NC (4.665 to NC)	NC (4.862 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5909		0.9764	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.76 to 1.63)		0.99 (0.38 to 2.56)	
P-value	-	0.5907		0.9764	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (11.1)	14 (11.9)	4 (21.1)	3 (12.5)	0.4288
Number (%) of patients censored	112 (88.9)	104 (88.1)	15 (78.9)	21 (87.5)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (0.986 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9132		0.4604	
Hazard ratio (95% CI) vs Pd	-	0.96 (0.46 to 2.01)		0.57 (0.13 to 2.56)	
P-value	-	0.9132		0.4661	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imppl_race_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (15.1)	17 (14.4)	3 (15.8)	5 (20.8)	0.5872
Number (%) of patients censored	107 (84.9)	101 (85.6)	16 (84.2)	19 (79.2)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (11.006 to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6861		0.6105	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.45 to 1.68)		1.45 (0.35 to 6.07)	
P-value	-	0.6865		0.6125	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_race_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	2 (50.0)	33 (24.6)	27 (20.8)	0.6865
Number (%) of patients censored	2 (66.7)	2 (50.0)	101 (75.4)	103 (79.2)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	5.26 (NC to NC)	1.02 (1.018 to NC)	7.62 (1.150 to NC)	NC (2.267 to NC)	
Median (95% CI)	5.26 (NC to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	5.26 (NC to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	1.0000		0.3392	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.09 to 11.03)		0.78 (0.47 to 1.30)	
P-value	-	1.0000		0.3404	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_impl_ethn_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	2 (50.0)	56 (41.8)	56 (43.1)	0.7676
Number (%) of patients censored	2 (66.7)	2 (50.0)	78 (58.2)	74 (56.9)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	2.78 (2.497 to NC)	3.09 (2.464 to 3.975)	2.33 (1.741 to 4.140)	
Median (95% CI)	NC (1.281 to NC)	NC (2.497 to NC)	13.90 (6.637 to NC)	NC (8.706 to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (2.497 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7741		0.9086	
Hazard ratio (95% CI) vs Pd	-	0.70 (0.06 to 7.92)		1.02 (0.71 to 1.48)	
P-value	-	0.7751		0.9086	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detl_ethn_de_i_t_x.rtf (08APR2021 14:57)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	2 (50.0)	15 (11.2)	14 (10.8)	0.6926
Number (%) of patients censored	2 (66.7)	2 (50.0)	119 (88.8)	116 (89.2)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	5.26 (NC to NC)	10.61 (9.626 to NC)	NC (NC to NC)	NC (13.634 to NC)	
Median (95% CI)	5.26 (NC to NC)	11.60 (9.626 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	5.26 (NC to NC)	NC (9.626 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0455		0.7311	
Hazard ratio (95% CI) vs Pd	-			0.88 (0.42 to 1.82)	
P-value	-	0.9986		0.7311	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	0 (0.0)	20 (14.9)	20 (15.4)	0.9892
Number (%) of patients censored	2 (66.7)	4 (100.0)	114 (85.1)	110 (84.6)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (NC to NC)	NC (13.832 to NC)	NC (9.396 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.8845	
Hazard ratio (95% CI) vs Pd	-			0.96 (0.51 to 1.78)	
P-value	-	0.9990		0.8845	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_ethn_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	18 (23.7)	5 (9.1)	8 (40.0)	6 (21.4)	2 (40.0)	2 (28.6)	6 (40.0)	7 (33.3)	6 (16.2)	11 (25.6)	0.2593
Number (%) of patients censored	58 (76.3)	50 (90.9)	12 (60.0)	22 (78.6)	3 (60.0)	5 (71.4)	9 (60.0)	14 (66.7)	31 (83.8)	32 (74.4)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	7.62 (1.084 to NC)	NC (NC to NC)	1.22 (0.953 to 9.429)	NC (0.986 to NC)	5.26 (0.986 to NC)	1.25 (1.018 to NC)	1.15 (0.986 to NC)	2.17 (1.018 to NC)	NC (1.117 to NC)	12.94 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.216 to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (1.018 to NC)	NC (1.117 to NC)	NC (2.168 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_impl_greg_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.0216		0.1533		0.7019		0.6270		0.3725	
Hazard ratio (95% CI) vs Pd	-	0.33 (0.12 to 0.89)		0.47 (0.16 to 1.36)		0.68 (0.10 to 4.87)		0.76 (0.26 to 2.27)		1.57 (0.58 to 4.24)	
P-value	-	0.0289		0.1631		0.7036		0.6281		0.3765	
Improvement probability (95% CI)[b]											
2 Months	0.196 (0.114 to 0.295)	0.074 (0.024 to 0.164)	0.263 (0.096 to 0.468)	0.214 (0.087 to 0.378)	0.200 (0.008 to 0.582)	0.286 (0.041 to 0.612)	0.400 (0.165 to 0.628)	0.241 (0.088 to 0.436)	0.140 (0.051 to 0.272)	0.192 (0.090 to 0.322)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_impl_greg_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	23 (30.3)	24 (43.6)	9 (45.0)	13 (46.4)	2 (40.0)	2 (28.6)	6 (40.0)	8 (38.1)	20 (54.1)	20 (46.5)	0.3194
Number (%) of patients censored	53 (69.7)	31 (56.4)	11 (55.0)	15 (53.6)	3 (60.0)	5 (71.4)	9 (60.0)	13 (61.9)	17 (45.9)	23 (53.5)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	4.63 (2.825 to 13.897)	2.04 (1.018 to 2.760)	3.42 (0.986 to 7.491)	2.79 (0.953 to 10.612)	6.87 (2.825 to NC)	3.06 (2.628 to NC)	4.67 (1.117 to NC)	4.86 (0.986 to NC)	2.33 (0.986 to 2.924)	2.17 (1.117 to 4.140)	
Median (95% CI)	NC (13.897 to NC)	NC (2.760 to NC)	NC (3.417 to NC)	10.74 (3.844 to NC)	NC (2.825 to NC)	NC (2.628 to NC)	NC (3.154 to NC)	NC (4.862 to NC)	5.45 (2.661 to NC)	12.06 (2.858 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.743 to NC)	NC (2.825 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.458 to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detl_greg_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.0642		0.8823		0.7737		0.8925		0.2718	
Hazard ratio (95% CI) vs Pd	-	1.71 (0.96 to 3.04)		1.07 (0.45 to 2.50)		0.75 (0.11 to 5.34)		1.08 (0.37 to 3.10)		0.71 (0.38 to 1.32)	
P-value	-	0.0674		0.8829		0.7744		0.8930		0.2741	
Deterioration probability (95% CI)[b]											
2 Months	0.915 (0.821 to 0.961)	0.759 (0.621 to 0.852)	0.895 (0.641 to 0.973)	0.821 (0.623 to 0.921)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.933 (0.613 to 0.990)	0.902 (0.662 to 0.975)	0.804 (0.632 to 0.901)	0.760 (0.599 to 0.863)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detl_greg_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	10 (13.2)	3 (5.5)	3 (15.0)	4 (14.3)	1 (20.0)	2 (28.6)	3 (20.0)	2 (9.5)	3 (8.1)	7 (16.3)	0.5049
Number (%) of patients censored	66 (86.8)	52 (94.5)	17 (85.0)	24 (85.7)	4 (80.0)	5 (71.4)	12 (80.0)	19 (90.5)	34 (91.9)	36 (83.7)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (11.138 to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (1.018 to NC)	NC (5.257 to NC)	11.60 (1.248 to NC)	NC (1.150 to NC)	NC (1.084 to NC)	NC (NC to NC)	NC (8.805 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.257 to NC)	11.60 (1.248 to NC)	NC (1.938 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imppl_greg_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.257 to NC)	NC (11.598 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.1281		0.8933		0.8086		0.4113		0.4787	
Hazard ratio (95% CI) vs Pd	-	0.38 (0.10 to 1.39)		0.90 (0.20 to 4.03)		1.35 (0.12 to 15.02)		0.48 (0.08 to 2.87)		1.62 (0.42 to 6.30)	
P-value	-	0.1431		0.8934		0.8093		0.4217		0.4831	
Improvement probability (95% CI)[b]											

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imppl_greg_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	10 (13.2)	8 (14.5)	3 (15.0)	5 (17.9)	0 (0.0)	1 (14.3)	2 (13.3)	4 (19.0)	7 (18.9)	5 (11.6)	0.7888
Number (%) of patients censored	66 (86.8)	47 (85.5)	17 (85.0)	23 (82.1)	5 (100.0)	6 (85.7)	13 (86.7)	17 (81.0)	30 (81.1)	38 (88.4)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (11.006 to NC)	NC (5.125 to NC)	NC (0.986 to NC)	NC (3.318 to NC)	NC (NC to NC)	NC (2.628 to NC)	NC (3.154 to NC)	NC (2.825 to NC)	NC (1.610 to NC)	NC (9.396 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.628 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_greg_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.8211		0.8849		0.3980		0.5835		0.2521	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.44 to 2.82)		1.11 (0.27 to 4.65)				1.60 (0.29 to 8.74)		0.52 (0.16 to 1.63)	
P-value	-	0.8212		0.8850		0.9984		0.5870		0.2606	
Deterioration probability (95% CI)[b]											
2 Months	0.958 (0.874 to 0.986)	0.944 (0.838 to 0.982)	0.947 (0.681 to 0.992)	0.964 (0.772 to 0.995)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.888 (0.729 to 0.956)	0.952 (0.821 to 0.988)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_greg_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (22.7)	11 (14.3)	18 (32.1)	20 (26.0)	0.5119
Number (%) of patients censored	75 (77.3)	66 (85.7)	38 (67.9)	57 (74.0)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	7.62 (1.117 to NC)	NC (6.637 to NC)	1.94 (1.051 to NC)	5.03 (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1064		0.4002	
Hazard ratio (95% CI) vs Pd	-	0.56 (0.27 to 1.15)		0.76 (0.40 to 1.44)	
P-value	-	0.1115		0.4017	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (34.0)	32 (41.6)	27 (48.2)	35 (45.5)	0.3061
Number (%) of patients censored	64 (66.0)	45 (58.4)	29 (51.8)	42 (54.5)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	3.45 (2.464 to 6.144)	2.14 (1.117 to 2.990)	3.09 (2.333 to 4.665)	2.66 (1.873 to 4.862)	
Median (95% CI)	NC (12.025 to NC)	NC (5.224 to NC)	7.49 (4.665 to NC)	12.06 (5.815 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2703		0.7148	
Hazard ratio (95% CI) vs Pd	-	1.31 (0.81 to 2.14)		0.91 (0.55 to 1.51)	
P-value	-	0.2717		0.7149	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (13.4)	7 (9.1)	7 (12.5)	11 (14.3)	0.4144
Number (%) of patients censored	84 (86.6)	70 (90.9)	49 (87.5)	66 (85.7)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (11.138 to NC)	NC (11.598 to NC)	NC (3.023 to NC)	NC (9.856 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2716		0.9091	
Hazard ratio (95% CI) vs Pd	-	0.60 (0.24 to 1.51)		1.06 (0.41 to 2.73)	
P-value	-	0.2769		0.9096	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (12.4)	13 (16.9)	10 (17.9)	10 (13.0)	0.2362
Number (%) of patients censored	85 (87.6)	64 (83.1)	46 (82.1)	67 (87.0)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (13.832 to NC)	NC (5.290 to NC)	NC (4.665 to NC)	NC (7.918 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4597		0.3512	
Hazard ratio (95% CI) vs Pd	-	1.34 (0.61 to 2.94)		0.66 (0.27 to 1.59)	
P-value	-	0.4614		0.3546	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_rreg_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (23.4)	28 (20.3)	8 (50.0)	3 (18.8)	0.1866
Number (%) of patients censored	105 (76.6)	110 (79.7)	8 (50.0)	13 (81.3)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	9.43 (1.938 to NC)	NC (2.267 to NC)	0.99 (0.953 to 1.906)	NC (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	1.94 (0.986 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.938 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3777		0.0767	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.48 to 1.32)		0.32 (0.08 to 1.21)	
P-value	-	0.3782		0.0932	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_impl_ecog_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	56 (40.9)	59 (42.8)	4 (25.0)	8 (50.0)	0.1645
Number (%) of patients censored	81 (59.1)	79 (57.2)	12 (75.0)	8 (50.0)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	3.15 (2.825 to 4.665)	2.33 (1.873 to 3.745)	2.00 (0.986 to NC)	1.91 (1.018 to 3.055)	
Median (95% CI)	13.90 (6.637 to NC)	NC (9.659 to NC)	NC (1.281 to NC)	3.06 (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.055 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7915		0.1780	
Hazard ratio (95% CI) vs Pd	-	1.05 (0.73 to 1.51)		2.24 (0.67 to 7.50)	
P-value	-	0.7916		0.1895	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (10.9)	15 (10.9)	5 (31.3)	3 (18.8)	0.4851
Number (%) of patients censored	122 (89.1)	123 (89.1)	11 (68.8)	13 (81.3)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	1.91 (0.953 to NC)	11.60 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.150 to NC)	NC (11.598 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.598 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7479		0.3622	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.43 to 1.82)		0.52 (0.12 to 2.18)	
P-value	-	0.7475		0.3707	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (13.1)	20 (14.5)	4 (25.0)	3 (18.8)	0.7001
Number (%) of patients censored	119 (86.9)	118 (85.5)	12 (75.0)	13 (81.3)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	13.83 (0.986 to NC)	NC (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	13.83 (1.281 to NC)	NC (4.600 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.832 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9420		0.6664	
Hazard ratio (95% CI) vs Pd	-	1.02 (0.54 to 1.94)		0.72 (0.16 to 3.22)	
P-value	-	0.9420		0.6678	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (33.3)	10 (15.6)	10 (17.9)	10 (18.9)	11 (25.6)	10 (29.4)	0.2019
Number (%) of patients censored	34 (66.7)	54 (84.4)	46 (82.1)	43 (81.1)	32 (74.4)	24 (70.6)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	1.22 (0.986 to NC)	NC (5.027 to NC)	NC (2.168 to NC)	NC (1.906 to NC)	1.12 (0.986 to NC)	1.05 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0259		0.9578		0.8567	
Hazard ratio (95% CI) vs Pd	-	0.42 (0.19 to 0.92)		1.02 (0.43 to 2.46)		1.08 (0.46 to 2.55)	
P-value	-	0.0308		0.9578		0.8563	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (45.1)	33 (51.6)	23 (41.1)	22 (41.5)	13 (30.2)	10 (29.4)	0.6081
Number (%) of patients censored	28 (54.9)	31 (48.4)	33 (58.9)	31 (58.5)	30 (69.8)	24 (70.6)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	3.88 (2.004 to 6.637)	2.04 (1.117 to 3.055)	3.09 (2.333 to 3.877)	2.50 (1.051 to 3.844)	3.15 (1.281 to 12.025)	5.13 (1.051 to NC)	
Median (95% CI)	13.90 (5.651 to NC)	10.61 (4.140 to NC)	NC (3.778 to NC)	NC (3.844 to NC)	NC (4.665 to NC)	NC (5.224 to NC)	
75% quantile (95% CI)	NC (13.897 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3153		0.8129		0.7038	
Hazard ratio (95% CI) vs Pd	-	1.31 (0.77 to 2.24)		1.07 (0.60 to 1.93)		0.85 (0.37 to 1.95)	
P-value	-	0.3168		0.8127		0.7041	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (15.7)	7 (10.9)	6 (10.7)	5 (9.4)	4 (9.3)	5 (14.7)	0.7584
Number (%) of patients censored	43 (84.3)	57 (89.1)	50 (89.3)	48 (90.6)	39 (90.7)	29 (85.3)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	NC (7.622 to NC)	NC (11.598 to NC)	NC (9.758 to NC)	NC (NC to NC)	NC (11.138 to NC)	NC (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.138 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5028		0.7230		0.7060	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.26 to 1.95)		0.81 (0.25 to 2.65)		1.29 (0.34 to 4.82)	
P-value	-	0.5049		0.7236		0.7067	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imppl_seiss_de_i_t_x.rtf (08APR2021 14:59)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (17.6)	12 (18.8)	3 (5.4)	9 (17.0)	10 (23.3)	1 (2.9)	0.0161
Number (%) of patients censored	42 (82.4)	52 (81.3)	53 (94.6)	44 (83.0)	33 (76.7)	33 (97.1)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	NC (7.458 to NC)	NC (7.885 to NC)	NC (NC to NC)	NC (4.632 to NC)	5.59 (1.281 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.735 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7396		0.0647		0.0052	
Hazard ratio (95% CI) vs Pd	-	1.16 (0.49 to 2.75)		3.21 (0.87 to 11.84)		0.09 (0.01 to 0.74)	
P-value	-	0.7398		0.0806		0.0247	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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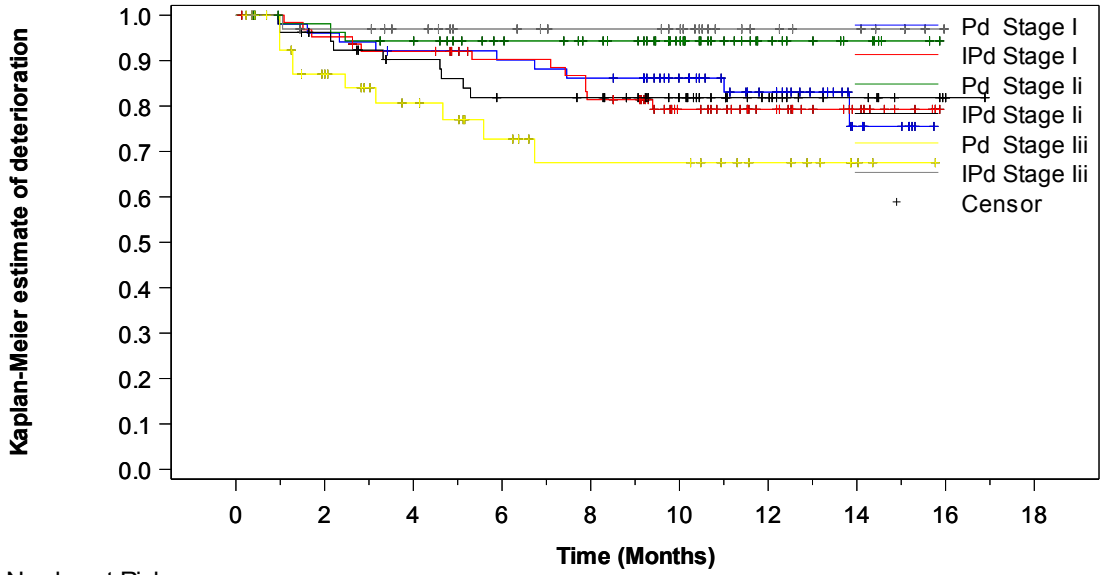
16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to ISS staging (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd Stage I	51	48	45	42	23	6	0
IPd Stage I	64	57	51	44	20	5	0
Pd Stage Ii	56	50	42	36	12	2	0
IPd Stage Ii	53	45	38	33	16	5	0
Pd Stage Iii	43	26	17	13	8	1	0
IPd Stage Iii	34	31	24	21	8	4	0

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_seiss_de_i_f_x.rtf (08APR2021 14:35)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (29.0)	6 (15.4)	24 (24.5)	22 (22.2)	7 (29.2)	3 (18.8)	0.5632
Number (%) of patients censored	22 (71.0)	33 (84.6)	74 (75.5)	77 (77.8)	17 (70.8)	13 (81.3)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	2.99 (0.986 to NC)	NC (1.906 to NC)	7.62 (1.938 to NC)	NC (1.906 to NC)	1.08 (0.986 to NC)	NC (0.723 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.084 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1649		0.6026		0.4254	
Hazard ratio (95% CI) vs Pd	-	0.49 (0.17 to 1.37)		0.86 (0.48 to 1.53)		0.58 (0.15 to 2.25)	
P-value	-	0.1740		0.6027		0.4312	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_impl_seriss_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (45.2)	17 (43.6)	42 (42.9)	47 (47.5)	4 (16.7)	3 (18.8)	0.7695
Number (%) of patients censored	17 (54.8)	22 (56.4)	56 (57.1)	52 (52.5)	20 (83.3)	13 (81.3)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	2.83 (1.117 to 6.867)	3.06 (1.873 to 10.612)	3.19 (2.464 to 4.665)	2.14 (1.117 to 2.661)	3.15 (1.281 to NC)	NC (0.953 to NC)	
Median (95% CI)	13.90 (3.877 to NC)	12.06 (8.246 to NC)	NC (5.585 to NC)	10.74 (3.844 to NC)	NC (3.154 to NC)	NC (3.745 to NC)	
75% quantile (95% CI)	NC (13.897 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8398		0.3080		0.8856	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.46 to 1.89)		1.24 (0.82 to 1.88)		0.90 (0.20 to 4.04)	
P-value	-	0.8391		0.3081		0.8857	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (9.7)	5 (12.8)	14 (14.3)	12 (12.1)	3 (12.5)	1 (6.3)	0.6340
Number (%) of patients censored	28 (90.3)	34 (87.2)	84 (85.7)	87 (87.9)	21 (87.5)	15 (93.8)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	NC (11.466 to NC)	NC (9.856 to NC)	NC (9.758 to NC)	NC (NC to NC)	11.14 (0.986 to NC)	NC (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.138 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.138 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6988		0.4982		0.3439	
Hazard ratio (95% CI) vs Pd	-	1.33 (0.32 to 5.56)		0.77 (0.35 to 1.66)		0.34 (0.03 to 3.46)	
P-value	-	0.6997		0.4988		0.3636	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (16.1)	4 (10.3)	14 (14.3)	19 (19.2)	3 (12.5)	0 (0.0)	0.6583
Number (%) of patients censored	26 (83.9)	35 (89.7)	84 (85.7)	80 (80.8)	21 (87.5)	16 (100.0)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	13.83 (5.881 to NC)	NC (7.885 to NC)	NC (11.006 to NC)	NC (5.322 to NC)	NC (1.281 to NC)	NC (NC to NC)	
Median (95% CI)	NC (13.832 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5144		0.4363		0.0918	
Hazard ratio (95% CI) vs Pd	-	0.65 (0.17 to 2.41)		1.31 (0.66 to 2.62)			
P-value	-	0.5177		0.4377		0.9972	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (21.7)	0 (0.0)	27 (28.4)	27 (22.9)	0.9882
Number (%) of patients censored	18 (78.3)	14 (100.0)	68 (71.6)	91 (77.1)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (0.953 to NC)	NC (NC to NC)	2.83 (1.084 to NC)	12.94 (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0650		0.2687	
Hazard ratio (95% CI) vs Pd	-			0.74 (0.43 to 1.26)	
P-value	-	0.9965		0.2704	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (34.8)	4 (28.6)	36 (37.9)	55 (46.6)	0.4734
Number (%) of patients censored	15 (65.2)	10 (71.4)	59 (62.1)	63 (53.4)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	3.09 (1.281 to 5.224)	3.32 (0.986 to NC)	3.19 (2.004 to 5.651)	2.17 (1.248 to 2.858)	
Median (95% CI)	5.22 (3.088 to NC)	10.74 (2.990 to NC)	13.90 (12.025 to NC)	12.06 (5.717 to NC)	
75% quantile (95% CI)	NC (5.224 to NC)	NC (10.743 to NC)	NC (13.897 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6414		0.2590	
Hazard ratio (95% CI) vs Pd	-	0.75 (0.23 to 2.51)		1.27 (0.84 to 1.94)	
P-value	-	0.6425		0.2601	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (17.4)	0 (0.0)	13 (13.7)	16 (13.6)	0.9876
Number (%) of patients censored	19 (82.6)	14 (100.0)	82 (86.3)	102 (86.4)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	11.14 (0.953 to NC)	NC (NC to NC)	NC (11.466 to NC)	NC (11.598 to NC)	
Median (95% CI)	NC (11.138 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1259		0.7241	
Hazard ratio (95% CI) vs Pd	-			0.88 (0.42 to 1.82)	
P-value	-	0.9970		0.7243	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (8.7)	2 (14.3)	15 (15.8)	19 (16.1)	0.5592
Number (%) of patients censored	21 (91.3)	12 (85.7)	80 (84.2)	99 (83.9)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (1.281 to NC)	NC (0.986 to NC)	NC (7.458 to NC)	NC (9.396 to NC)	
Median (95% CI)	NC (11.006 to NC)	NC (3.318 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5030		0.8844	
Hazard ratio (95% CI) vs Pd	-	1.96 (0.26 to 14.48)		0.95 (0.48 to 1.87)	
P-value	-	0.5103		0.8841	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_cyto_de_i_t_x.rtf (20APR2021 10:51)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (30.6)	4 (16.7)	19 (24.4)	22 (21.4)	0.4152
Number (%) of patients censored	25 (69.4)	20 (83.3)	59 (75.6)	81 (78.6)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	1.15 (0.953 to NC)	NC (1.018 to NC)	5.95 (1.084 to NC)	NC (1.906 to NC)	
Median (95% CI)	NC (5.257 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1757		0.4935	
Hazard ratio (95% CI) vs Pd	-	0.46 (0.15 to 1.45)		0.81 (0.44 to 1.49)	
P-value	-	0.1864		0.4943	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_impl_care_de_i_t_x.rtf (20APR2021 10:51)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (30.6)	9 (37.5)	33 (42.3)	48 (46.6)	0.6157
Number (%) of patients censored	25 (69.4)	15 (62.5)	45 (57.7)	55 (53.4)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	3.98 (2.825 to 7.491)	2.99 (0.986 to 10.743)	2.83 (1.281 to 4.665)	2.14 (1.117 to 2.858)	
Median (95% CI)	NC (5.224 to NC)	10.74 (2.990 to NC)	13.90 (5.454 to NC)	12.06 (5.224 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.743 to NC)	NC (13.897 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4552		0.6914	
Hazard ratio (95% CI) vs Pd	-	1.40 (0.58 to 3.38)		1.09 (0.70 to 1.70)	
P-value	-	0.4572		0.6915	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detl_care_de_i_t_x.rtf (20APR2021 10:51)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (22.2)	1 (4.2)	8 (10.3)	14 (13.6)	0.0945
Number (%) of patients censored	28 (77.8)	23 (95.8)	70 (89.7)	89 (86.4)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	11.14 (1.117 to NC)	NC (6.637 to NC)	NC (11.466 to NC)	NC (11.598 to NC)	
Median (95% CI)	NC (11.138 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0534		0.7144	
Hazard ratio (95% CI) vs Pd	-	0.17 (0.02 to 1.32)		1.18 (0.49 to 2.80)	
P-value	-	0.0900		0.7147	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imppl_care_de_i_t_x.rtf (20APR2021 10:51)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (5.6)	4 (16.7)	15 (19.2)	17 (16.5)	0.1439
Number (%) of patients censored	34 (94.4)	20 (83.3)	63 (80.8)	86 (83.5)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (11.006 to NC)	9.40 (0.986 to NC)	13.83 (5.881 to NC)	NC (7.885 to NC)	
Median (95% CI)	NC (NC to NC)	NC (9.396 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1387		0.5097	
Hazard ratio (95% CI) vs Pd	-	3.36 (0.61 to 18.49)		0.79 (0.40 to 1.59)	
P-value	-	0.1629		0.5106	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_care_de_i_t_x.rtf (20APR2021 10:51)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (28.9)	13 (15.7)	14 (22.2)	18 (25.4)	0.1629
Number (%) of patients censored	64 (71.1)	70 (84.3)	49 (77.8)	53 (74.6)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	3.91 (1.084 to NC)	NC (2.267 to NC)	NC (1.117 to NC)	12.94 (1.446 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0405		0.9960	
Hazard ratio (95% CI) vs Pd	-	0.51 (0.26 to 0.98)		1.00 (0.50 to 2.01)	
P-value	-	0.0446		0.9960	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_impl_auto_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (42.2)	32 (38.6)	22 (34.9)	35 (49.3)	0.2610
Number (%) of patients censored	52 (57.8)	51 (61.4)	41 (65.1)	36 (50.7)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	3.15 (2.366 to 5.224)	2.50 (1.938 to 7.655)	3.42 (1.281 to 5.585)	2.04 (1.117 to 2.825)	
Median (95% CI)	13.90 (6.144 to NC)	NC (10.612 to NC)	NC (5.585 to NC)	9.66 (3.745 to NC)	
75% quantile (95% CI)	NC (13.897 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7909		0.1912	
Hazard ratio (95% CI) vs Pd	-	0.94 (0.59 to 1.50)		1.42 (0.84 to 2.43)	
P-value	-	0.7914		0.1935	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (12.2)	8 (9.6)	9 (14.3)	10 (14.1)	0.9934
Number (%) of patients censored	79 (87.8)	75 (90.4)	54 (85.7)	61 (85.9)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (11.466 to NC)	NC (13.634 to NC)	NC (3.023 to NC)	NC (9.856 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6136		0.6565	
Hazard ratio (95% CI) vs Pd	-	0.79 (0.32 to 1.97)		0.82 (0.33 to 2.01)	
P-value	-	0.6144		0.6571	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (14.4)	11 (13.3)	9 (14.3)	12 (16.9)	0.8973
Number (%) of patients censored	77 (85.6)	72 (86.7)	54 (85.7)	59 (83.1)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (11.006 to NC)	NC (7.885 to NC)	NC (5.585 to NC)	NC (7.885 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8459		0.9705	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.41 to 2.06)		1.02 (0.43 to 2.41)	
P-value	-	0.8463		0.9706	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_auto_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	39 (25.8)	30 (19.7)	0.9024
Number (%) of patients censored	1 (50.0)	1 (50.0)	112 (74.2)	122 (80.3)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	1.08 (1.084 to NC)	2.27 (2.267 to NC)	5.26 (1.150 to NC)	NC (3.285 to NC)	
Median (95% CI)	NC (1.084 to NC)	NC (2.267 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.084 to NC)	NC (2.267 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.1340	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		0.70 (0.43 to 1.12)	
P-value	-	0.8092		0.1361	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	60 (39.7)	66 (43.4)	0.9832
Number (%) of patients censored	2 (100.0)	1 (50.0)	91 (60.3)	86 (56.6)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	2.04 (2.037 to NC)	3.15 (2.825 to 4.665)	2.33 (1.873 to 3.055)	
Median (95% CI)	NC (NC to NC)	NC (2.037 to NC)	13.90 (6.867 to NC)	12.06 (8.246 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (2.037 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.5414	
Hazard ratio (95% CI) vs Pd	-			1.12 (0.79 to 1.58)	
P-value	-	0.9990		0.5418	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	19 (12.6)	18 (11.8)	0.9856
Number (%) of patients censored	1 (50.0)	2 (100.0)	132 (87.4)	134 (88.2)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	11.47 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.634 to NC)	
Median (95% CI)	11.47 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	11.47 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.6105	
Hazard ratio (95% CI) vs Pd	-			0.85 (0.44 to 1.61)	
P-value	-			0.6101	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imppl_allt_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	22 (14.6)	23 (15.1)	1.0000
Number (%) of patients censored	2 (100.0)	2 (100.0)	129 (85.4)	129 (84.9)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.832 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.9139	
Hazard ratio (95% CI) vs Pd	-			0.97 (0.54 to 1.74)	
P-value	-			0.9139	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_allt_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (29.7)	22 (21.2)	8 (19.5)	7 (21.2)	0.6769
Number (%) of patients censored	71 (70.3)	82 (78.8)	33 (80.5)	26 (78.8)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	2.83 (1.084 to NC)	NC (1.938 to NC)	NC (1.117 to NC)	NC (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1039		0.9377	
Hazard ratio (95% CI) vs Pd	-	0.64 (0.37 to 1.10)		1.04 (0.38 to 2.87)	
P-value	-	0.1071		0.9376	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_impl_semm_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (42.6)	48 (46.2)	12 (29.3)	10 (30.3)	0.8937
Number (%) of patients censored	58 (57.4)	56 (53.8)	29 (70.7)	23 (69.7)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	3.09 (2.333 to 3.877)	2.50 (1.708 to 3.318)	5.22 (2.464 to NC)	2.20 (1.117 to NC)	
Median (95% CI)	13.90 (5.618 to NC)	10.74 (5.717 to NC)	NC (9.298 to NC)	NC (5.815 to NC)	
75% quantile (95% CI)	NC (13.897 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7333		0.8272	
Hazard ratio (95% CI) vs Pd	-	1.07 (0.71 to 1.62)		1.10 (0.47 to 2.54)	
P-value	-	0.7337		0.8272	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detl_semm_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (14.9)	12 (11.5)	4 (9.8)	4 (12.1)	0.7700
Number (%) of patients censored	86 (85.1)	92 (88.5)	37 (90.2)	29 (87.9)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (11.138 to NC)	NC (11.598 to NC)	NC (5.257 to NC)	NC (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3168		0.8542	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.32 to 1.45)		1.14 (0.28 to 4.56)	
P-value	-	0.3197		0.8539	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imppl_semm_de_i_t_x.rtf (08APR2021 14:59)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (14.9)	17 (16.3)	6 (14.6)	3 (9.1)	0.5538
Number (%) of patients censored	86 (85.1)	87 (83.7)	35 (85.4)	30 (90.9)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (7.458 to NC)	NC (7.885 to NC)	NC (2.464 to NC)	NC (9.396 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9062		0.3592	
Hazard ratio (95% CI) vs Pd	-	1.04 (0.52 to 2.09)		0.53 (0.13 to 2.12)	
P-value	-	0.9063		0.3673	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (30.0)	22 (21.6)	10 (19.2)	9 (17.6)	0.5884
Number (%) of patients censored	70 (70.0)	80 (78.4)	42 (80.8)	42 (82.4)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	2.17 (1.084 to NC)	12.94 (1.938 to NC)	NC (1.117 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1109		0.7257	
Hazard ratio (95% CI) vs Pd	-	0.64 (0.37 to 1.11)		0.85 (0.35 to 2.10)	
P-value	-	0.1139		0.7259	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (42.0)	46 (45.1)	17 (32.7)	20 (39.2)	0.5746
Number (%) of patients censored	58 (58.0)	56 (54.9)	35 (67.3)	31 (60.8)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	3.09 (2.333 to 3.975)	2.71 (1.708 to 3.844)	4.99 (2.464 to 12.025)	2.17 (1.248 to 4.862)	
Median (95% CI)	13.90 (5.618 to NC)	12.06 (6.604 to NC)	NC (9.298 to NC)	NC (4.862 to NC)	
75% quantile (95% CI)	NC (13.897 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8065		0.3779	
Hazard ratio (95% CI) vs Pd	-	1.05 (0.69 to 1.60)		1.34 (0.70 to 2.55)	
P-value	-	0.8067		0.3795	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detl_dghc_de_i_t_x.rtf (08APR2021 14:57)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (15.0)	12 (11.8)	5 (9.6)	6 (11.8)	0.4977
Number (%) of patients censored	85 (85.0)	90 (88.2)	47 (90.4)	45 (88.2)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (11.138 to NC)	NC (11.598 to NC)	NC (NC to NC)	NC (8.805 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3237		0.8523	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.32 to 1.46)		1.12 (0.34 to 3.67)	
P-value	-	0.3266		0.8529	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imppl_dghc_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (15.0)	15 (14.7)	7 (13.5)	7 (13.7)	0.9986
Number (%) of patients censored	85 (85.0)	87 (85.3)	45 (86.5)	44 (86.3)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (7.458 to NC)	NC (7.885 to NC)	NC (4.665 to NC)	NC (7.918 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8233		0.8780	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.45 to 1.89)		0.92 (0.32 to 2.63)	
P-value	-	0.8232		0.8779	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_dghc_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	3 (21.4)	40 (28.0)	28 (20.0)	0.9847
Number (%) of patients censored	10 (100.0)	11 (78.6)	103 (72.0)	112 (80.0)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (1.084 to NC)	3.91 (1.117 to NC)	NC (3.285 to NC)	
Median (95% CI)	NC (NC to NC)	NC (2.267 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1571		0.0818	
Hazard ratio (95% CI) vs Pd	-			0.65 (0.40 to 1.06)	
P-value	-	0.9973		0.0841	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_impl_mri_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (50.0)	6 (42.9)	55 (38.5)	61 (43.6)	0.1410
Number (%) of patients censored	5 (50.0)	8 (57.1)	88 (61.5)	79 (56.4)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	1.94 (0.986 to 2.661)	4.14 (0.986 to 10.743)	3.45 (2.825 to 5.224)	2.17 (1.873 to 2.858)	
Median (95% CI)	2.66 (0.986 to NC)	10.74 (2.661 to NC)	13.90 (7.491 to NC)	NC (7.655 to NC)	
75% quantile (95% CI)	NC (2.333 to NC)	NC (10.743 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2557		0.3084	
Hazard ratio (95% CI) vs Pd	-	0.50 (0.15 to 1.69)		1.21 (0.84 to 1.74)	
P-value	-	0.2640		0.3086	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detl_mri_de_i_t_x.rtf (08APR2021 14:57)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (14.3)	20 (14.0)	16 (11.4)	0.9900
Number (%) of patients censored	10 (100.0)	12 (85.7)	123 (86.0)	124 (88.6)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (1.084 to NC)	NC (11.466 to NC)	NC (13.634 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2957		0.3773	
Hazard ratio (95% CI) vs Pd	-			0.74 (0.39 to 1.44)	
P-value	-	0.9979		0.3790	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (30.0)	1 (7.1)	19 (13.3)	22 (15.7)	0.0713
Number (%) of patients censored	7 (70.0)	13 (92.9)	124 (86.7)	118 (84.3)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	2.33 (0.986 to NC)	NC (7.885 to NC)	NC (13.832 to NC)	NC (9.396 to NC)	
Median (95% CI)	NC (0.986 to NC)	NC (7.885 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0493		0.6763	
Hazard ratio (95% CI) vs Pd	-	0.13 (0.01 to 1.35)		1.14 (0.62 to 2.10)	
P-value	-	0.0883		0.6771	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (28.1)	18 (20.7)	11 (22.4)	12 (21.8)	0.6101
Number (%) of patients censored	69 (71.9)	69 (79.3)	38 (77.6)	43 (78.2)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	4.11 (1.084 to NC)	NC (1.938 to NC)	NC (0.986 to NC)	12.94 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.945 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1862		0.7768	
Hazard ratio (95% CI) vs Pd	-	0.67 (0.37 to 1.22)		0.89 (0.39 to 2.01)	
P-value	-	0.1891		0.7769	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (41.7)	47 (54.0)	20 (40.8)	16 (29.1)	0.0247
Number (%) of patients censored	56 (58.3)	40 (46.0)	29 (59.2)	39 (70.9)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	3.09 (2.333 to 4.994)	1.91 (1.084 to 2.760)	3.15 (1.938 to 5.454)	4.86 (2.168 to NC)	
Median (95% CI)	13.90 (6.144 to NC)	8.25 (3.055 to NC)	12.02 (4.665 to NC)	NC (12.057 to NC)	
75% quantile (95% CI)	NC (13.897 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0871		0.1334	
Hazard ratio (95% CI) vs Pd	-	1.44 (0.95 to 2.20)		0.61 (0.31 to 1.17)	
P-value	-	0.0889		0.1375	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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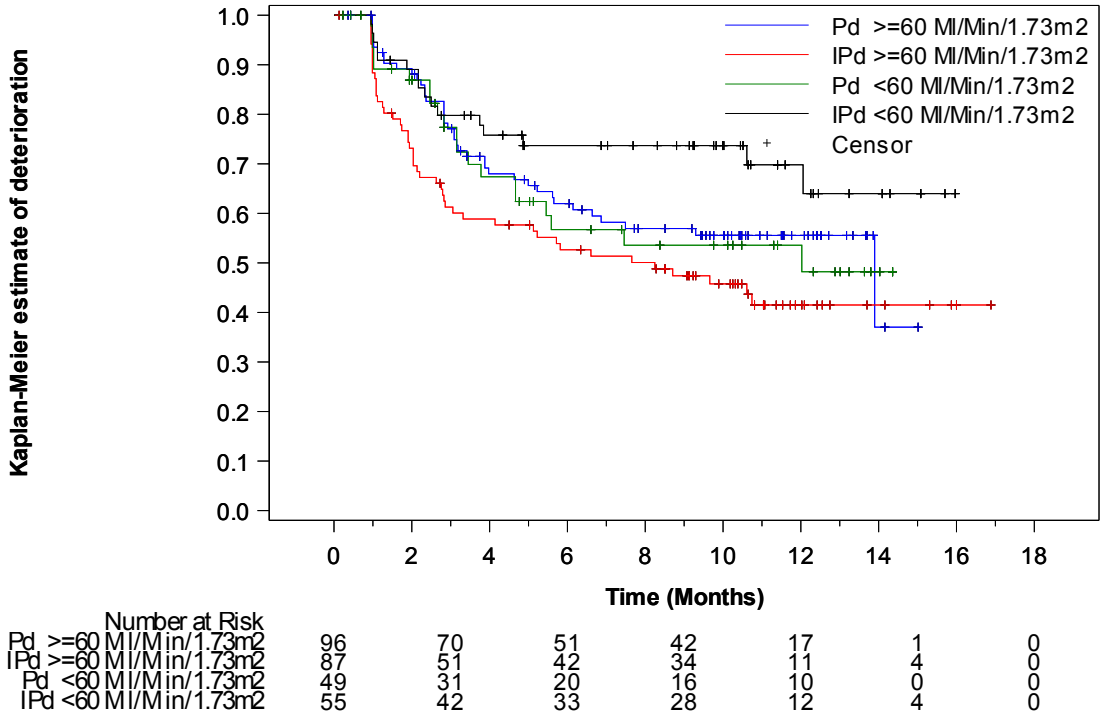
16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to baseline creatinine clearance (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd >=60 Ml/Min/1.73m2	96	70	51	42	17	1	0
IPd >=60 Ml/Min/1.73m2	87	51	42	34	11	4	0
Pd <60 Ml/Min/1.73m2	49	31	20	16	10	0	0
IPd <60 Ml/Min/1.73m2	55	42	33	28	12	4	0

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (12.5)	10 (11.5)	6 (12.2)	7 (12.7)	0.8985
Number (%) of patients censored	84 (87.5)	77 (88.5)	43 (87.8)	48 (87.3)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (11.466 to NC)	NC (11.598 to NC)	NC (5.585 to NC)	NC (9.626 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6721		0.8599	
Hazard ratio (95% CI) vs Pd	-	0.83 (0.36 to 1.93)		0.91 (0.30 to 2.70)	
P-value	-	0.6725		0.8600	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (11.5)	19 (21.8)	11 (22.4)	3 (5.5)	0.0022
Number (%) of patients censored	85 (88.5)	68 (78.2)	38 (77.6)	52 (94.5)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (13.832 to NC)	NC (4.632 to NC)	7.46 (3.154 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0879		0.0040	
Hazard ratio (95% CI) vs Pd	-	1.89 (0.90 to 3.97)		0.19 (0.05 to 0.67)	
P-value	-	0.0933		0.0101	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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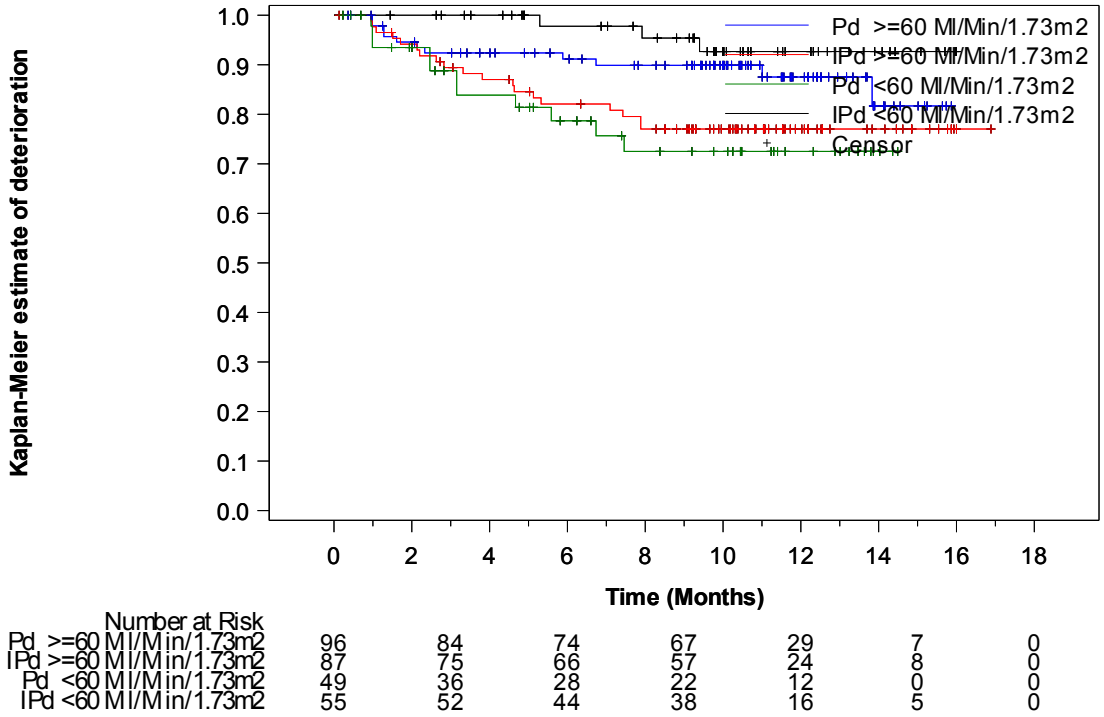
16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.8 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to baseline creatinine clearance (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd >=60 Ml/Min/1.73m2	96	84	74	67	29	7	0
IPd >=60 Ml/Min/1.73m2	87	75	66	57	24	8	0
Pd <60 Ml/Min/1.73m2	49	36	28	22	12	0	0
IPd <60 Ml/Min/1.73m2	55	52	44	38	16	5	0

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (100.0)	40 (26.5)	29 (19.1)	0.9809
Number (%) of patients censored	2 (100.0)	0 (0.0)	111 (73.5)	123 (80.9)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	1.91 (1.906 to 1.971)	4.11 (1.150 to NC)	NC (5.027 to NC)	
Median (95% CI)	NC (NC to NC)	1.94 (1.906 to 1.971)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	1.97 (1.906 to 1.971)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.0784	
Hazard ratio (95% CI) vs Pd	-			0.65 (0.40 to 1.05)	
P-value	-	0.9991		0.0807	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	59 (39.1)	66 (43.4)	0.6489
Number (%) of patients censored	1 (50.0)	1 (50.0)	92 (60.9)	86 (56.6)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	4.14 (4.140 to NC)	3.15 (2.825 to 4.665)	2.20 (1.873 to 2.990)	
Median (95% CI)	NC (1.281 to NC)	NC (4.140 to NC)	13.90 (7.458 to NC)	12.06 (8.246 to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (4.140 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.4370	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		1.15 (0.81 to 1.63)	
P-value	-	0.8092		0.4376	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	20 (13.2)	17 (11.2)	0.9882
Number (%) of patients censored	2 (100.0)	1 (50.0)	131 (86.8)	135 (88.8)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	5.09 (5.092 to NC)	NC (11.466 to NC)	NC (13.634 to NC)	
Median (95% CI)	NC (NC to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.4083	
Hazard ratio (95% CI) vs Pd	-			0.76 (0.40 to 1.45)	
P-value	-	0.9991		0.4091	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	21 (13.9)	23 (15.1)	0.9855
Number (%) of patients censored	1 (50.0)	2 (100.0)	130 (86.1)	129 (84.9)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (NC to NC)	NC (13.832 to NC)	NC (NC to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.9398	
Hazard ratio (95% CI) vs Pd	-			1.02 (0.57 to 1.85)	
P-value	-	0.9990		0.9398	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_prmab_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (25.2)	26 (22.0)	11 (28.9)	5 (13.9)	0.3189
Number (%) of patients censored	86 (74.8)	92 (78.0)	27 (71.1)	31 (86.1)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	5.26 (1.150 to NC)	NC (1.938 to NC)	3.91 (0.986 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3974		0.1092	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.47 to 1.35)		0.43 (0.15 to 1.24)	
P-value	-	0.3984		0.1198	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (34.8)	50 (42.4)	20 (52.6)	17 (47.2)	0.3849
Number (%) of patients censored	75 (65.2)	68 (57.6)	18 (47.4)	19 (52.8)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	3.45 (2.825 to 5.585)	2.17 (1.281 to 3.745)	2.83 (1.117 to 5.224)	2.20 (1.873 to 3.844)	
Median (95% CI)	NC (12.025 to NC)	NC (8.706 to NC)	6.14 (3.088 to NC)	9.66 (2.661 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.491 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2790		0.7429	
Hazard ratio (95% CI) vs Pd	-	1.26 (0.83 to 1.91)		0.90 (0.47 to 1.72)	
P-value	-	0.2801		0.7436	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (13.9)	13 (11.0)	4 (10.5)	5 (13.9)	0.3711
Number (%) of patients censored	99 (86.1)	105 (89.0)	34 (89.5)	31 (86.1)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (11.466 to NC)	NC (13.634 to NC)	NC (11.138 to NC)	NC (6.637 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2904		0.6686	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.32 to 1.40)		1.33 (0.36 to 4.96)	
P-value	-	0.2934		0.6696	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (13.0)	20 (16.9)	7 (18.4)	3 (8.3)	0.1976
Number (%) of patients censored	100 (87.0)	98 (83.1)	31 (81.6)	33 (91.7)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (13.832 to NC)	NC (7.918 to NC)	NC (2.464 to NC)	NC (7.097 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6046		0.2192	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.61 to 2.33)		0.44 (0.11 to 1.70)	
P-value	-	0.6051		0.2324	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (25.0)	31 (21.1)	4 (44.4)	0 (0.0)	0.9858
Number (%) of patients censored	108 (75.0)	116 (78.9)	5 (55.6)	7 (100.0)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	5.95 (1.150 to NC)	NC (2.168 to NC)	2.83 (0.986 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.990 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2794		0.0513	
Hazard ratio (95% CI) vs Pd	-	0.77 (0.47 to 1.24)			
P-value	-	0.2800		0.9968	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	54 (37.5)	64 (43.5)	6 (66.7)	3 (42.9)	0.4159
Number (%) of patients censored	90 (62.5)	83 (56.5)	3 (33.3)	4 (57.1)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	3.42 (2.825 to 5.224)	2.20 (1.906 to 3.055)	2.83 (0.986 to 4.665)	1.12 (0.986 to NC)	
Median (95% CI)	13.90 (9.298 to NC)	12.06 (8.246 to NC)	4.67 (0.986 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.825 to NC)	NC (2.825 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3399		0.5188	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.83 to 1.71)		0.64 (0.16 to 2.55)	
P-value	-	0.3417		0.5224	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (12.5)	18 (12.2)	2 (22.2)	0 (0.0)	0.9902
Number (%) of patients censored	126 (87.5)	129 (87.8)	7 (77.8)	7 (100.0)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (11.466 to NC)	NC (13.634 to NC)	NC (2.825 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.825 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6727		0.2600	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.45 to 1.67)			
P-value	-	0.6729		0.9978	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (14.6)	21 (14.3)	1 (11.1)	2 (28.6)	0.2663
Number (%) of patients censored	123 (85.4)	126 (85.7)	8 (88.9)	5 (71.4)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (11.006 to NC)	NC (NC to NC)	NC (6.735 to NC)	2.83 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.735 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7084		0.3411	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.49 to 1.63)		3.04 (0.27 to 33.67)	
P-value	-	0.7079		0.3653	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (21.6)	17 (18.3)	21 (32.3)	14 (23.0)	0.5860
Number (%) of patients censored	69 (78.4)	76 (81.7)	44 (67.7)	47 (77.0)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (1.084 to NC)	NC (5.027 to NC)	2.17 (1.117 to 9.429)	NC (1.446 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.429 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5063		0.1426	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.42 to 1.54)		0.61 (0.31 to 1.19)	
P-value	-	0.5063		0.1467	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (42.0)	39 (41.9)	23 (35.4)	28 (45.9)	0.3900
Number (%) of patients censored	51 (58.0)	54 (58.1)	42 (64.6)	33 (54.1)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	3.15 (2.136 to 5.454)	2.66 (2.037 to 5.717)	3.78 (2.825 to 6.637)	1.91 (1.051 to 2.825)	
Median (95% CI)	13.90 (5.651 to NC)	12.06 (8.246 to NC)	NC (6.637 to NC)	NC (2.990 to NC)	
75% quantile (95% CI)	NC (13.897 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9882		0.2478	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.64 to 1.57)		1.38 (0.80 to 2.40)	
P-value	-	0.9882		0.2498	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (9.1)	11 (11.8)	12 (18.5)	7 (11.5)	0.1731
Number (%) of patients censored	80 (90.9)	82 (88.2)	53 (81.5)	54 (88.5)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.598 to NC)	NC (2.825 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6342		0.1569	
Hazard ratio (95% CI) vs Pd	-	1.25 (0.50 to 3.10)		0.52 (0.20 to 1.31)	
P-value	-	0.6349		0.1645	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imppl_llen_de_i_t_x.rtf (08APR2021 14:58)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (19.3)	9 (9.7)	5 (7.7)	14 (23.0)	0.0078
Number (%) of patients censored	71 (80.7)	84 (90.3)	60 (92.3)	47 (77.0)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	13.83 (5.585 to NC)	NC (NC to NC)	NC (NC to NC)	9.40 (4.600 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0613		0.0440	
Hazard ratio (95% CI) vs Pd	-	0.47 (0.21 to 1.06)		2.74 (0.99 to 7.60)	
P-value	-	0.0676		0.0534	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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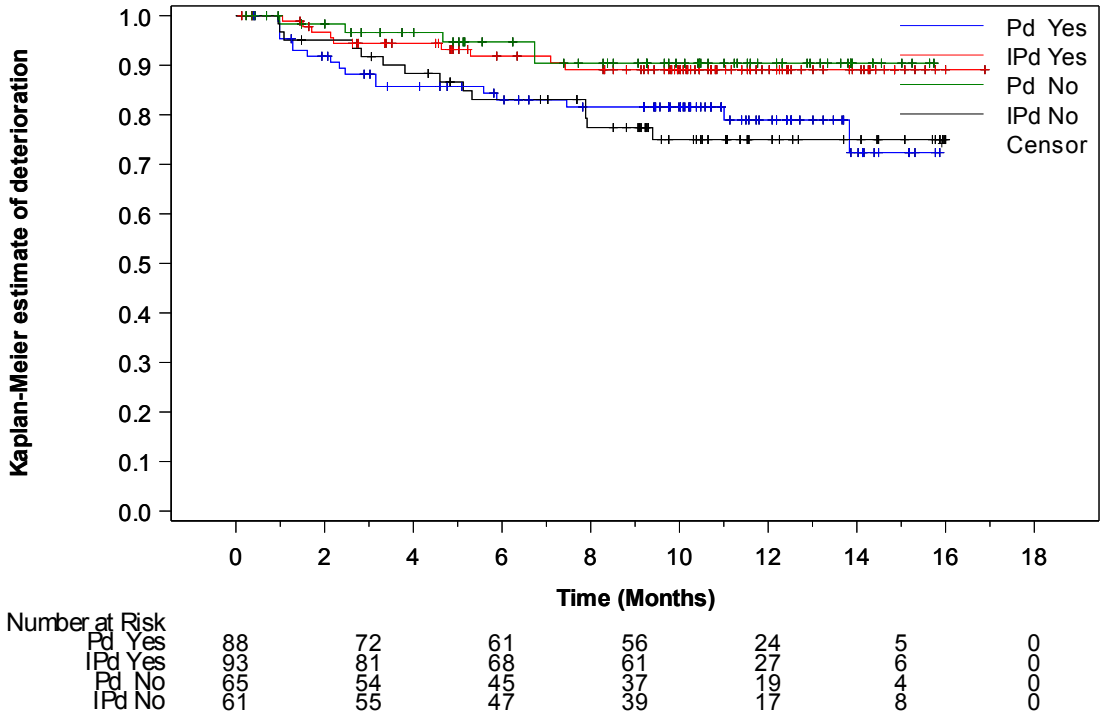
16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Body image
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to refractory to lenalidomide in last previous regimen (LOCF) - Kaplan-Meier curve - ITT population



A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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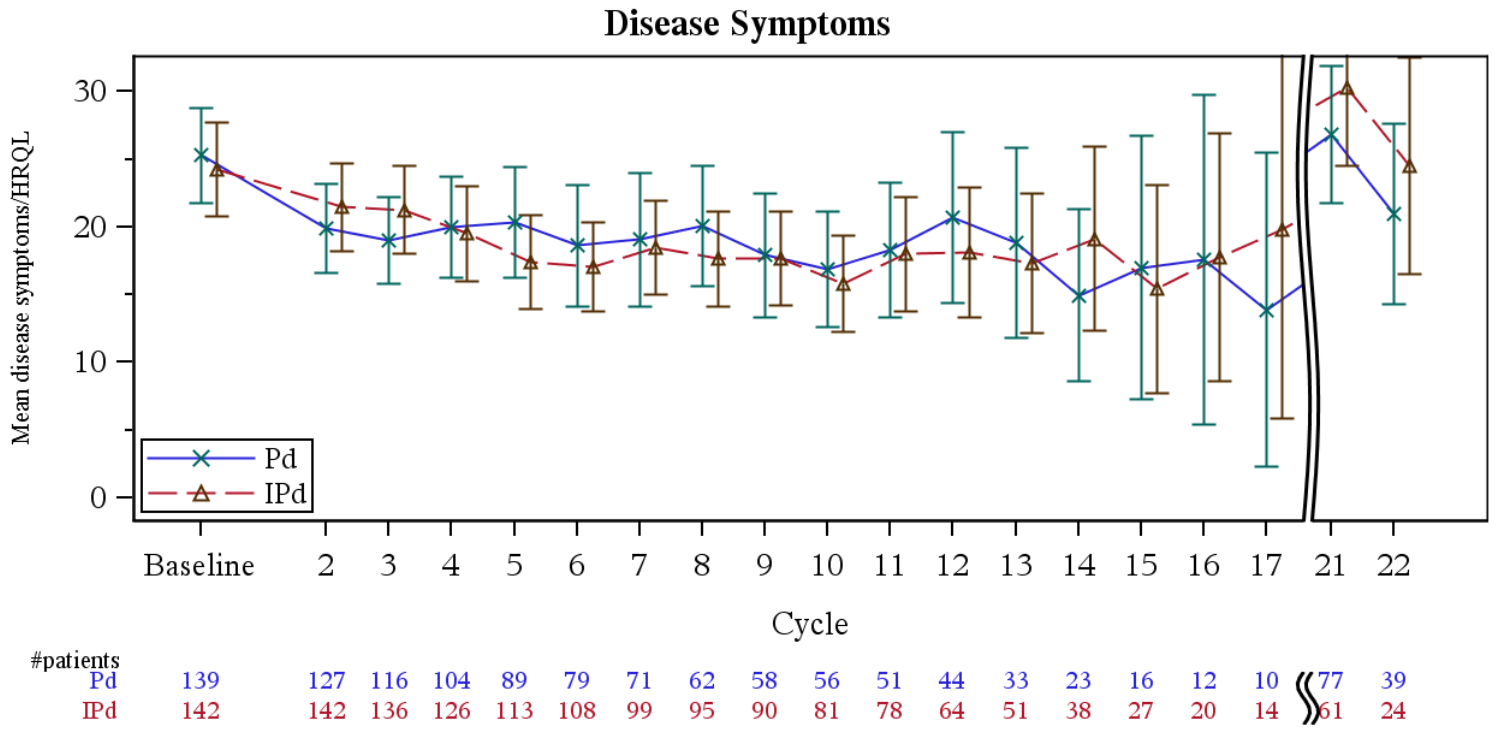
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Disease symptoms
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-MY20 - Mean and 95% CI for disease symptoms score over time (LOCF) - ITT population



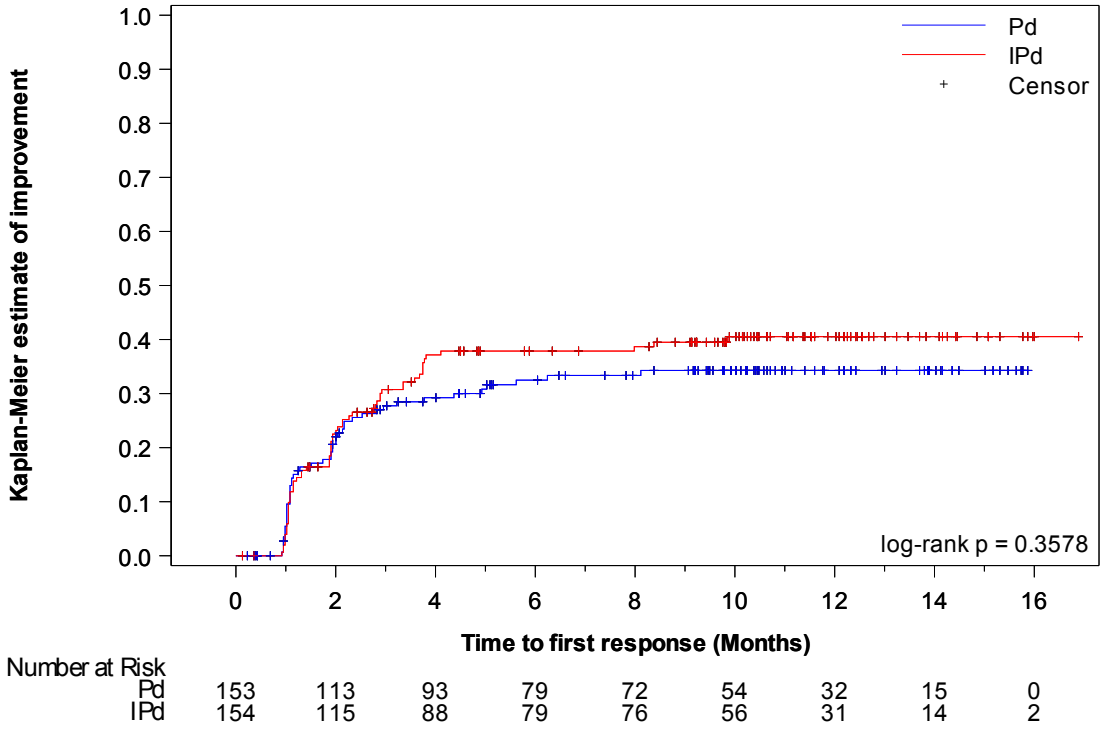
A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_line_i_f.sas OUT=REPORT/OUTPUT/eff_qlq_line_my20_dis_de_i_f_x.rtf (12FEB2021 17:15)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Disease symptoms
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-MY20 - Time to first improvement by 15 pt in disease symptoms (LOCF) - ITT population

First improvement 15 points Disease symptoms (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	48 (31.4)	59 (38.3)
Number (%) of patients censored	105 (68.6)	95 (61.7)
Kaplan-Meier estimates of disease symptoms in months		
25% quantile (95% CI)	2.33 (1.741 to 5.618)	2.14 (1.873 to 3.351)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3578
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.20 (0.82 to 1.75)
P-value	-	0.3585
Probability (95% CI)[c]		
2 Months	0.21 (0.145 to 0.275)	0.23 (0.162 to 0.294)
4 Months	0.29 (0.220 to 0.368)	0.37 (0.294 to 0.449)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_imp15l_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Disease symptoms
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-MY20 - Time to first improvement by 15 pt in disease symptoms - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_imp15l_de_i_f_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Disease symptoms
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-MY20 - Time to first deterioration by 15 pt in disease symptoms (LOCF) - ITT population

First deterioration 15 points Disease symptoms (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	45 (29.4)	50 (32.5)
Number (%) of patients censored	108 (70.6)	104 (67.5)
Kaplan-Meier estimates of disease symptoms in months		
25% quantile (95% CI)	5.78 (3.811 to 9.331)	4.93 (3.220 to 6.702)
Median (95% CI)	NC (NC to NC)	NC (14.324 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.7746
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.06 (0.71 to 1.59)
P-value	-	0.7748
Probability (95% CI)[c]		
2 Months	0.93 (0.876 to 0.962)	0.87 (0.809 to 0.918)
4 Months	0.81 (0.739 to 0.870)	0.79 (0.715 to 0.848)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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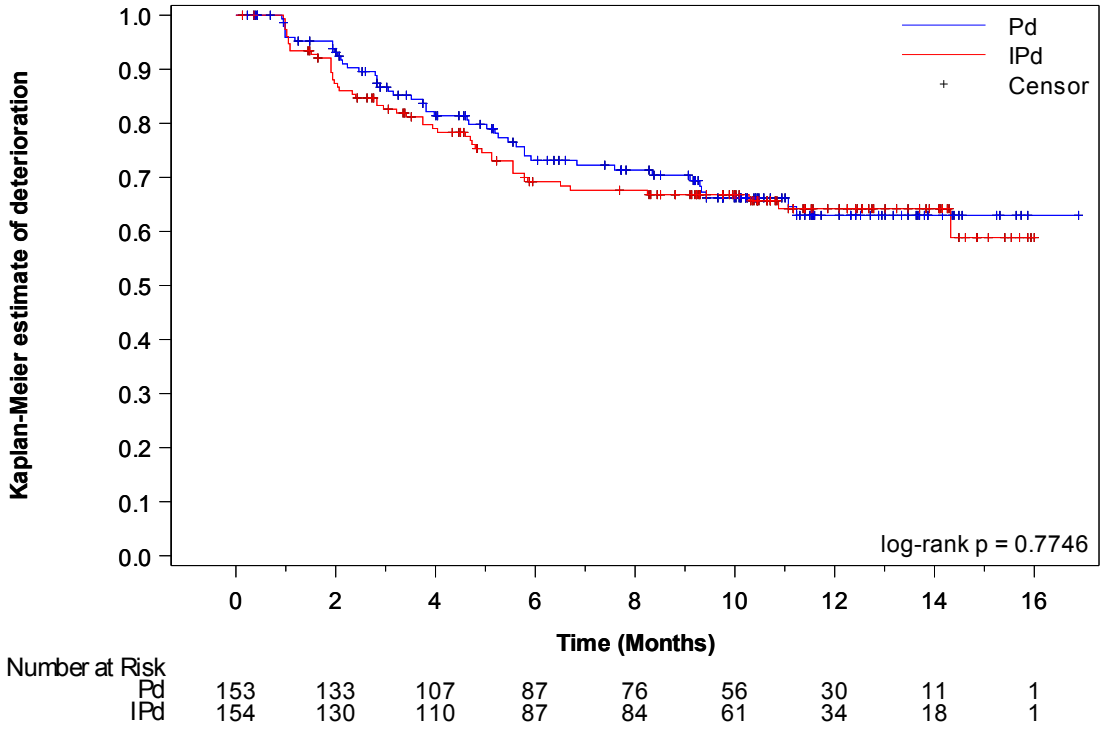
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Disease symptoms
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-MY20 - Time to first deterioration by 15 pt in disease symptoms - Kaplan-Meier curve (LOCF) - ITT population



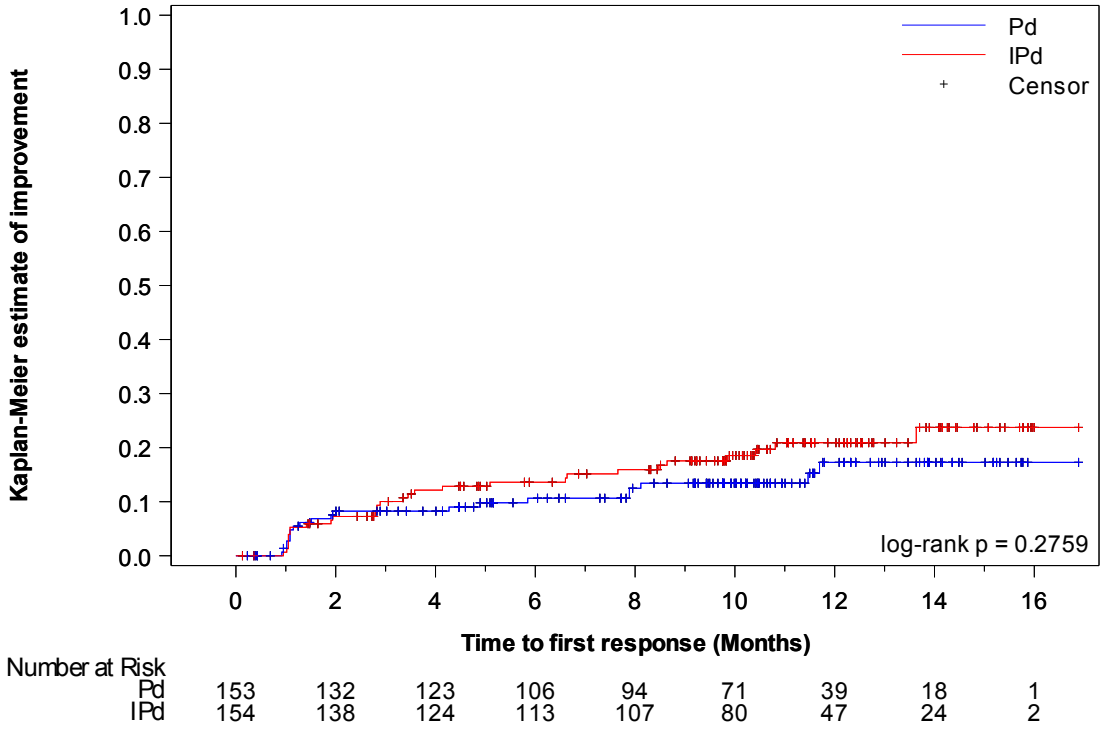
A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_det15l_de_i_f_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Disease symptoms
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-MY20 - Time until permanent improvement by 15 pt in disease symptoms (LOCF) - ITT population

First permanent improvement 15 points Disease symptoms (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	20 (13.1)	29 (18.8)
Number (%) of patients censored	133 (86.9)	125 (81.2)
Kaplan-Meier estimates of disease symptoms in months		
25% quantile (95% CI)	NC (11.696 to NC)	NC (9.856 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2759
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.37 (0.78 to 2.43)
P-value	-	0.2778
Probability (95% CI)[c]		
2 Months	0.08 (0.040 to 0.126)	0.07 (0.038 to 0.121)
4 Months	0.08 (0.045 to 0.134)	0.12 (0.075 to 0.180)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_imp15pl_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Disease symptoms
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-MY20 - Time until permanent improvement by 15 pt in disease symptoms - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Disease symptoms
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-MY20 - Time until permanent deterioration by 15 pt in disease symptoms (LOCF) - ITT population

First permanent deterioration 15 points Disease symptoms (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	19 (12.4)	15 (9.7)
Number (%) of patients censored	134 (87.6)	139 (90.3)
Kaplan-Meier estimates of disease symptoms in months		
25% quantile (95% CI)	NC (11.236 to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2723
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.69 (0.35 to 1.35)
P-value	-	0.2751
Probability (95% CI)[c]		
2 Months	0.98 (0.938 to 0.993)	0.97 (0.930 to 0.990)
4 Months	0.93 (0.871 to 0.961)	0.96 (0.912 to 0.982)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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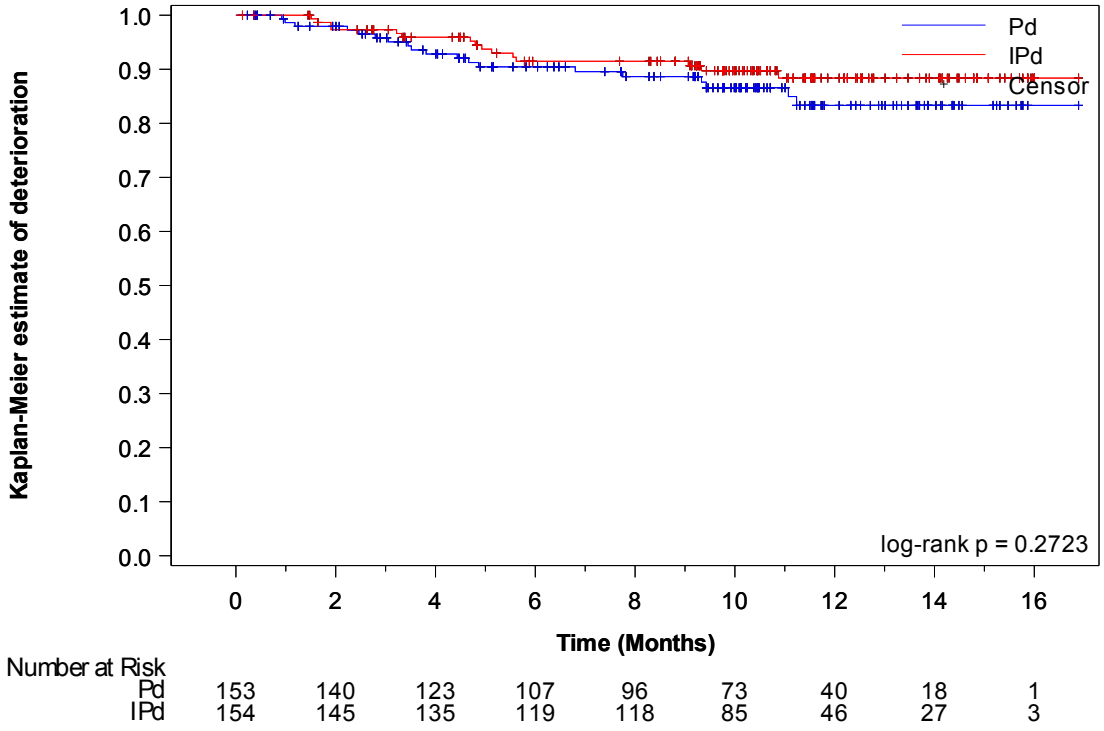
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Disease symptoms
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-MY20 - Time until permanent deterioration by 15 pt in disease symptoms - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (35.7)	28 (51.9)	27 (50.0)	34 (50.0)	10 (34.5)	15 (46.9)	0.4537
Number (%) of patients censored	45 (64.3)	26 (48.1)	27 (50.0)	34 (50.0)	19 (65.5)	17 (53.1)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	1.51 (1.018 to 2.891)	1.15 (1.018 to 1.840)	1.12 (0.986 to 1.906)	1.08 (1.051 to 1.938)	3.52 (1.018 to NC)	1.95 (1.051 to 3.745)	
Median (95% CI)	NC (5.618 to NC)	3.78 (1.840 to NC)	4.93 (1.906 to NC)	6.54 (2.103 to NC)	NC (3.778 to NC)	NC (2.037 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1207		0.8943		0.4593	
Hazard ratio (95% CI) vs Pd	-	1.53 (0.89 to 2.62)		0.97 (0.58 to 1.60)		1.35 (0.61 to 3.01)	
P-value	-	0.1235		0.8941		0.4609	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (35.7)	26 (48.1)	16 (29.6)	36 (52.9)	19 (65.5)	17 (53.1)	0.0112
Number (%) of patients censored	45 (64.3)	28 (51.9)	38 (70.4)	32 (47.1)	10 (34.5)	15 (46.9)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	5.78 (2.793 to 8.936)	2.83 (1.938 to 5.027)	5.55 (1.938 to NC)	2.40 (1.183 to 4.600)	1.12 (0.953 to 1.938)	2.45 (1.084 to 5.125)	
Median (95% CI)	NC (9.298 to NC)	7.79 (5.027 to NC)	NC (NC to NC)	8.25 (4.632 to NC)	2.46 (1.183 to 5.027)	6.70 (2.957 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	6.83 (3.055 to NC)	NC (7.984 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1698		0.0279		0.0617	
Hazard ratio (95% CI) vs Pd	-	1.47 (0.85 to 2.54)		1.92 (1.06 to 3.45)		0.54 (0.28 to 1.04)	
P-value	-	0.1724		0.0307		0.0658	
Hazard ratio inverted (95% CI) vs IPd		-		0.52 (0.29 to 0.94)		1.85 (0.96 to 3.58)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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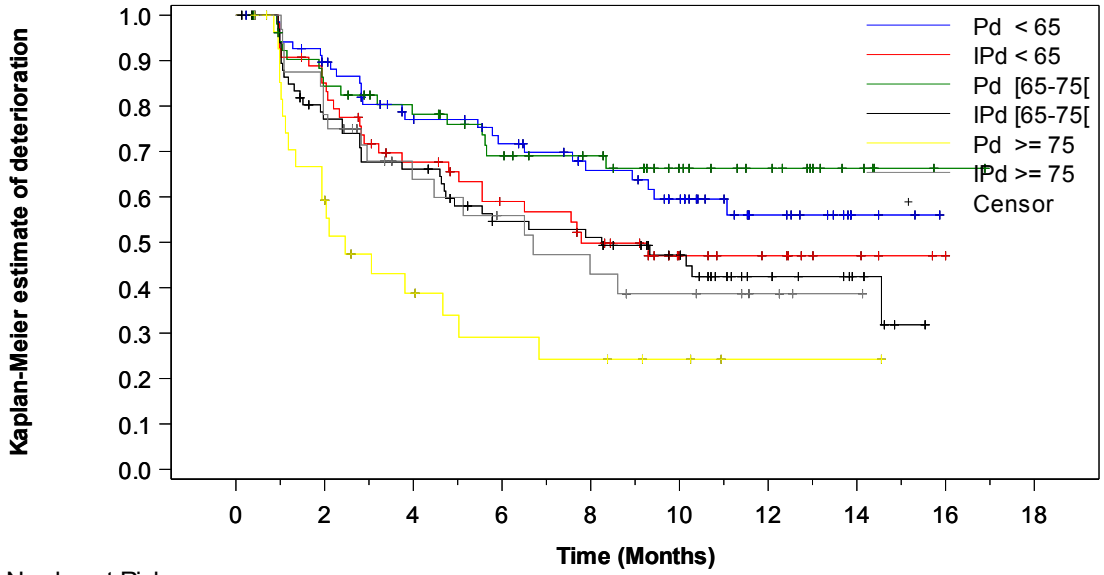
16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to age (IRT) (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd < 65	70	51	40	31	12	2	0
IPd < 65	54	37	26	19	8	2	0
Pd [65-75[	54	40	30	23	12	2	0
IPd [65-75[	68	43	31	26	10	1	0
Pd >= 75	29	11	6	4	1	0	0
IPd >= 75	32	19	13	7	4	0	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_detl_age_de_i_f_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (17.1)	10 (18.5)	14 (25.9)	19 (27.9)	4 (13.8)	8 (25.0)	0.7797
Number (%) of patients censored	58 (82.9)	44 (81.5)	40 (74.1)	49 (72.1)	25 (86.2)	24 (75.0)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	NC (7.622 to NC)	NC (3.844 to NC)	11.70 (1.511 to NC)	9.86 (2.793 to NC)	NC (1.281 to NC)	10.81 (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.259 to NC)	NC (12.945 to NC)	NC (NC to NC)	NC (10.809 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9394		0.9770		0.4972	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.45 to 2.39)		0.99 (0.50 to 1.98)		1.51 (0.45 to 5.03)	
P-value	-	0.9393		0.9770		0.5002	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_imppl_age_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (20.0)	10 (18.5)	8 (14.8)	9 (13.2)	11 (37.9)	5 (15.6)	0.2366
Number (%) of patients censored	56 (80.0)	44 (81.5)	46 (85.2)	59 (86.8)	18 (62.1)	27 (84.4)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	13.34 (6.801 to NC)	14.82 (6.538 to NC)	NC (5.552 to NC)	NC (11.466 to NC)	2.46 (0.986 to 8.378)	NC (5.125 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.811 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6446		0.7296		0.0209	
Hazard ratio (95% CI) vs Pd	-	0.83 (0.37 to 1.86)		0.85 (0.33 to 2.19)		0.31 (0.11 to 0.89)	
P-value	-	0.6451		0.7299		0.0291	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_detpl_age_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	39 (38.6)	48 (47.1)	23 (44.2)	29 (55.8)	0.9573
Number (%) of patients censored	62 (61.4)	54 (52.9)	29 (55.8)	23 (44.2)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.28 (1.084 to 2.891)	1.26 (1.084 to 1.906)	1.74 (0.986 to 2.004)	1.10 (1.051 to 1.906)	
Median (95% CI)	NC (4.928 to NC)	NC (2.267 to NC)	7.92 (1.938 to NC)	3.75 (1.906 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3198		0.4040	
Hazard ratio (95% CI) vs Pd	-	1.24 (0.81 to 1.89)		1.26 (0.73 to 2.18)	
P-value	-	0.3207		0.4051	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_impl_plne_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	41 (40.6)	51 (50.0)	19 (36.5)	28 (53.8)	0.8478
Number (%) of patients censored	60 (59.4)	51 (50.0)	33 (63.5)	24 (46.2)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	2.83 (1.938 to 4.665)	2.33 (1.511 to 3.220)	4.76 (1.150 to 6.834)	2.89 (1.938 to 5.125)	
Median (95% CI)	NC (7.589 to NC)	8.25 (4.731 to NC)	NC (5.914 to NC)	7.69 (5.027 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2315		0.2599	
Hazard ratio (95% CI) vs Pd	-	1.28 (0.85 to 1.94)		1.40 (0.78 to 2.50)	
P-value	-	0.2328		0.2621	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	23 (22.8)	24 (23.5)	7 (13.5)	13 (25.0)	0.2216
Number (%) of patients censored	78 (77.2)	78 (76.5)	45 (86.5)	39 (75.0)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	10.74 (4.928 to NC)	12.52 (7.458 to NC)	14.26 (7.885 to NC)	6.60 (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.259 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8138		0.1937	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.53 to 1.65)		1.82 (0.73 to 4.57)	
P-value	-	0.8136		0.2004	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_imppl_plne_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	19 (18.8)	15 (14.7)	14 (26.9)	9 (17.3)	0.5654
Number (%) of patients censored	82 (81.2)	87 (85.3)	38 (73.1)	43 (82.7)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	13.34 (5.191 to NC)	NC (10.875 to NC)	8.38 (3.811 to NC)	NC (5.125 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.236 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3164		0.1097	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.36 to 1.40)		0.51 (0.22 to 1.18)	
P-value	-	0.3191		0.1164	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_detpl_plne_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (38.6)	44 (49.4)	35 (42.2)	33 (50.8)	0.6127
Number (%) of patients censored	43 (61.4)	45 (50.6)	48 (57.8)	32 (49.2)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.51 (1.051 to 4.928)	1.12 (1.051 to 1.873)	1.28 (1.018 to 2.168)	1.40 (1.051 to 1.906)	
Median (95% CI)	NC (5.618 to NC)	4.93 (2.103 to NC)	NC (2.825 to NC)	6.54 (1.938 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2082		0.5489	
Hazard ratio (95% CI) vs Pd	-	1.36 (0.84 to 2.20)		1.16 (0.72 to 1.86)	
P-value	-	0.2099		0.5492	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_impl_sex_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (37.1)	45 (50.6)	34 (41.0)	34 (52.3)	0.6206
Number (%) of patients censored	44 (62.9)	44 (49.4)	49 (59.0)	31 (47.7)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	3.19 (1.938 to 5.914)	2.79 (1.643 to 4.698)	2.86 (1.347 to 5.618)	2.40 (1.511 to 3.745)	
Median (95% CI)	NC (7.885 to NC)	7.69 (5.027 to NC)	NC (5.782 to NC)	8.61 (3.975 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1357		0.4212	
Hazard ratio (95% CI) vs Pd	-	1.44 (0.89 to 2.34)		1.22 (0.76 to 1.96)	
P-value	-	0.1378		0.4219	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_detl_sex_de_i_t_x.rtf (08APR2021 15:01)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (17.1)	23 (25.8)	18 (21.7)	14 (21.5)	0.2539
Number (%) of patients censored	58 (82.9)	66 (74.2)	65 (78.3)	51 (78.5)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	14.26 (7.885 to NC)	12.52 (3.351 to NC)	10.74 (4.731 to NC)	NC (3.450 to NC)	
Median (95% CI)	NC (14.259 to NC)	NC (13.634 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2334		0.6636	
Hazard ratio (95% CI) vs Pd	-	1.52 (0.76 to 3.06)		0.86 (0.43 to 1.72)	
P-value	-	0.2369		0.6639	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_imppl_sex_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (20.0)	11 (12.4)	19 (22.9)	13 (20.0)	0.5890
Number (%) of patients censored	56 (80.0)	78 (87.6)	64 (77.1)	52 (80.0)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	NC (5.191 to NC)	NC (11.466 to NC)	11.24 (4.435 to NC)	14.82 (5.125 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.339 to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1388		0.3948	
Hazard ratio (95% CI) vs Pd	-	0.56 (0.25 to 1.22)		0.74 (0.36 to 1.50)	
P-value	-	0.1445		0.3966	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_detpl_sex_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	54 (42.9)	60 (50.8)	8 (42.1)	13 (54.2)	0.8068
Number (%) of patients censored	72 (57.1)	58 (49.2)	11 (57.9)	11 (45.8)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.51 (1.084 to 2.136)	1.18 (1.051 to 1.906)	1.12 (0.986 to NC)	1.22 (0.986 to 2.004)	
Median (95% CI)	NC (3.778 to NC)	4.93 (2.267 to NC)	NC (1.117 to NC)	4.93 (1.314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.979 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3775		0.5532	
Hazard ratio (95% CI) vs Pd	-	1.18 (0.82 to 1.70)		1.30 (0.54 to 3.15)	
P-value	-	0.3779		0.5544	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_impl_race_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	52 (41.3)	64 (54.2)	5 (26.3)	13 (54.2)	0.3168
Number (%) of patients censored	74 (58.7)	54 (45.8)	14 (73.7)	11 (45.8)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	2.83 (1.938 to 4.665)	2.07 (1.446 to 2.825)	8.34 (1.906 to NC)	4.80 (2.037 to 7.786)	
Median (95% CI)	NC (6.834 to NC)	7.56 (4.698 to NC)	NC (8.345 to NC)	8.61 (4.928 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (8.608 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1404		0.0830	
Hazard ratio (95% CI) vs Pd	-	1.32 (0.91 to 1.90)		2.43 (0.86 to 6.86)	
P-value	-	0.1416		0.0931	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_detl_race_de_i_t_x.rtf (08APR2021 15:01)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (21.4)	29 (24.6)	3 (15.8)	4 (16.7)	0.9298
Number (%) of patients censored	99 (78.6)	89 (75.4)	16 (84.2)	20 (83.3)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	11.47 (7.425 to NC)	12.52 (5.092 to NC)	NC (1.084 to NC)	NC (1.051 to NC)	
Median (95% CI)	NC (14.259 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8629		0.9271	
Hazard ratio (95% CI) vs Pd	-	1.05 (0.62 to 1.77)		0.93 (0.20 to 4.23)	
P-value	-	0.8630		0.9267	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_imppl_race_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (23.0)	17 (14.4)	2 (10.5)	6 (25.0)	0.0859
Number (%) of patients censored	97 (77.0)	101 (85.6)	17 (89.5)	18 (75.0)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	11.07 (4.468 to NC)	NC (11.466 to NC)	NC (5.191 to NC)	10.87 (4.797 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.875 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0366		0.2684	
Hazard ratio (95% CI) vs Pd	-	0.53 (0.29 to 0.97)		2.42 (0.48 to 12.18)	
P-value	-	0.0397		0.2833	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_detpl_race_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	1 (25.0)	55 (41.0)	69 (53.1)	0.3780
Number (%) of patients censored	2 (66.7)	3 (75.0)	79 (59.0)	61 (46.9)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (2.136 to NC)	1.61 (1.084 to 2.168)	1.15 (1.051 to 1.873)	
Median (95% CI)	NC (1.281 to NC)	NC (2.136 to NC)	NC (5.618 to NC)	3.78 (2.037 to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (2.136 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4504		0.0977	
Hazard ratio (95% CI) vs Pd	-	0.35 (0.02 to 5.89)		1.35 (0.95 to 1.92)	
P-value	-	0.4689		0.0990	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_impl_ethn_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	3 (75.0)	52 (38.8)	68 (52.3)	0.9325
Number (%) of patients censored	2 (66.7)	1 (25.0)	82 (61.2)	62 (47.7)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	2.27 (2.267 to NC)	1.17 (1.018 to 7.556)	2.86 (1.971 to 5.454)	2.83 (1.971 to 3.975)	
Median (95% CI)	NC (2.267 to NC)	4.44 (1.018 to NC)	NC (8.345 to NC)	7.98 (5.552 to NC)	
75% quantile (95% CI)	NC (2.267 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (14.554 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7822		0.1129	
Hazard ratio (95% CI) vs Pd	-	1.41 (0.12 to 15.84)		1.34 (0.93 to 1.92)	
P-value	-	0.7832		0.1141	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	1 (25.0)	27 (20.1)	31 (23.8)	0.3041
Number (%) of patients censored	2 (66.7)	3 (75.0)	107 (79.9)	99 (76.2)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	12.52 (12.517 to NC)	11.70 (7.885 to NC)	12.94 (6.078 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (12.517 to NC)	NC (14.259 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (12.517 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.6996	
Hazard ratio (95% CI) vs Pd	-			1.11 (0.66 to 1.85)	
P-value	-	0.9985		0.7002	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (25.0)	30 (22.4)	22 (16.9)	0.9867
Number (%) of patients censored	3 (100.0)	3 (75.0)	104 (77.6)	108 (83.1)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.466 to NC)	11.24 (4.764 to NC)	NC (9.758 to NC)	
Median (95% CI)	NC (NC to NC)	NC (11.466 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (11.466 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.1352	
Hazard ratio (95% CI) vs Pd	-			0.66 (0.38 to 1.14)	
P-value	-			0.1380	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	27 (35.5)	26 (47.3)	6 (30.0)	15 (53.6)	3 (60.0)	5 (71.4)	6 (40.0)	12 (57.1)	20 (54.1)	19 (44.2)	0.2326
Number (%) of patients censored	49 (64.5)	29 (52.7)	14 (70.0)	13 (46.4)	2 (40.0)	2 (28.6)	9 (60.0)	9 (42.9)	17 (45.9)	24 (55.8)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	1.94 (1.084 to 4.107)	1.15 (1.018 to 1.873)	2.89 (1.084 to NC)	1.05 (0.953 to 1.906)	1.12 (0.986 to NC)	1.15 (0.953 to 2.136)	1.12 (0.986 to NC)	1.12 (0.986 to 2.004)	1.03 (0.986 to 1.741)	1.91 (1.051 to 3.187)	
Median (95% CI)	NC (5.618 to NC)	NC (1.873 to NC)	NC (2.891 to NC)	2.89 (1.084 to NC)	4.93 (0.986 to NC)	2.14 (0.953 to NC)	NC (1.117 to NC)	4.93 (1.117 to NC)	2.53 (1.511 to NC)	NC (2.431 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (2.004 to NC)	NC (NC to NC)	NC (4.928 to NC)	NC (5.618 to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.2549		0.0852		0.7140		0.3749		0.2114	
Hazard ratio (95% CI) vs Pd	-	1.37 (0.80 to 2.34)		2.25 (0.87 to 5.81)		1.31 (0.31 to 5.58)		1.55 (0.58 to 4.14)		0.67 (0.36 to 1.26)	
P-value	-	0.2568		0.0939		0.7148		0.3788		0.2144	
Improvement probability (95% CI)[b]											
2 Months	0.254 (0.160 to 0.359)	0.391 (0.262 to 0.518)	0.158 (0.039 to 0.349)	0.464 (0.276 to 0.633)	0.400 (0.052 to 0.753)	0.286 (0.041 to 0.612)	0.333 (0.122 to 0.564)	0.381 (0.183 to 0.578)	0.421 (0.259 to 0.575)	0.287 (0.160 to 0.427)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_impl_greg_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	28 (36.8)	27 (49.1)	12 (60.0)	13 (46.4)	2 (40.0)	3 (42.9)	5 (33.3)	12 (57.1)	13 (35.1)	24 (55.8)	0.4404
Number (%) of patients censored	48 (63.2)	28 (50.9)	8 (40.0)	15 (53.6)	3 (60.0)	4 (57.1)	10 (66.7)	9 (42.9)	24 (64.9)	19 (44.2)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	2.86 (1.281 to 5.027)	2.40 (1.511 to 4.600)	1.05 (0.986 to 6.505)	2.83 (1.018 to 7.556)	2.27 (0.986 to NC)	1.08 (1.018 to NC)	5.91 (1.906 to NC)	3.98 (2.037 to 7.786)	3.81 (1.938 to 9.298)	1.94 (0.986 to 2.957)	
Median (95% CI)	NC (5.618 to NC)	7.69 (4.600 to NC)	6.83 (1.051 to NC)	14.55 (4.632 to NC)	NC (0.986 to NC)	NC (1.018 to NC)	NC (5.782 to NC)	7.89 (3.975 to NC)	NC (5.651 to NC)	6.51 (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.834 to NC)	NC (14.554 to NC)	NC (0.986 to NC)	NC (2.793 to NC)	NC (NC to NC)	NC (7.885 to NC)	NC (NC to NC)	NC (10.152 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_detl_greg_de_i_t_x.rtf (08APR2021 15:01)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.2910		0.3299		0.9998		0.2006		0.1090	
Hazard ratio (95% CI) vs Pd	-	1.33 (0.78 to 2.26)		0.68 (0.31 to 1.49)		1.00 (0.17 to 6.00)		1.97 (0.68 to 5.64)		1.73 (0.88 to 3.39)	
P-value	-	0.2926		0.3329		1.0000		0.2090		0.1135	
Deterioration probability (95% CI)[b]											
2 Months	0.804 (0.691 to 0.879)	0.814 (0.682 to 0.895)	0.737 (0.479 to 0.881)	0.786 (0.584 to 0.898)	0.800 (0.204 to 0.969)	0.714 (0.258 to 0.920)	0.867 (0.564 to 0.965)	1.000 (1.000 to 1.000)	0.887 (0.727 to 0.956)	0.712 (0.549 to 0.825)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_detl_greg_de_i_t_x.rtf (08APR2021 15:01)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	13 (17.1)	11 (20.0)	2 (10.0)	9 (32.1)	2 (40.0)	4 (57.1)	2 (13.3)	3 (14.3)	11 (29.7)	10 (23.3)	0.3464
Number (%) of patients censored	63 (82.9)	44 (80.0)	18 (90.0)	19 (67.9)	3 (60.0)	3 (42.9)	13 (86.7)	18 (85.7)	26 (70.3)	33 (76.7)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (7.425 to NC)	NC (1.183 to NC)	NC (4.731 to NC)	2.83 (1.051 to NC)	4.90 (0.986 to NC)	3.45 (0.953 to 12.517)	NC (1.084 to NC)	NC (1.051 to NC)	7.62 (1.051 to 14.259)	12.94 (6.604 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.891 to NC)	NC (0.986 to NC)	12.52 (0.953 to 12.517)	NC (NC to NC)	NC (NC to NC)	14.26 (7.885 to NC)	NC (13.634 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	12.52 (7.458 to 12.517)	NC (NC to NC)	NC (NC to NC)	NC (14.259 to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.7289		0.0771		0.9344		0.9390		0.1752	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.52 to 2.57)		3.64 (0.79 to 16.87)		1.08 (0.18 to 6.47)		1.07 (0.18 to 6.42)		0.56 (0.23 to 1.32)	
P-value	-	0.7292		0.0987		0.9344		0.9391		0.1812	
Improvement probability (95% CI)[b]											

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	15 (19.7)	9 (16.4)	9 (45.0)	4 (14.3)	0 (0.0)	1 (14.3)	2 (13.3)	5 (23.8)	7 (18.9)	5 (11.6)	0.4790
Number (%) of patients censored	61 (80.3)	46 (83.6)	11 (55.0)	24 (85.7)	5 (100.0)	6 (85.7)	13 (86.7)	16 (76.2)	30 (81.1)	38 (88.4)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	13.34 (4.764 to NC)	14.82 (9.331 to NC)	4.47 (0.986 to 11.236)	NC (1.906 to NC)	NC (NC to NC)	9.76 (9.758 to NC)	NC (5.191 to NC)	10.87 (4.797 to NC)	NC (2.136 to NC)	NC (4.698 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (4.468 to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.758 to NC)	NC (NC to NC)	NC (10.875 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.758 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.4551		0.0290		0.3173		0.5017		0.3126	
Hazard ratio (95% CI) vs Pd	-	0.73 (0.32 to 1.67)		0.29 (0.09 to 0.94)				1.76 (0.33 to 9.29)		0.56 (0.18 to 1.76)	
P-value	-	0.4569		0.0400		0.9990		0.5072		0.3194	
Deterioration probability (95% CI)[b]											
2 Months	0.888 (0.788 to 0.942)	0.944 (0.838 to 0.982)	0.947 (0.681 to 0.992)	0.929 (0.743 to 0.982)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.916 (0.761 to 0.972)	0.928 (0.793 to 0.976)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (41.2)	38 (49.4)	22 (39.3)	39 (50.6)	0.7710
Number (%) of patients censored	57 (58.8)	39 (50.6)	34 (60.7)	38 (49.4)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.61 (1.084 to 2.168)	1.15 (1.051 to 1.873)	1.15 (1.051 to 2.825)	1.31 (1.051 to 1.906)	
Median (95% CI)	NC (3.778 to NC)	4.93 (1.938 to NC)	NC (2.825 to NC)	5.98 (2.037 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4147		0.2891	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.77 to 1.88)		1.33 (0.79 to 2.24)	
P-value	-	0.4153		0.2907	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (34.0)	39 (50.6)	27 (48.2)	40 (51.9)	0.4073
Number (%) of patients censored	64 (66.0)	38 (49.4)	29 (51.8)	37 (48.1)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	3.06 (1.938 to 5.618)	2.40 (1.938 to 4.468)	2.83 (1.906 to 5.914)	2.79 (1.183 to 4.632)	
Median (95% CI)	NC (11.072 to NC)	7.69 (4.731 to NC)	9.30 (5.782 to NC)	8.25 (4.797 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0948		0.6500	
Hazard ratio (95% CI) vs Pd	-	1.48 (0.93 to 2.36)		1.12 (0.69 to 1.82)	
P-value	-	0.0969		0.6502	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (20.6)	17 (22.1)	10 (17.9)	20 (26.0)	0.4687
Number (%) of patients censored	77 (79.4)	60 (77.9)	46 (82.1)	57 (74.0)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	11.70 (5.848 to NC)	12.52 (3.450 to NC)	14.26 (7.622 to NC)	9.86 (2.891 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.259 to NC)	NC (13.634 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9569		0.3724	
Hazard ratio (95% CI) vs Pd	-	0.98 (0.51 to 1.88)		1.41 (0.66 to 3.01)	
P-value	-	0.9570		0.3748	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (17.5)	12 (15.6)	16 (28.6)	12 (15.6)	0.4275
Number (%) of patients censored	80 (82.5)	65 (84.4)	40 (71.4)	65 (84.4)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	13.34 (5.552 to NC)	14.82 (9.758 to NC)	7.75 (3.811 to NC)	NC (8.082 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (11.236 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4373		0.0609	
Hazard ratio (95% CI) vs Pd	-	0.75 (0.35 to 1.57)		0.50 (0.23 to 1.05)	
P-value	-	0.4389		0.0663	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	54 (39.4)	67 (48.6)	8 (50.0)	10 (62.5)	0.9485
Number (%) of patients censored	83 (60.6)	71 (51.4)	8 (50.0)	6 (37.5)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.91 (1.084 to 2.530)	1.18 (1.084 to 1.873)	0.99 (0.953 to 1.150)	1.05 (0.953 to 1.938)	
Median (95% CI)	NC (5.618 to NC)	9.86 (2.891 to NC)	1.28 (0.986 to NC)	2.14 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.281 to NC)	6.54 (2.136 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2159		0.7073	
Hazard ratio (95% CI) vs Pd	-	1.25 (0.88 to 1.79)		1.20 (0.47 to 3.03)	
P-value	-	0.2168		0.7077	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_impl_ecog_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	54 (39.4)	74 (53.6)	6 (37.5)	5 (31.3)	0.4286
Number (%) of patients censored	83 (60.6)	64 (46.4)	10 (62.5)	11 (68.8)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	3.19 (1.971 to 5.454)	2.40 (1.906 to 2.957)	2.79 (0.986 to NC)	6.51 (1.018 to 7.984)	
Median (95% CI)	NC (7.885 to NC)	7.79 (5.027 to 14.554)	NC (1.347 to NC)	7.98 (4.600 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (8.345 to NC)	NC (6.505 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0735		0.8777	
Hazard ratio (95% CI) vs Pd	-	1.38 (0.97 to 1.95)		0.91 (0.28 to 3.01)	
P-value	-	0.0747		0.8781	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (17.5)	30 (21.7)	6 (37.5)	7 (43.8)	0.8663
Number (%) of patients censored	113 (82.5)	108 (78.3)	10 (62.5)	9 (56.3)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	14.26 (8.608 to NC)	12.94 (7.458 to NC)	1.08 (0.953 to NC)	1.31 (0.953 to 12.517)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.084 to NC)	12.52 (1.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.517 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6069		0.9026	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.67 to 1.97)		1.07 (0.36 to 3.20)	
P-value	-	0.6072		0.9028	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (20.4)	23 (16.7)	5 (31.3)	1 (6.3)	0.1584
Number (%) of patients censored	109 (79.6)	115 (83.3)	11 (68.8)	15 (93.8)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	13.34 (7.754 to NC)	NC (10.875 to NC)	2.79 (0.986 to NC)	14.82 (14.817 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.347 to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2550		0.0189	
Hazard ratio (95% CI) vs Pd	-	0.73 (0.42 to 1.26)			
P-value	-	0.2564		0.9964	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (49.0)	29 (45.3)	22 (39.3)	29 (54.7)	14 (32.6)	19 (55.9)	0.2043
Number (%) of patients censored	26 (51.0)	35 (54.7)	34 (60.7)	24 (45.3)	29 (67.4)	15 (44.1)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	1.08 (0.986 to 1.150)	1.08 (1.018 to 2.136)	2.17 (1.248 to 4.928)	1.38 (1.084 to 2.004)	1.51 (1.018 to 6.242)	1.05 (0.986 to 1.840)	
Median (95% CI)	NC (1.117 to NC)	NC (3.187 to NC)	NC (4.107 to NC)	3.68 (1.938 to NC)	NC (2.168 to NC)	2.89 (1.314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.928 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6735		0.0819		0.1166	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.52 to 1.52)		1.63 (0.94 to 2.84)		1.73 (0.87 to 3.44)	
P-value	-	0.6736		0.0849		0.1212	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (41.2)	34 (53.1)	25 (44.6)	27 (50.9)	13 (30.2)	15 (44.1)	0.7114
Number (%) of patients censored	30 (58.8)	30 (46.9)	31 (55.4)	26 (49.1)	30 (69.8)	19 (55.9)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	3.75 (1.971 to 8.345)	2.04 (1.084 to 3.745)	2.27 (1.150 to 5.027)	2.33 (1.314 to 4.632)	3.98 (0.986 to 6.505)	3.75 (1.183 to 6.505)	
Median (95% CI)	NC (7.885 to NC)	7.89 (4.698 to NC)	NC (4.764 to NC)	9.30 (4.600 to NC)	NC (4.665 to NC)	7.98 (4.928 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	14.55 (14.554 to NC)	NC (NC to NC)	NC (8.608 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1231		0.6939		0.6801	
Hazard ratio (95% CI) vs Pd	-	1.53 (0.89 to 2.64)		1.12 (0.65 to 1.92)		1.17 (0.56 to 2.46)	
P-value	-	0.1260		0.6941		0.6808	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (25.5)	13 (20.3)	7 (12.5)	13 (24.5)	9 (20.9)	11 (32.4)	0.3696
Number (%) of patients censored	38 (74.5)	51 (79.7)	49 (87.5)	40 (75.5)	34 (79.1)	23 (67.6)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	11.47 (4.731 to NC)	12.94 (7.655 to NC)	NC (8.608 to NC)	10.81 (2.793 to NC)	7.62 (1.084 to NC)	2.89 (1.051 to NC)	
Median (95% CI)	NC (14.259 to NC)	NC (13.634 to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.984 to NC)	NC (6.604 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5960		0.1619		0.5419	
Hazard ratio (95% CI) vs Pd	-	0.81 (0.38 to 1.75)		1.91 (0.76 to 4.78)		1.31 (0.54 to 3.17)	
P-value	-	0.5966		0.1692		0.5437	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (19.6)	9 (14.1)	13 (23.2)	8 (15.1)	10 (23.3)	7 (20.6)	0.8878
Number (%) of patients censored	41 (80.4)	55 (85.9)	43 (76.8)	45 (84.9)	33 (76.7)	27 (79.4)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	NC (5.552 to NC)	NC (9.331 to NC)	9.43 (2.464 to NC)	NC (9.758 to NC)	8.38 (1.347 to NC)	14.82 (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	13.34 (8.378 to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.339 to NC)	NC (14.817 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4801		0.1881		0.3151	
Hazard ratio (95% CI) vs Pd	-	0.72 (0.29 to 1.78)		0.56 (0.23 to 1.35)		0.60 (0.22 to 1.65)	
P-value	-	0.4820		0.1943		0.3204	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (51.6)	18 (46.2)	40 (40.8)	50 (50.5)	6 (25.0)	9 (56.3)	0.1720
Number (%) of patients censored	15 (48.4)	21 (53.8)	58 (59.2)	49 (49.5)	18 (75.0)	7 (43.8)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	1.08 (0.986 to 1.117)	1.15 (1.018 to 3.187)	1.94 (1.084 to 2.957)	1.22 (1.084 to 1.906)	1.51 (0.986 to NC)	1.02 (0.723 to 1.380)	
Median (95% CI)	5.62 (1.117 to NC)	NC (1.906 to NC)	NC (4.928 to NC)	5.98 (2.267 to NC)	NC (1.511 to NC)	1.84 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.840 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5657		0.1870		0.0821	
Hazard ratio (95% CI) vs Pd	-	0.82 (0.42 to 1.61)		1.32 (0.87 to 2.00)		2.43 (0.86 to 6.84)	
P-value	-	0.5664		0.1884		0.0924	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_impl_seriss_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (38.7)	21 (53.8)	41 (41.8)	51 (51.5)	7 (29.2)	7 (43.8)	0.8172
Number (%) of patients censored	19 (61.3)	18 (46.2)	57 (58.2)	48 (48.5)	17 (70.8)	9 (56.3)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	3.75 (1.281 to NC)	1.97 (1.018 to 4.731)	2.83 (1.938 to 5.454)	2.40 (1.938 to 4.600)	2.83 (0.953 to NC)	3.22 (1.051 to 6.505)	
Median (95% CI)	NC (7.589 to NC)	9.33 (2.891 to NC)	NC (6.505 to NC)	7.89 (5.027 to NC)	NC (2.825 to NC)	6.51 (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	NC (5.914 to NC)	NC (6.505 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1863		0.2545		0.8483	
Hazard ratio (95% CI) vs Pd	-	1.61 (0.79 to 3.27)		1.27 (0.84 to 1.92)		1.11 (0.39 to 3.18)	
P-value	-	0.1904		0.2556		0.8481	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (25.8)	7 (17.9)	18 (18.4)	27 (27.3)	4 (16.7)	3 (18.8)	0.3670
Number (%) of patients censored	23 (74.2)	32 (82.1)	80 (81.6)	72 (72.7)	20 (83.3)	13 (81.3)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	11.47 (1.084 to NC)	13.63 (9.856 to NC)	NC (7.622 to NC)	7.66 (2.825 to NC)	NC (1.018 to NC)	NC (1.018 to NC)	
Median (95% CI)	14.26 (14.259 to NC)	NC (12.945 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.604 to NC)	
75% quantile (95% CI)	NC (14.259 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3596		0.2010		0.8914	
Hazard ratio (95% CI) vs Pd	-	0.62 (0.23 to 1.73)		1.47 (0.81 to 2.67)		0.90 (0.20 to 4.08)	
P-value	-	0.3640		0.2038		0.8915	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (19.4)	4 (10.3)	22 (22.4)	15 (15.2)	5 (20.8)	5 (31.3)	0.6363
Number (%) of patients censored	25 (80.6)	35 (89.7)	76 (77.6)	84 (84.8)	19 (79.2)	11 (68.8)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	NC (1.873 to NC)	NC (9.331 to NC)	11.07 (4.665 to NC)	NC (10.875 to NC)	7.75 (1.117 to NC)	4.70 (1.938 to 14.817)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.435 to NC)	14.82 (3.220 to 14.817)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.378 to NC)	14.82 (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2883		0.1366		0.8890	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (34.8)	6 (42.9)	39 (41.1)	62 (52.5)	0.8658
Number (%) of patients censored	15 (65.2)	8 (57.1)	56 (58.9)	56 (47.5)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.61 (0.986 to NC)	1.31 (0.986 to 3.778)	1.94 (1.084 to 2.891)	1.12 (1.051 to 1.906)	
Median (95% CI)	NC (1.610 to NC)	3.78 (1.150 to NC)	NC (4.928 to NC)	4.93 (2.267 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (3.778 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7375		0.1257	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.42 to 3.46)		1.37 (0.91 to 2.04)	
P-value	-	0.7379		0.1272	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (39.1)	5 (35.7)	39 (41.1)	67 (56.8)	0.4200
Number (%) of patients censored	14 (60.9)	9 (64.3)	56 (58.9)	51 (43.2)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	3.06 (1.051 to 8.936)	4.70 (1.018 to NC)	2.79 (1.347 to 4.764)	2.40 (1.906 to 2.825)	
Median (95% CI)	8.94 (3.055 to NC)	9.30 (3.220 to NC)	NC (5.782 to NC)	6.70 (4.731 to 9.331)	
75% quantile (95% CI)	NC (8.936 to NC)	NC (9.298 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7762		0.0931	
Hazard ratio (95% CI) vs Pd	-	0.85 (0.28 to 2.55)		1.40 (0.94 to 2.08)	
P-value	-	0.7764		0.0947	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (17.4)	3 (21.4)	18 (18.9)	28 (23.7)	0.9451
Number (%) of patients censored	19 (82.6)	11 (78.6)	77 (81.1)	90 (76.3)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	7.43 (1.018 to NC)	8.48 (1.314 to NC)	11.70 (7.984 to NC)	12.52 (6.078 to NC)	
Median (95% CI)	NC (4.928 to NC)	NC (7.458 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (8.476 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9708		0.5773	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.23 to 4.60)		1.18 (0.65 to 2.14)	
P-value	-	0.9707		0.5778	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (17.4)	3 (21.4)	21 (22.1)	18 (15.3)	0.3676
Number (%) of patients censored	19 (82.6)	11 (78.6)	74 (77.9)	100 (84.7)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	11.07 (1.051 to NC)	4.70 (1.018 to NC)	13.34 (4.665 to NC)	NC (11.466 to NC)	
Median (95% CI)	NC (11.072 to NC)	NC (3.220 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7588		0.1114	
Hazard ratio (95% CI) vs Pd	-	1.26 (0.28 to 5.68)		0.60 (0.32 to 1.13)	
P-value	-	0.7593		0.1152	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (33.3)	9 (37.5)	33 (42.3)	57 (55.3)	0.6183
Number (%) of patients censored	24 (66.7)	15 (62.5)	45 (57.7)	46 (44.7)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.91 (1.018 to NC)	1.84 (0.986 to NC)	1.91 (1.084 to 2.825)	1.08 (1.051 to 1.873)	
Median (95% CI)	NC (2.891 to NC)	NC (1.840 to NC)	NC (3.778 to NC)	3.75 (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8453		0.1217	
Hazard ratio (95% CI) vs Pd	-	1.09 (0.46 to 2.59)		1.40 (0.91 to 2.15)	
P-value	-	0.8453		0.1234	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (44.4)	12 (50.0)	30 (38.5)	59 (57.3)	0.5378
Number (%) of patients censored	20 (55.6)	12 (50.0)	48 (61.5)	44 (42.7)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	2.83 (1.183 to 4.764)	2.40 (1.018 to 3.220)	2.86 (1.906 to 5.782)	2.40 (1.511 to 3.745)	
Median (95% CI)	8.94 (3.811 to NC)	7.89 (2.398 to NC)	NC (6.505 to NC)	6.70 (5.027 to 10.152)	
75% quantile (95% CI)	NC (11.072 to NC)	NC (7.885 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5931		0.0532	
Hazard ratio (95% CI) vs Pd	-	1.23 (0.58 to 2.60)		1.54 (0.99 to 2.39)	
P-value	-	0.5937		0.0550	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (16.7)	5 (20.8)	15 (19.2)	25 (24.3)	0.9945
Number (%) of patients censored	30 (83.3)	19 (79.2)	63 (80.8)	78 (75.7)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	NC (1.281 to NC)	8.48 (1.314 to NC)	11.70 (7.984 to NC)	12.52 (3.844 to NC)	
Median (95% CI)	NC (NC to NC)	NC (7.458 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8834		0.5642	
Hazard ratio (95% CI) vs Pd	-	1.09 (0.33 to 3.58)		1.21 (0.64 to 2.29)	
P-value	-	0.8835		0.5648	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (22.2)	6 (25.0)	16 (20.5)	15 (14.6)	0.2897
Number (%) of patients censored	28 (77.8)	18 (75.0)	62 (79.5)	88 (85.4)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	11.07 (1.347 to NC)	4.70 (1.018 to NC)	13.34 (4.665 to NC)	NC (11.466 to NC)	
Median (95% CI)	NC (11.072 to NC)	NC (4.698 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7603		0.1631	
Hazard ratio (95% CI) vs Pd	-	1.18 (0.41 to 3.40)		0.61 (0.30 to 1.23)	
P-value	-	0.7606		0.1674	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (38.9)	36 (43.4)	27 (42.9)	41 (57.7)	0.7442
Number (%) of patients censored	55 (61.1)	47 (56.6)	36 (57.1)	30 (42.3)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.74 (1.084 to 2.530)	1.15 (1.051 to 1.873)	1.28 (1.018 to 2.957)	1.15 (1.051 to 1.938)	
Median (95% CI)	NC (4.928 to NC)	NC (1.906 to NC)	NC (2.957 to NC)	3.68 (2.037 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5312		0.2691	
Hazard ratio (95% CI) vs Pd	-	1.16 (0.73 to 1.85)		1.31 (0.81 to 2.14)	
P-value	-	0.5305		0.2706	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (37.8)	42 (50.6)	26 (41.3)	37 (52.1)	0.6063
Number (%) of patients censored	56 (62.2)	41 (49.4)	37 (58.7)	34 (47.9)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	3.98 (2.267 to 5.914)	2.40 (1.938 to 4.797)	2.04 (1.117 to 4.665)	2.79 (1.084 to 3.975)	
Median (95% CI)	NC (6.834 to NC)	8.25 (5.552 to NC)	11.07 (4.665 to NC)	7.89 (4.468 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1347		0.5450	
Hazard ratio (95% CI) vs Pd	-	1.41 (0.90 to 2.22)		1.17 (0.71 to 1.93)	
P-value	-	0.1367		0.5454	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (17.8)	14 (16.9)	14 (22.2)	23 (32.4)	0.5517
Number (%) of patients censored	74 (82.2)	69 (83.1)	49 (77.8)	48 (67.6)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	NC (5.848 to NC)	NC (7.458 to NC)	11.70 (7.425 to NC)	7.66 (2.431 to 12.945)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.259 to NC)	NC (12.517 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8400		0.5471	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.45 to 1.90)		1.23 (0.63 to 2.39)	
P-value	-	0.8403		0.5478	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (20.0)	14 (16.9)	15 (23.8)	10 (14.1)	0.3460
Number (%) of patients censored	72 (80.0)	69 (83.1)	48 (76.2)	61 (85.9)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	13.34 (5.552 to NC)	14.82 (9.758 to NC)	11.07 (2.825 to NC)	NC (9.331 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.236 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4713		0.0670	
Hazard ratio (95% CI) vs Pd	-	0.77 (0.38 to 1.56)		0.48 (0.22 to 1.07)	
P-value	-	0.4725		0.0732	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	2 (100.0)	60 (39.7)	75 (49.3)	0.5655
Number (%) of patients censored	0 (0.0)	0 (0.0)	91 (60.3)	77 (50.7)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.02 (1.018 to 1.084)	1.08 (1.084 to 1.117)	1.61 (1.084 to 2.168)	1.18 (1.084 to 1.873)	
Median (95% CI)	1.05 (1.018 to 1.084)	1.10 (1.084 to 1.117)	NC (5.618 to NC)	6.54 (2.891 to NC)	
75% quantile (95% CI)	1.08 (1.018 to 1.084)	1.12 (1.084 to 1.117)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.1812	
Hazard ratio (95% CI) vs Pd	-	0.31 (0.03 to 3.50)		1.26 (0.90 to 1.77)	
P-value	-	0.3429		0.1822	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (100.0)	60 (39.7)	77 (50.7)	0.9817
Number (%) of patients censored	2 (100.0)	0 (0.0)	91 (60.3)	75 (49.3)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	NC (NC to NC)	5.03 (5.027 to 7.786)	2.86 (1.971 to 5.027)	2.79 (1.938 to 3.220)	
Median (95% CI)	NC (NC to NC)	6.41 (5.027 to 7.786)	NC (7.885 to NC)	7.98 (5.552 to NC)	
75% quantile (95% CI)	NC (NC to NC)	7.79 (5.027 to 7.786)	NC (NC to NC)	NC (14.554 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.1487	
Hazard ratio (95% CI) vs Pd	-			1.28 (0.91 to 1.80)	
P-value	-	0.9991		0.1498	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	29 (19.2)	37 (24.3)	0.9825
Number (%) of patients censored	1 (50.0)	2 (100.0)	122 (80.8)	115 (75.7)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	11.47 (NC to NC)	NC (NC to NC)	14.26 (7.885 to NC)	12.52 (6.078 to NC)	
Median (95% CI)	11.47 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	11.47 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.5070	
Hazard ratio (95% CI) vs Pd	-			1.18 (0.72 to 1.92)	
P-value	-			0.5075	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	33 (21.9)	24 (15.8)	0.9998
Number (%) of patients censored	2 (100.0)	2 (100.0)	118 (78.1)	128 (84.2)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	11.24 (5.552 to NC)	NC (11.466 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0811	
Hazard ratio (95% CI) vs Pd	-			0.63 (0.37 to 1.06)	
P-value	-			0.0838	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (41.6)	55 (52.9)	15 (36.6)	15 (45.5)	0.7547
Number (%) of patients censored	59 (58.4)	49 (47.1)	26 (63.4)	18 (54.5)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.28 (1.084 to 2.825)	1.22 (1.084 to 1.906)	1.94 (1.018 to 4.928)	1.12 (0.986 to 2.037)	
Median (95% CI)	NC (4.107 to NC)	4.93 (2.103 to NC)	NC (2.168 to NC)	NC (1.314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2218		0.4847	
Hazard ratio (95% CI) vs Pd	-	1.28 (0.86 to 1.92)		1.29 (0.63 to 2.64)	
P-value	-	0.2230		0.4859	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (40.6)	52 (50.0)	14 (34.1)	17 (51.5)	0.6796
Number (%) of patients censored	60 (59.4)	52 (50.0)	27 (65.9)	16 (48.5)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	3.06 (1.938 to 5.027)	3.22 (2.037 to 4.797)	5.55 (1.873 to 11.072)	2.40 (1.018 to 4.731)	
Median (95% CI)	NC (6.834 to NC)	8.61 (5.552 to NC)	NC (8.936 to NC)	7.89 (2.793 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (10.152 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4263		0.1993	
Hazard ratio (95% CI) vs Pd	-	1.18 (0.78 to 1.78)		1.58 (0.78 to 3.21)	
P-value	-	0.4268		0.2032	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (20.8)	27 (26.0)	7 (17.1)	8 (24.2)	0.7791
Number (%) of patients censored	80 (79.2)	77 (74.0)	34 (82.9)	25 (75.8)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	11.47 (7.622 to NC)	10.81 (5.092 to NC)	NC (1.084 to NC)	8.64 (1.084 to NC)	
Median (95% CI)	NC (14.259 to NC)	NC (13.634 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6261		0.6162	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.65 to 2.04)		1.30 (0.47 to 3.57)	
P-value	-	0.6263		0.6171	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_imppl_semm_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (20.8)	15 (14.4)	9 (22.0)	4 (12.1)	0.7346
Number (%) of patients censored	80 (79.2)	89 (85.6)	32 (78.0)	29 (87.9)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	13.34 (4.764 to NC)	NC (10.875 to NC)	11.07 (2.825 to NC)	14.82 (9.758 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.072 to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1406		0.1550	
Hazard ratio (95% CI) vs Pd	-	0.61 (0.31 to 1.18)		0.43 (0.13 to 1.42)	
P-value	-	0.1446		0.1669	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_detpl_semm_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (41.0)	53 (52.0)	20 (38.5)	23 (45.1)	0.8994
Number (%) of patients censored	59 (59.0)	49 (48.0)	32 (61.5)	28 (54.9)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.28 (1.084 to 2.825)	1.35 (1.084 to 1.906)	1.94 (1.018 to 2.530)	1.08 (1.018 to 2.004)	
Median (95% CI)	NC (5.618 to NC)	4.93 (2.136 to NC)	NC (2.168 to NC)	NC (1.380 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2476		0.5636	
Hazard ratio (95% CI) vs Pd	-	1.27 (0.85 to 1.91)		1.19 (0.65 to 2.17)	
P-value	-	0.2488		0.5645	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (41.0)	52 (51.0)	19 (36.5)	27 (52.9)	0.3924
Number (%) of patients censored	59 (59.0)	50 (49.0)	33 (63.5)	24 (47.1)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	2.86 (1.938 to 5.027)	2.89 (2.037 to 4.698)	4.67 (1.873 to 8.936)	1.91 (1.051 to 2.825)	
Median (95% CI)	NC (5.914 to NC)	8.25 (5.552 to NC)	NC (6.505 to NC)	6.51 (2.793 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3890		0.1109	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.79 to 1.80)		1.61 (0.89 to 2.89)	
P-value	-	0.3897		0.1142	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (20.0)	26 (25.5)	9 (17.3)	11 (21.6)	0.9294
Number (%) of patients censored	80 (80.0)	76 (74.5)	43 (82.7)	40 (78.4)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	11.70 (7.885 to NC)	10.81 (5.092 to NC)	NC (1.084 to NC)	NC (2.825 to NC)	
Median (95% CI)	NC (14.259 to NC)	NC (13.634 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5845		0.7696	
Hazard ratio (95% CI) vs Pd	-	1.18 (0.66 to 2.11)		1.14 (0.47 to 2.75)	
P-value	-	0.5849		0.7698	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (21.0)	15 (14.7)	12 (23.1)	9 (17.6)	0.8719
Number (%) of patients censored	79 (79.0)	87 (85.3)	40 (76.9)	42 (82.4)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	13.34 (4.468 to NC)	NC (10.875 to NC)	11.07 (2.825 to NC)	14.82 (4.698 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.236 to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1467		0.3196	
Hazard ratio (95% CI) vs Pd	-	0.61 (0.32 to 1.19)		0.65 (0.27 to 1.54)	
P-value	-	0.1507		0.3235	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_detpl_dghc_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (40.0)	11 (78.6)	58 (40.6)	66 (47.1)	0.3448
Number (%) of patients censored	6 (60.0)	3 (21.4)	85 (59.4)	74 (52.9)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.74 (0.920 to NC)	1.08 (0.986 to 1.380)	1.51 (1.084 to 2.168)	1.18 (1.084 to 1.938)	
Median (95% CI)	NC (0.920 to NC)	1.61 (1.084 to 1.906)	NC (5.618 to NC)	NC (3.680 to NC)	
75% quantile (95% CI)	NC (1.938 to NC)	1.91 (1.380 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1627		0.3897	
Hazard ratio (95% CI) vs Pd	-	2.24 (0.70 to 7.13)		1.17 (0.82 to 1.66)	
P-value	-	0.1733		0.3906	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (30.0)	6 (42.9)	57 (39.9)	73 (52.1)	0.5298
Number (%) of patients censored	7 (70.0)	8 (57.1)	86 (60.1)	67 (47.9)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.94 (0.920 to NC)	3.22 (0.986 to NC)	3.06 (2.037 to 5.454)	2.79 (1.938 to 3.745)	
Median (95% CI)	NC (0.920 to NC)	NC (1.971 to NC)	NC (8.345 to NC)	7.89 (5.552 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (5.027 to NC)	NC (NC to NC)	NC (14.554 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9996		0.0806	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.25 to 4.03)		1.36 (0.96 to 1.92)	
P-value	-	1.0000		0.0818	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	6 (42.9)	29 (20.3)	31 (22.1)	0.2777
Number (%) of patients censored	9 (90.0)	8 (57.1)	114 (79.7)	109 (77.9)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	NC (0.920 to NC)	3.84 (1.051 to NC)	11.70 (7.885 to NC)	12.94 (7.458 to NC)	
Median (95% CI)	NC (0.920 to NC)	NC (1.314 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (7.655 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2236		0.9426	
Hazard ratio (95% CI) vs Pd	-	3.44 (0.41 to 28.65)		1.02 (0.61 to 1.69)	
P-value	-	0.2529		0.9426	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (30.0)	2 (14.3)	30 (21.0)	22 (15.7)	0.1749
Number (%) of patients censored	7 (70.0)	12 (85.7)	113 (79.0)	118 (84.3)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.94 (0.920 to NC)	NC (3.220 to NC)	13.34 (6.801 to NC)	NC (11.466 to NC)	
Median (95% CI)	NC (0.920 to NC)	NC (6.538 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1285		0.1642	
Hazard ratio (95% CI) vs Pd	-	0.26 (0.04 to 1.65)		0.68 (0.39 to 1.18)	
P-value	-	0.1540		0.1668	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (44.8)	49 (56.3)	19 (38.8)	24 (43.6)	0.6893
Number (%) of patients censored	53 (55.2)	38 (43.7)	30 (61.2)	31 (56.4)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.12 (1.018 to 1.938)	1.12 (1.084 to 1.873)	2.14 (1.018 to 5.618)	1.38 (1.051 to 2.891)	
Median (95% CI)	NC (2.530 to NC)	3.75 (1.906 to NC)	NC (3.778 to NC)	NC (2.891 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2503		0.7514	
Hazard ratio (95% CI) vs Pd	-	1.27 (0.84 to 1.92)		1.10 (0.60 to 2.01)	
P-value	-	0.2507		0.7525	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_impl_crcl_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (38.5)	50 (57.5)	20 (40.8)	27 (49.1)	0.3292
Number (%) of patients censored	59 (61.5)	37 (42.5)	29 (59.2)	28 (50.9)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	3.81 (1.971 to 7.589)	2.40 (1.938 to 3.745)	2.79 (1.347 to 5.454)	2.79 (1.183 to 4.698)	
Median (95% CI)	NC (8.936 to NC)	7.69 (4.731 to 14.554)	NC (3.975 to NC)	8.61 (4.468 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0340		0.7205	
Hazard ratio (95% CI) vs Pd	-	1.58 (1.03 to 2.42)		1.11 (0.62 to 1.98)	
P-value	-	0.0355		0.7206	
Hazard ratio inverted (95% CI) vs IPd		-		0.90 (0.50 to 1.60)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (22.9)	19 (21.8)	8 (16.3)	14 (25.5)	0.3684
Number (%) of patients censored	74 (77.1)	68 (78.2)	41 (83.7)	41 (74.5)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	11.70 (4.895 to NC)	12.52 (5.092 to NC)	NC (7.885 to NC)	10.81 (2.891 to NC)	
Median (95% CI)	NC (14.259 to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.945 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6745		0.4416	
Hazard ratio (95% CI) vs Pd	-	0.88 (0.47 to 1.62)		1.40 (0.59 to 3.35)	
P-value	-	0.6753		0.4438	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (19.8)	11 (12.6)	12 (24.5)	12 (21.8)	0.6910
Number (%) of patients censored	77 (80.2)	76 (87.4)	37 (75.5)	43 (78.2)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	13.34 (6.801 to NC)	NC (NC to NC)	4.67 (1.938 to NC)	11.47 (4.928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1293		0.3288	
Hazard ratio (95% CI) vs Pd	-	0.57 (0.27 to 1.19)		0.67 (0.29 to 1.51)	
P-value	-	0.1344		0.3320	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	61 (40.4)	76 (50.0)	0.8198
Number (%) of patients censored	1 (50.0)	1 (50.0)	90 (59.6)	76 (50.0)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	1.91 (1.906 to NC)	1.61 (1.084 to 2.168)	1.15 (1.084 to 1.873)	
Median (95% CI)	NC (1.281 to NC)	NC (1.906 to NC)	NC (5.618 to NC)	5.98 (2.431 to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (1.906 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.1862	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		1.25 (0.90 to 1.76)	
P-value	-	0.8092		0.1872	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	2 (100.0)	60 (39.7)	77 (50.7)	0.9739
Number (%) of patients censored	2 (100.0)	0 (0.0)	91 (60.3)	75 (49.3)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	NC (NC to NC)	0.99 (0.986 to 1.971)	2.86 (1.971 to 5.027)	2.79 (1.971 to 3.745)	
Median (95% CI)	NC (NC to NC)	1.48 (0.986 to 1.971)	NC (8.345 to NC)	7.98 (5.552 to NC)	
75% quantile (95% CI)	NC (NC to NC)	1.97 (0.986 to 1.971)	NC (NC to NC)	NC (14.554 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.1558	
Hazard ratio (95% CI) vs Pd	-			1.28 (0.91 to 1.79)	
P-value	-	0.9991		0.1568	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	29 (19.2)	36 (23.7)	0.6120
Number (%) of patients censored	1 (50.0)	1 (50.0)	122 (80.8)	116 (76.3)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	5.09 (5.092 to NC)	14.26 (7.984 to NC)	12.52 (6.604 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.5702	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		1.15 (0.71 to 1.88)	
P-value	-	0.8092		0.5705	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	33 (21.9)	24 (15.8)	0.9998
Number (%) of patients censored	2 (100.0)	2 (100.0)	118 (78.1)	128 (84.2)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	11.24 (5.552 to NC)	NC (11.466 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0873	
Hazard ratio (95% CI) vs Pd	-			0.63 (0.37 to 1.07)	
P-value	-			0.0900	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (41.7)	64 (54.2)	14 (36.8)	13 (36.1)	0.3158
Number (%) of patients censored	67 (58.3)	54 (45.8)	24 (63.2)	23 (63.9)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.74 (1.084 to 2.168)	1.12 (1.051 to 1.314)	1.12 (1.018 to NC)	2.14 (1.084 to NC)	
Median (95% CI)	NC (4.107 to NC)	3.75 (1.906 to NC)	NC (2.530 to NC)	NC (3.351 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1031		0.7673	
Hazard ratio (95% CI) vs Pd	-	1.36 (0.94 to 1.98)		0.89 (0.42 to 1.90)	
P-value	-	0.1045		0.7674	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (37.4)	59 (50.0)	17 (44.7)	20 (55.6)	0.8953
Number (%) of patients censored	72 (62.6)	59 (50.0)	21 (55.3)	16 (44.4)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	3.75 (2.136 to 5.618)	2.79 (1.938 to 3.975)	2.04 (0.986 to 7.589)	2.20 (1.018 to 4.632)	
Median (95% CI)	NC (7.885 to NC)	9.30 (5.552 to NC)	NC (2.825 to NC)	6.51 (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (7.688 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1732		0.3375	
Hazard ratio (95% CI) vs Pd	-	1.31 (0.89 to 1.95)		1.37 (0.72 to 2.63)	
P-value	-	0.1745		0.3395	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (20.9)	30 (25.4)	6 (15.8)	7 (19.4)	0.8223
Number (%) of patients censored	91 (79.1)	88 (74.6)	32 (84.2)	29 (80.6)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	11.47 (7.622 to NC)	10.81 (3.844 to NC)	NC (1.281 to NC)	12.52 (3.351 to NC)	
Median (95% CI)	NC (14.259 to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.517 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7499		0.7045	
Hazard ratio (95% CI) vs Pd	-	1.09 (0.64 to 1.87)		1.23 (0.41 to 3.68)	
P-value	-	0.7509		0.7052	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (21.7)	18 (15.3)	8 (21.1)	6 (16.7)	0.6036
Number (%) of patients censored	90 (78.3)	100 (84.7)	30 (78.9)	30 (83.3)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	11.07 (5.191 to NC)	NC (10.875 to NC)	13.34 (2.464 to NC)	14.82 (3.220 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.339 to NC)	NC (14.817 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0915		0.7528	
Hazard ratio (95% CI) vs Pd	-	0.60 (0.33 to 1.09)		0.84 (0.29 to 2.45)	
P-value	-	0.0951		0.7531	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	56 (38.9)	74 (50.3)	6 (66.7)	3 (42.9)	0.1819
Number (%) of patients censored	88 (61.1)	73 (49.7)	3 (33.3)	4 (57.1)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.74 (1.084 to 2.530)	1.15 (1.084 to 1.873)	0.99 (0.986 to 2.168)	1.05 (0.986 to NC)	
Median (95% CI)	NC (6.242 to NC)	4.93 (2.431 to NC)	2.17 (0.986 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.084 to NC)	NC (2.037 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1077		0.4636	
Hazard ratio (95% CI) vs Pd	-	1.33 (0.94 to 1.88)		0.60 (0.15 to 2.40)	
P-value	-	0.1089		0.4686	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_impl_refr1_de_i_t_x.rtf (08APR2021 15:02)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	56 (38.9)	75 (51.0)	4 (44.4)	4 (57.1)	0.9157
Number (%) of patients censored	88 (61.1)	72 (49.0)	5 (55.6)	3 (42.9)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	2.86 (1.971 to 5.454)	2.40 (1.938 to 3.220)	3.98 (0.986 to NC)	4.93 (1.446 to 9.298)	
Median (95% CI)	NC (8.345 to NC)	7.89 (5.552 to NC)	NC (0.986 to NC)	9.30 (1.446 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (7.589 to NC)	NC (7.688 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1099		0.8121	
Hazard ratio (95% CI) vs Pd	-	1.33 (0.94 to 1.87)		1.18 (0.29 to 4.75)	
P-value	-	0.1111		0.8123	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (18.1)	36 (24.5)	4 (44.4)	1 (14.3)	0.3058
Number (%) of patients censored	118 (81.9)	111 (75.5)	5 (55.6)	6 (85.7)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	NC (7.885 to NC)	10.81 (6.078 to NC)	7.98 (2.168 to 14.259)	NC (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	14.26 (2.168 to NC)	NC (1.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.259 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3874		0.4891	
Hazard ratio (95% CI) vs Pd	-	1.25 (0.75 to 2.07)		0.46 (0.05 to 4.41)	
P-value	-	0.3884		0.4999	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (22.2)	23 (15.6)	1 (11.1)	1 (14.3)	0.5239
Number (%) of patients censored	112 (77.8)	124 (84.4)	8 (88.9)	6 (85.7)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	11.07 (5.191 to NC)	NC (11.466 to NC)	NC (3.450 to NC)	NC (4.928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.450 to NC)	NC (4.928 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0590		0.8917	
Hazard ratio (95% CI) vs Pd	-	0.60 (0.35 to 1.03)		1.21 (0.08 to 19.40)	
P-value	-	0.0615		0.8918	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (37.5)	40 (43.0)	29 (44.6)	37 (60.7)	0.6697
Number (%) of patients censored	55 (62.5)	53 (57.0)	36 (55.4)	24 (39.3)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.61 (1.018 to 3.515)	1.31 (1.084 to 2.103)	1.51 (1.084 to 2.136)	1.15 (1.018 to 1.873)	
Median (95% CI)	NC (5.618 to NC)	NC (3.351 to NC)	7.92 (2.136 to NC)	2.89 (1.906 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5201		0.2137	
Hazard ratio (95% CI) vs Pd	-	1.16 (0.73 to 1.84)		1.36 (0.84 to 2.21)	
P-value	-	0.5205		0.2155	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (43.2)	46 (49.5)	22 (33.8)	33 (54.1)	0.5754
Number (%) of patients censored	50 (56.8)	47 (50.5)	43 (66.2)	28 (45.9)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	2.79 (1.938 to 3.811)	2.07 (1.511 to 2.825)	5.03 (1.347 to 7.885)	3.75 (1.938 to 5.125)	
Median (95% CI)	NC (5.782 to NC)	7.98 (4.632 to NC)	NC (7.885 to NC)	7.89 (5.125 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3674		0.1400	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.79 to 1.87)		1.50 (0.87 to 2.57)	
P-value	-	0.3682		0.1427	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (20.5)	21 (22.6)	12 (18.5)	16 (26.2)	0.6933
Number (%) of patients censored	70 (79.5)	72 (77.4)	53 (81.5)	45 (73.8)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	11.70 (7.425 to NC)	12.52 (7.458 to NC)	14.26 (4.895 to NC)	6.08 (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (14.259 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8976		0.5125	
Hazard ratio (95% CI) vs Pd	-	1.04 (0.56 to 1.96)		1.28 (0.61 to 2.71)	
P-value	-	0.8978		0.5136	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Disease symptoms
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (21.6)	16 (17.2)	14 (21.5)	8 (13.1)	0.4283
Number (%) of patients censored	69 (78.4)	77 (82.8)	51 (78.5)	53 (86.9)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	13.34 (3.811 to NC)	14.82 (9.331 to NC)	11.07 (4.468 to NC)	NC (10.875 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3802		0.0955	
Hazard ratio (95% CI) vs Pd	-	0.74 (0.38 to 1.45)		0.48 (0.20 to 1.16)	
P-value	-	0.3820		0.1028	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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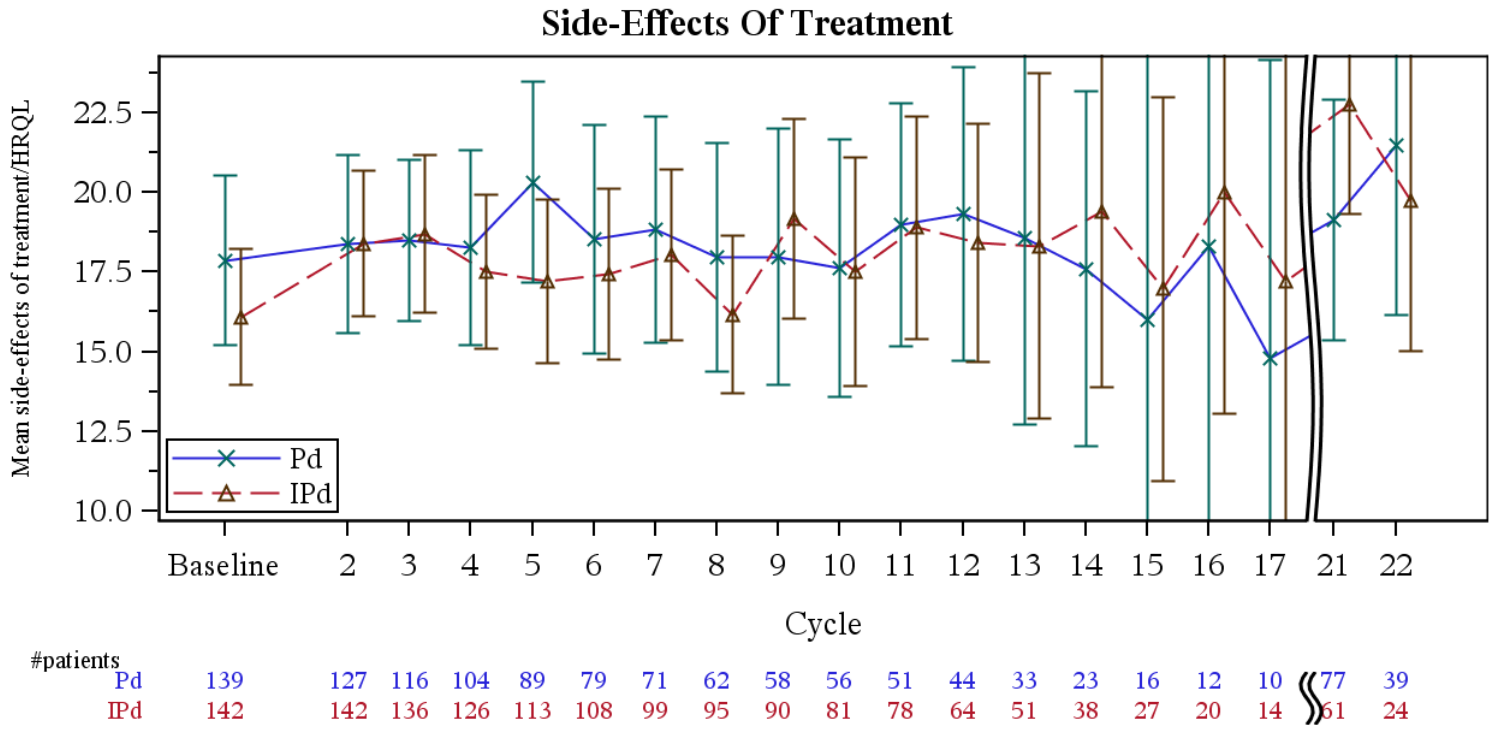
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Side-effects of treatment
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-MY20 - Mean and 95% CI for side-effects of treatment score over time - ITT population



A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Side-effects of treatment
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-MY20 - Time to first improvement by 15 pt in side-effects of treatment (LOCF) - ITT population

First improvement 15 points Side effects of treatment (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	17 (11.1)	18 (11.7)
Number (%) of patients censored	136 (88.9)	136 (88.3)
Kaplan-Meier estimates of side-effects of treatment in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9576
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.02 (0.52 to 1.98)
P-value	-	0.9576
Probability (95% CI)[c]		
2 Months	0.07 (0.035 to 0.117)	0.07 (0.039 to 0.121)
4 Months	0.10 (0.056 to 0.153)	0.11 (0.064 to 0.163)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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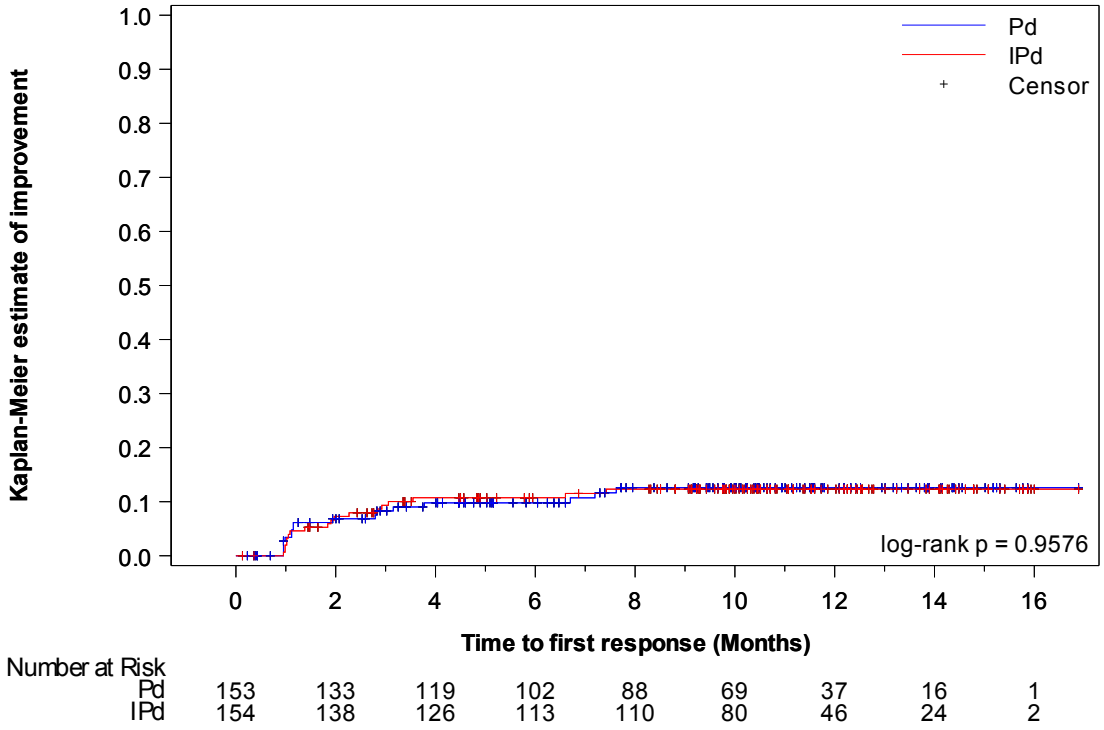
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Side-effects of treatment
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-MY20 - Time to first improvement by 15 pt in side-effects of treatment - Kaplan-Meier curve (LOCF) - ITT population



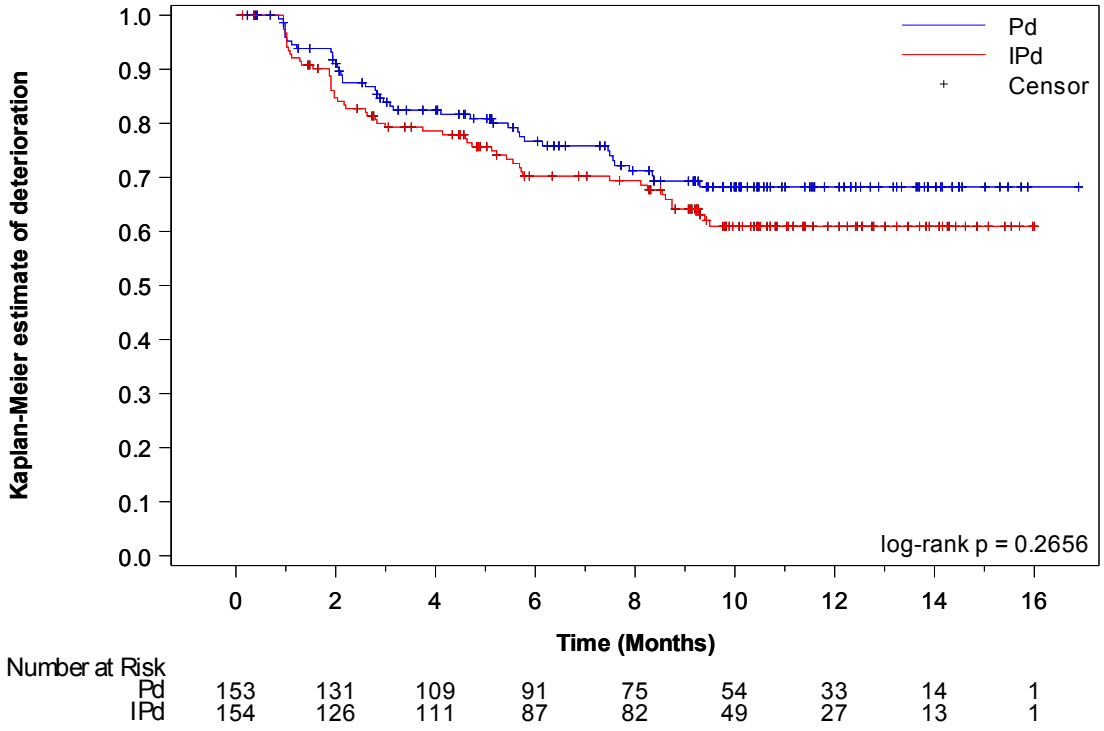
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_imp15l_de_i_f_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Side-effects of treatment
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-MY20 - Time to first deterioration by 15 pt in side-effects of treatment (LOCF) - ITT population

First deterioration 15 points Side effects of treatment (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	41 (26.8)	53 (34.4)
Number (%) of patients censored	112 (73.2)	101 (65.6)
Kaplan-Meier estimates of side-effects of treatment in months		
25% quantile (95% CI)	7.46 (4.107 to NC)	5.13 (2.595 to 8.246)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2656
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.26 (0.84 to 1.90)
P-value	-	0.2666
Probability (95% CI)[c]		
2 Months	0.92 (0.859 to 0.952)	0.85 (0.779 to 0.896)
4 Months	0.82 (0.751 to 0.878)	0.79 (0.711 to 0.844)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_det15l_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Side-effects of treatment
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-MY20 - Time to first deterioration by 15 pt in side-effects of treatment - Kaplan-Meier curve (LOCF) - ITT population



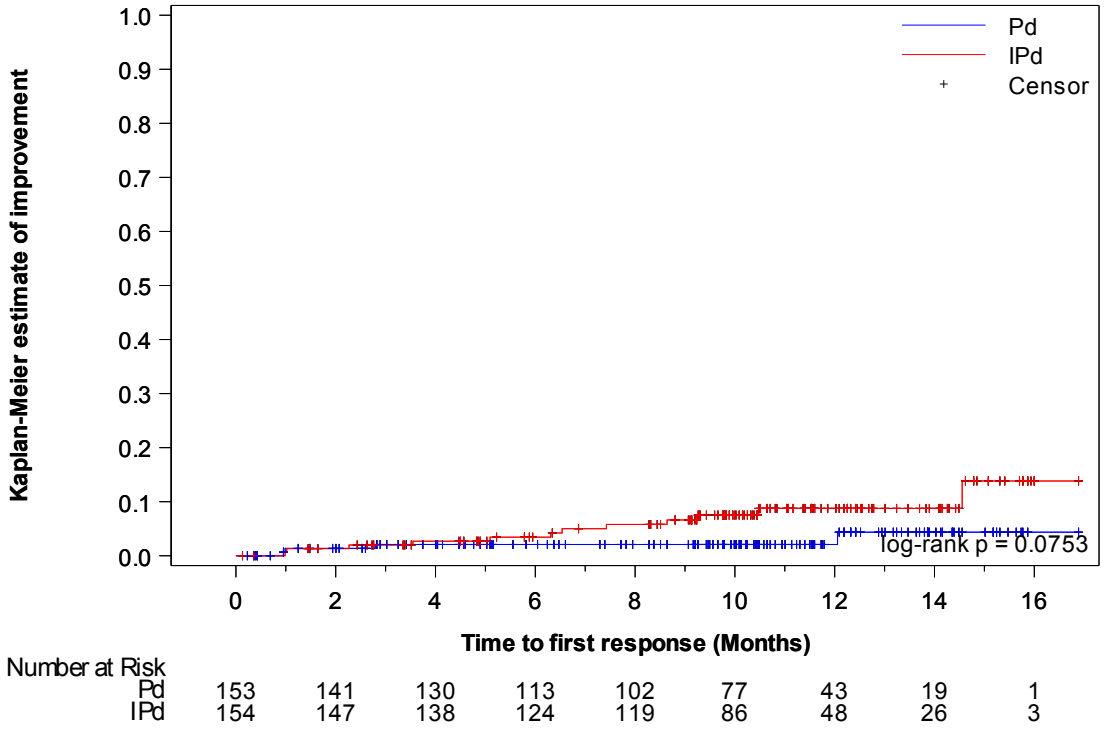
A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_det15l_de_i_f_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Side-effects of treatment
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-MY20 - Time until permanent improvement by 15 pt in side-effects of treatment (LOCF) - ITT population

First permanent improvement 15 points Side effects of treatment (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	4 (2.6)	12 (7.8)
Number (%) of patients censored	149 (97.4)	142 (92.2)
Kaplan-Meier estimates of side-effects of treatment in months		
25% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0753
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.69 (0.86 to 8.34)
P-value	-	0.0875
Probability (95% CI)[c]		
2 Months	0.01 (0.003 to 0.044)	0.01 (0.003 to 0.043)
4 Months	0.02 (0.006 to 0.055)	0.03 (0.009 to 0.063)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_imp15pl_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Side-effects of treatment
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-MY20 - Time until permanent improvement by 15 pt in side-effects of treatment - Kaplan-Meier curve (LOCF) - ITT population



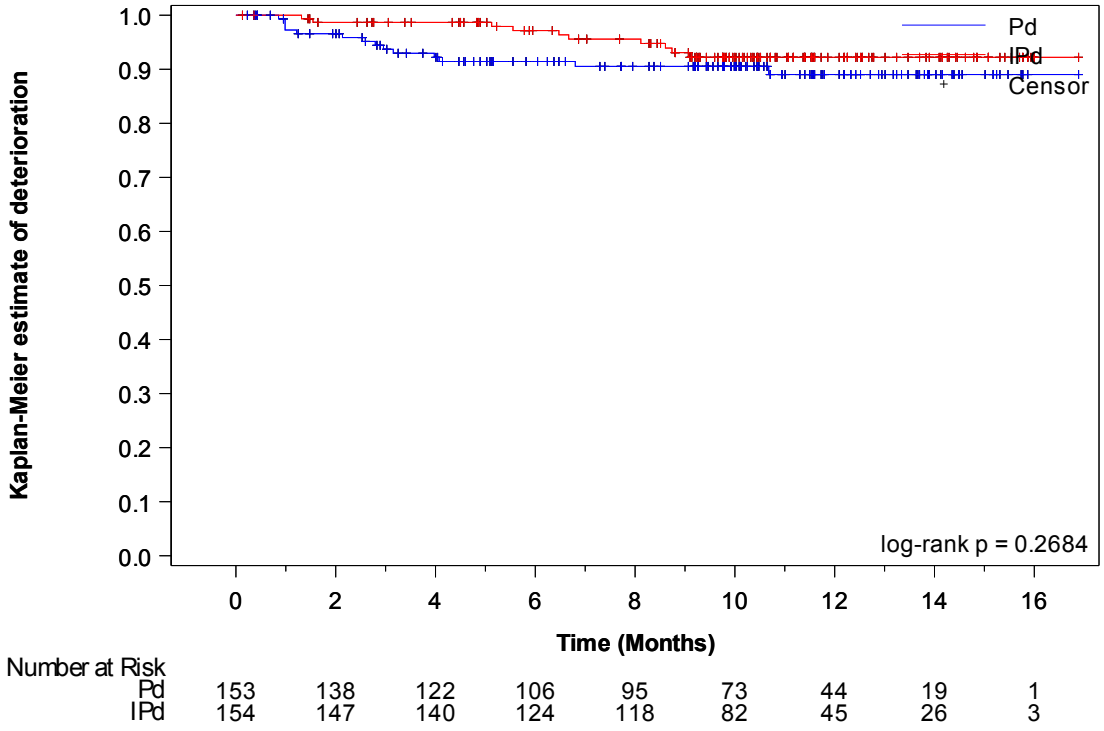
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_imp15pl_de_i_f_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Side-effects of treatment
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-MY20 - Time until permanent deterioration by 15 pt in side-effects of treatment (LOCF) - ITT population

First permanent deterioration 15 points Side effects of treatment (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	14 (9.2)	10 (6.5)
Number (%) of patients censored	139 (90.8)	144 (93.5)
Kaplan-Meier estimates of side-effects of treatment in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2684
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.63 (0.28 to 1.43)
P-value	-	0.2725
Probability (95% CI)[c]		
2 Months	0.97 (0.920 to 0.986)	0.99 (0.948 to 0.997)
4 Months	0.92 (0.864 to 0.956)	0.99 (0.948 to 0.997)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_det15pl_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Side-effects of treatment
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-MY20 - Time until permanent deterioration by 15 pt in side-effects of treatment - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_det15pl_de_i_f_x.rtf (08APR2021 15:30)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (17.1)	13 (24.1)	14 (25.9)	18 (26.5)	7 (24.1)	3 (9.4)	0.1908
Number (%) of patients censored	58 (82.9)	41 (75.9)	40 (74.1)	50 (73.5)	22 (75.9)	29 (90.6)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	NC (2.990 to NC)	NC (1.906 to NC)	5.55 (1.117 to NC)	6.44 (2.234 to NC)	5.62 (1.117 to NC)	NC (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.618 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3998		0.8682		0.0923	
Hazard ratio (95% CI) vs Pd	-	1.40 (0.64 to 3.07)		0.94 (0.47 to 1.89)		0.33 (0.09 to 1.28)	
P-value	-	0.4020		0.8677		0.1094	

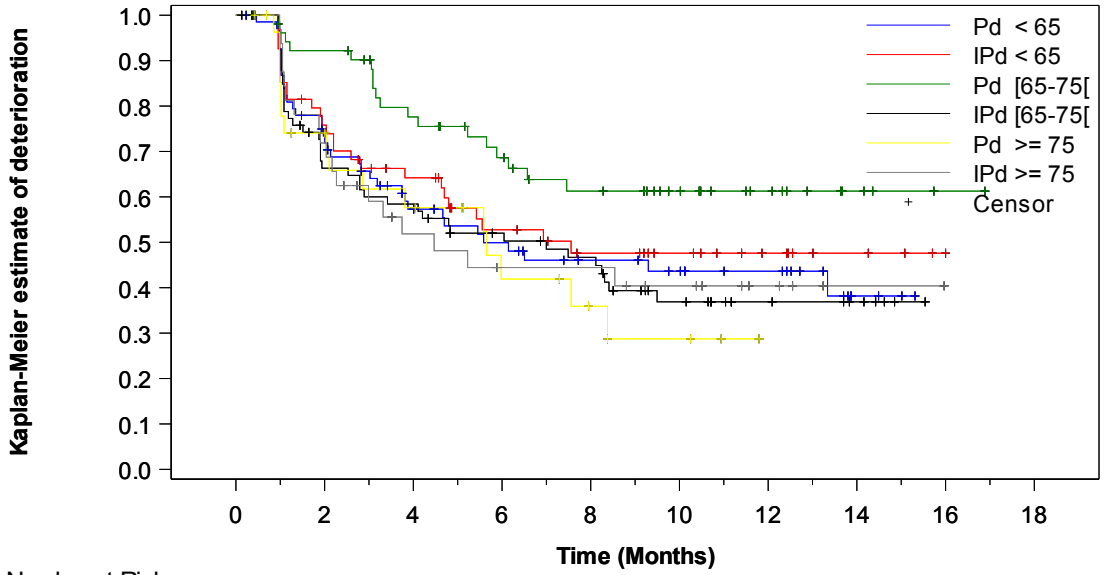
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_impl_age_de_i_t_x.rtf (08APR2021 15:03)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (51.4)	26 (48.1)	18 (33.3)	39 (57.4)	16 (55.2)	18 (56.3)	0.0498
Number (%) of patients censored	34 (48.6)	28 (51.9)	36 (66.7)	29 (42.6)	13 (44.8)	14 (43.8)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	1.94 (1.084 to 3.023)	2.04 (0.986 to 4.632)	5.22 (3.088 to 7.458)	1.51 (1.051 to 2.530)	1.08 (0.986 to 3.811)	1.89 (1.051 to 2.990)	
Median (95% CI)	5.59 (3.187 to NC)	7.56 (3.811 to NC)	NC (6.571 to NC)	7.00 (2.793 to 9.495)	5.65 (2.037 to 8.378)	4.47 (2.037 to NC)	
75% quantile (95% CI)	NC (13.339 to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.495 to NC)	NC (5.979 to NC)	NC (8.542 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6404		0.0090		0.6630	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.54 to 1.47)		2.07 (1.19 to 3.63)		0.86 (0.44 to 1.69)	
P-value	-	0.6406		0.0106		0.6633	
Hazard ratio inverted (95% CI) vs IPd		-		0.48 (0.28 to 0.84)		1.16 (0.59 to 2.29)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detl_age_de_i_t_x.rtf (08APR2021 15:03)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to age (IRT) (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd < 65	70	41	27	20	13	2	0
IPd < 65	54	34	22	17	8	3	0
Pd [65-75[	54	44	30	23	10	2	0
IPd [65-75[	68	38	30	19	8	1	0
Pd >= 75	29	15	8	3	0	0	0
IPd >= 75	32	17	11	9	4	1	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detl_age_de_i_f_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (7.1)	5 (9.3)	4 (7.4)	9 (13.2)	1 (3.4)	3 (9.4)	0.8774
Number (%) of patients censored	65 (92.9)	49 (90.7)	50 (92.6)	59 (86.8)	28 (96.6)	29 (90.6)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	NC (12.057 to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.480 to NC)	NC (NC to NC)	NC (8.641 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7237		0.4150		0.4865	
Hazard ratio (95% CI) vs Pd	-	1.25 (0.36 to 4.32)		1.62 (0.50 to 5.28)		2.19 (0.23 to 21.17)	
P-value	-	0.7243		0.4197		0.4974	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (22.9)	9 (16.7)	8 (14.8)	11 (16.2)	6 (20.7)	8 (25.0)	0.7916
Number (%) of patients censored	54 (77.1)	45 (83.3)	46 (85.2)	57 (83.8)	23 (79.3)	24 (75.0)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	10.68 (4.665 to NC)	NC (5.552 to NC)	15.08 (9.561 to NC)	NC (8.739 to NC)	5.65 (0.986 to NC)	10.68 (4.665 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (NC to NC)	NC (5.651 to NC)	13.67 (10.678 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.667 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2958		0.9974		0.9485	
Hazard ratio (95% CI) vs Pd	-	0.65 (0.29 to 1.47)		1.00 (0.40 to 2.49)		0.97 (0.33 to 2.79)	
P-value	-	0.2996		0.9974		0.9484	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detpl_age_de_i_t_x.rtf (08APR2021 15:04)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (21.8)	18 (17.6)	11 (21.2)	16 (30.8)	0.2305
Number (%) of patients censored	79 (78.2)	84 (82.4)	41 (78.8)	36 (69.2)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (2.825 to NC)	NC (3.778 to NC)	NC (1.906 to NC)	3.35 (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3781		0.4293	
Hazard ratio (95% CI) vs Pd	-	0.76 (0.41 to 1.41)		1.36 (0.63 to 2.94)	
P-value	-	0.3802		0.4311	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_impl_plne_de_i_t_x.rtf (08APR2021 15:04)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (43.6)	56 (54.9)	26 (50.0)	27 (51.9)	0.2599
Number (%) of patients censored	57 (56.4)	46 (45.1)	26 (50.0)	25 (48.1)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	2.83 (1.347 to 4.107)	1.71 (1.084 to 2.201)	2.14 (1.018 to 3.877)	2.04 (1.051 to 3.811)	
Median (95% CI)	13.34 (5.454 to NC)	4.83 (2.891 to NC)	6.57 (3.811 to NC)	8.41 (3.318 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1083		0.7851	
Hazard ratio (95% CI) vs Pd	-	1.38 (0.93 to 2.05)		0.93 (0.54 to 1.59)	
P-value	-	0.1098		0.7848	

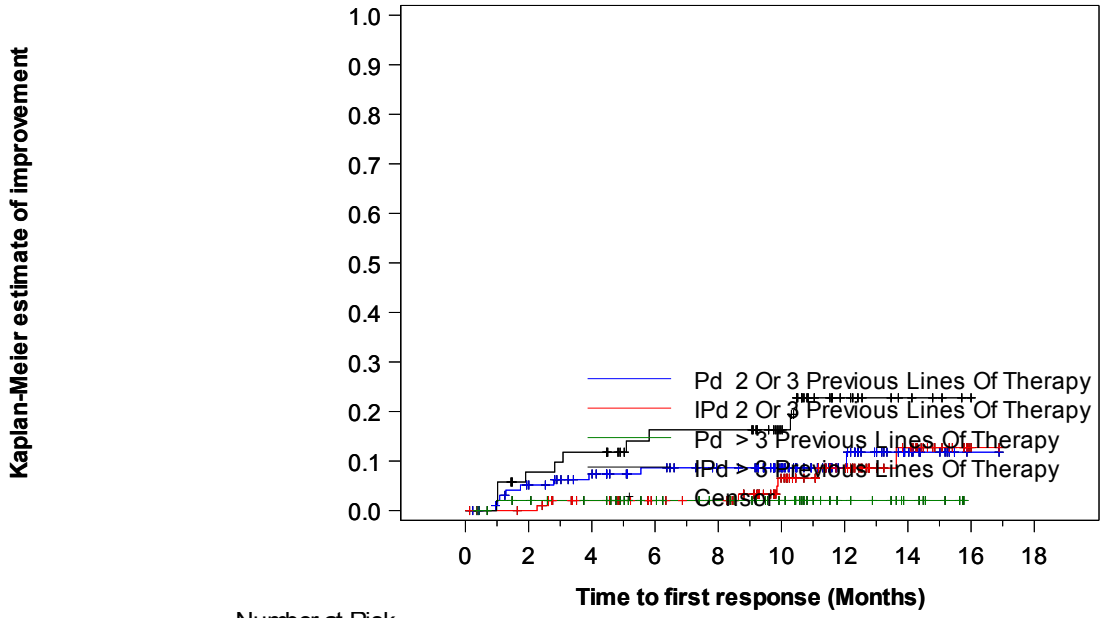
A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detl_plne_de_i_t_x.rtf (08APR2021 15:03)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	9 (8.9)	7 (6.9)	1 (1.9)	10 (19.2)	0.0236
Number (%) of patients censored	92 (91.1)	95 (93.1)	51 (98.1)	42 (80.8)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (NC to NC)	NC (5.092 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4666		0.0087	
Hazard ratio (95% CI) vs Pd	-	0.69 (0.26 to 1.87)		9.47 (1.21 to 73.99)	
P-value	-	0.4694		0.0321	
Hazard ratio inverted (95% CI) vs IPd		-		0.11 (0.01 to 0.83)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_imppl_plne_de_i_t_x.rtf (08APR2021 15:04)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to nb of prior lines (IRT) (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd 2 Or 3 Previous Lines Of Therapy	101	85	73	66	29	7	0
IPd 2 Or 3 Previous Lines Of Therapy	102	93	83	73	36	10	0
Pd > 3 Previous Lines Of Therapy	52	45	36	29	13	4	0
IPd > 3 Previous Lines Of Therapy	52	45	37	37	11	3	0

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (16.8)	16 (15.7)	13 (25.0)	12 (23.1)	0.8644
Number (%) of patients censored	84 (83.2)	86 (84.3)	39 (75.0)	40 (76.9)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	14.69 (7.655 to NC)	NC (8.969 to NC)	10.68 (3.154 to NC)	10.68 (5.552 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	15.08 (11.236 to NC)	NC (13.667 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6043		0.5088	
Hazard ratio (95% CI) vs Pd	-	0.83 (0.42 to 1.65)		0.77 (0.35 to 1.68)	
P-value	-	0.6048		0.5100	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (18.6)	22 (24.7)	20 (24.1)	12 (18.5)	0.1944
Number (%) of patients censored	57 (81.4)	67 (75.3)	63 (75.9)	53 (81.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (2.825 to NC)	8.44 (2.628 to NC)	5.55 (1.938 to NC)	NC (2.267 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4310		0.2931	
Hazard ratio (95% CI) vs Pd	-	1.32 (0.66 to 2.61)		0.68 (0.33 to 1.40)	
P-value	-	0.4324		0.2960	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (45.7)	44 (49.4)	38 (45.8)	39 (60.0)	0.3447
Number (%) of patients censored	38 (54.3)	45 (50.6)	45 (54.2)	26 (40.0)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	2.14 (1.117 to 4.107)	1.94 (1.084 to 3.417)	3.02 (1.084 to 3.877)	1.40 (1.051 to 2.037)	
Median (95% CI)	7.46 (5.454 to NC)	8.11 (4.797 to NC)	7.56 (4.698 to NC)	4.21 (2.201 to 8.312)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.339 to NC)	NC (8.312 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8044		0.1095	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.67 to 1.67)		1.44 (0.92 to 2.25)	
P-value	-	0.8051		0.1114	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (5.7)	9 (10.1)	6 (7.2)	8 (12.3)	0.8825
Number (%) of patients censored	66 (94.3)	80 (89.9)	77 (92.8)	57 (87.7)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (12.057 to NC)	NC (10.480 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3644		0.4387	
Hazard ratio (95% CI) vs Pd	-	1.71 (0.53 to 5.56)		1.52 (0.53 to 4.37)	
P-value	-	0.3703		0.4419	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (22.9)	14 (15.7)	14 (16.9)	14 (21.5)	0.2723
Number (%) of patients censored	54 (77.1)	75 (84.3)	69 (83.1)	51 (78.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	9.56 (5.585 to NC)	NC (8.345 to NC)	14.69 (9.298 to NC)	13.67 (7.885 to NC)	
Median (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1656		0.8638	
Hazard ratio (95% CI) vs Pd	-	0.61 (0.30 to 1.24)		1.07 (0.51 to 2.24)	
P-value	-	0.1701		0.8638	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (19.8)	25 (21.2)	7 (36.8)	8 (33.3)	0.8048
Number (%) of patients censored	101 (80.2)	93 (78.8)	12 (63.2)	16 (66.7)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (2.990 to NC)	NC (3.088 to NC)	1.15 (0.986 to NC)	2.92 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.150 to NC)	NC (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9616		0.7443	
Hazard ratio (95% CI) vs Pd	-	0.99 (0.57 to 1.72)		0.84 (0.31 to 2.33)	
P-value	-	0.9616		0.7445	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	58 (46.0)	70 (59.3)	9 (47.4)	10 (41.7)	0.3607
Number (%) of patients censored	68 (54.0)	48 (40.7)	10 (52.6)	14 (58.3)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	2.79 (1.281 to 3.811)	1.87 (1.084 to 2.168)	3.02 (0.986 to 5.881)	4.21 (0.953 to 8.115)	
Median (95% CI)	7.46 (5.224 to NC)	4.83 (2.891 to 8.312)	NC (3.023 to NC)	NC (4.632 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0915		0.7931	
Hazard ratio (95% CI) vs Pd	-	1.35 (0.95 to 1.91)		0.89 (0.36 to 2.18)	
P-value	-	0.0924		0.7933	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (5.6)	15 (12.7)	3 (15.8)	2 (8.3)	0.1023
Number (%) of patients censored	119 (94.4)	103 (87.3)	16 (84.2)	22 (91.7)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (0.986 to NC)	NC (9.889 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0832		0.2681	
Hazard ratio (95% CI) vs Pd	-	2.17 (0.88 to 5.32)		0.37 (0.06 to 2.29)	
P-value	-	0.0911		0.2858	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (18.3)	22 (18.6)	6 (31.6)	5 (20.8)	0.5718
Number (%) of patients censored	103 (81.7)	96 (81.4)	13 (68.4)	19 (79.2)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	14.69 (6.801 to NC)	NC (8.969 to NC)	7.66 (0.986 to 15.080)	13.67 (1.314 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	15.08 (7.655 to 15.080)	NC (13.667 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	15.08 (NC to NC)	NC (13.667 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6493		0.5204	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.49 to 1.57)		0.66 (0.19 to 2.33)	
P-value	-	0.6491		0.5231	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detpl_race_de_i_t_x.rtf (08APR2021 15:04)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	0 (0.0)	28 (20.9)	33 (25.4)	0.9822
Number (%) of patients censored	2 (66.7)	4 (100.0)	106 (79.1)	97 (74.6)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (NC to NC)	NC (2.990 to NC)	8.44 (2.825 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.5544	
Hazard ratio (95% CI) vs Pd	-			1.16 (0.70 to 1.93)	
P-value	-	0.9990		0.5557	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_impl_ethn_de_i_t_x.rtf (08APR2021 15:04)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	3 (75.0)	63 (47.0)	71 (54.6)	0.8721
Number (%) of patients censored	2 (66.7)	1 (25.0)	71 (53.0)	59 (45.4)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	1.35 (1.347 to NC)	2.22 (1.018 to 7.556)	2.83 (1.938 to 3.745)	1.91 (1.150 to 2.530)	
Median (95% CI)	NC (1.347 to NC)	5.49 (1.018 to NC)	7.46 (5.454 to NC)	6.93 (4.107 to 9.495)	
75% quantile (95% CI)	NC (1.347 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9835		0.3337	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.09 to 10.98)		1.18 (0.84 to 1.66)	
P-value	-	0.9834		0.3345	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detl_ethn_de_i_t_x.rtf (08APR2021 15:03)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	0 (0.0)	8 (6.0)	17 (13.1)	0.9899
Number (%) of patients censored	2 (66.7)	4 (100.0)	126 (94.0)	113 (86.9)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.138 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.0870	
Hazard ratio (95% CI) vs Pd	-			2.05 (0.88 to 4.75)	
P-value	-	0.9990		0.0940	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_imppl_ethn_de_i_t_x.rtf (08APR2021 15:04)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	27 (20.1)	25 (19.2)	0.9999
Number (%) of patients censored	3 (100.0)	4 (100.0)	107 (79.9)	105 (80.8)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	14.69 (6.801 to 15.080)	13.67 (8.969 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	15.08 (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.4632	
Hazard ratio (95% CI) vs Pd	-			0.82 (0.47 to 1.41)	
P-value	-			0.4640	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detpl_ethn_de_i_t_x.rtf (08APR2021 15:04)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	16 (21.1)	7 (12.7)	3 (15.0)	6 (21.4)	2 (40.0)	1 (14.3)	5 (33.3)	6 (28.6)	7 (18.9)	14 (32.6)	0.2972
Number (%) of patients censored	60 (78.9)	48 (87.3)	17 (85.0)	22 (78.6)	3 (60.0)	6 (85.7)	10 (66.7)	15 (71.4)	30 (81.1)	29 (67.4)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (2.267 to NC)	NC (6.439 to NC)	NC (1.018 to NC)	NC (1.018 to NC)	1.12 (0.953 to NC)	NC (2.628 to NC)	1.94 (1.084 to NC)	3.75 (1.084 to NC)	NC (2.825 to NC)	3.09 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (2.628 to NC)	NC (1.150 to NC)	NC (3.745 to NC)	NC (NC to NC)	NC (9.856 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.1699		0.6136		0.2663		0.7376		0.2368	
Hazard ratio (95% CI) vs Pd	-	0.54 (0.22 to 1.32)		1.43 (0.36 to 5.70)		0.28 (0.02 to 3.10)		0.82 (0.25 to 2.68)		1.72 (0.69 to 4.27)	
P-value	-	0.1767		0.6155		0.2978		0.7380		0.2426	
Improvement probability (95% CI)[b]											
2 Months	0.127 (0.062 to 0.216)	0.093 (0.034 to 0.189)	0.105 (0.018 to 0.284)	0.143 (0.045 to 0.295)	0.400 (0.052 to 0.753)		0.267 (0.083 to 0.496)	0.098 (0.017 to 0.267)	0.083 (0.021 to 0.201)	0.192 (0.090 to 0.322)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	23 (30.3)	27 (49.1)	15 (75.0)	14 (50.0)	2 (40.0)	5 (71.4)	8 (53.3)	10 (47.6)	22 (59.5)	27 (62.8)	0.0309
Number (%) of patients censored	53 (69.7)	28 (50.9)	5 (25.0)	14 (50.0)	3 (60.0)	2 (28.6)	7 (46.7)	11 (52.4)	15 (40.5)	16 (37.2)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	5.59 (2.793 to 13.339)	1.51 (1.018 to 3.417)	0.99 (0.953 to 1.216)	1.92 (0.986 to 3.318)	2.60 (1.347 to NC)	1.02 (0.953 to 2.793)	3.02 (1.084 to 5.651)	4.21 (0.953 to 5.552)	2.04 (1.018 to 3.088)	1.28 (0.986 to 2.037)	
Median (95% CI)	NC (13.339 to NC)	5.42 (3.417 to NC)	3.81 (0.986 to 6.505)	8.41 (2.168 to NC)	NC (1.347 to NC)	2.79 (0.953 to NC)	5.88 (1.971 to NC)	NC (4.205 to NC)	3.81 (2.825 to 9.298)	6.05 (1.906 to 8.312)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	6.51 (3.811 to NC)	NC (NC to NC)	NC (1.347 to NC)	NC (2.530 to NC)	NC (5.881 to NC)	NC (NC to NC)	NC (5.454 to NC)	NC (8.246 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.0188		0.0469		0.3446		0.9002		0.8626	
Hazard ratio (95% CI) vs Pd	-	1.93 (1.10 to 3.38)		0.48 (0.23 to 1.01)		2.17 (0.42 to 11.20)		0.94 (0.37 to 2.39)		0.95 (0.54 to 1.68)	
P-value	-	0.0209		0.0517		0.3564		0.8998		0.8623	
Hazard ratio inverted (95% CI) vs IPd		-		2.07 (0.99 to 4.31)		0.46 (0.09 to 2.39)		1.06 (0.42 to 2.69)		1.05 (0.60 to 1.86)	
Deterioration probability (95% CI)[b]											

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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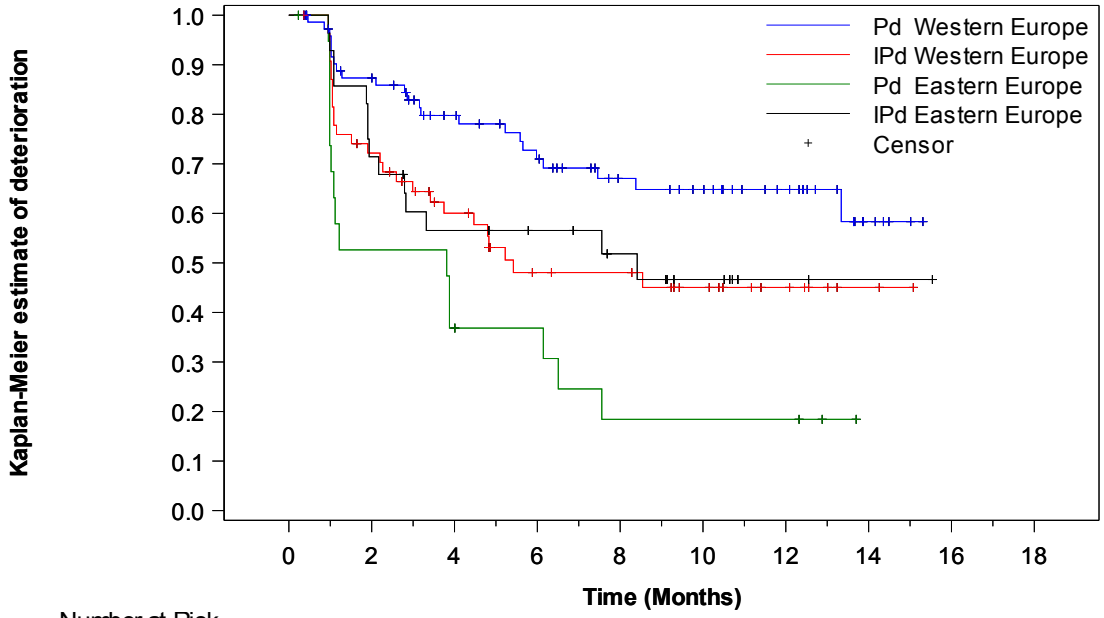
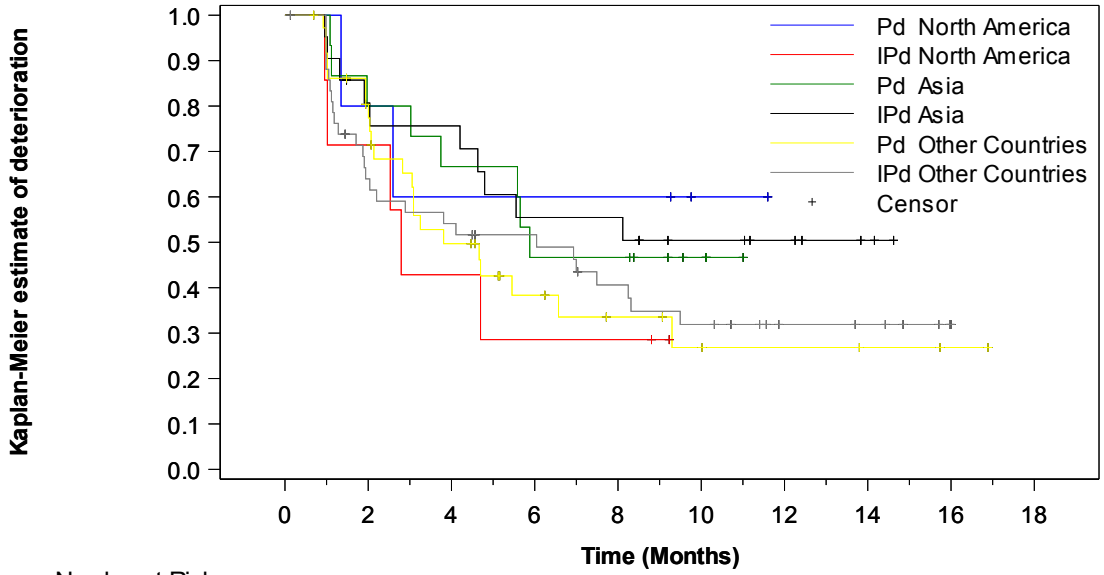
16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to geographical region (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd Western Europe	76	54	40	29	17	2	0
IPd Western Europe	55	32	18	15	7	1	0
Pd Eastern Europe	20	10	6	3	3	0	0
IPd Eastern Europe	28	16	13	9	2	1	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detl_greg_de_i_f_x.rtf (08APR2021 14:33)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to geographical region (LOCF) - Kaplan-Meier curve (2) - ITT population



Number at Risk							
Pd North America	5	3	3	3	0	0	0
IPd North America	7	3	2	1	0	0	0
Pd Asia	15	12	7	5	0	0	0
IPd Asia	21	15	11	8	5	0	0
Pd Other Countries	37	21	9	6	3	2	0
IPd Other Countries	43	23	19	12	6	3	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detl_greg2_de_i_f_x.rtf (08APR2021 14:33)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.7 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	7 (9.2)	2 (3.6)	0 (0.0)	3 (10.7)	0 (0.0)	1 (14.3)	2 (13.3)	1 (4.8)	1 (2.7)	10 (23.3)	0.1737
Number (%) of patients censored	69 (90.8)	53 (96.4)	20 (100.0)	25 (89.3)	5 (100.0)	6 (85.7)	13 (86.7)	20 (95.2)	36 (97.3)	33 (76.7)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (12.057 to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.825 to NC)	NC (NC to NC)	NC (2.628 to NC)	NC (1.084 to NC)	NC (10.283 to NC)	NC (NC to NC)	11.14 (5.815 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.628 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.634 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.7 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.1998		0.1409		0.3980		0.2244		0.0260	
Hazard ratio (95% CI) vs Pd	-	0.37 (0.08 to 1.79)						0.24 (0.02 to 2.85)		7.33 (0.94 to 57.35)	
P-value	-	0.2181		0.9958		0.9984		0.2569		0.0577	
Improvement probability (95% CI)[b]											
2 Months	0.057 (0.018 to 0.127)	0.019 (0.002 to 0.086)		0.036 (0.003 to 0.154)			0.067 (0.004 to 0.260)		0.028 (0.002 to 0.124)	0.048 (0.009 to 0.142)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.8 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	9 (11.8)	11 (20.0)	5 (25.0)	5 (17.9)	1 (20.0)	1 (14.3)	5 (33.3)	5 (23.8)	10 (27.0)	6 (14.0)	0.2696
Number (%) of patients censored	67 (88.2)	44 (80.0)	15 (75.0)	23 (82.1)	4 (80.0)	6 (85.7)	10 (66.7)	16 (76.2)	27 (73.0)	37 (86.0)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (10.678 to NC)	NC (5.585 to NC)	11.24 (0.986 to NC)	NC (6.472 to NC)	NC (2.595 to NC)	NC (8.969 to NC)	7.66 (1.084 to 15.080)	13.67 (1.314 to NC)	9.30 (3.055 to 14.686)	NC (8.115 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.236 to NC)	NC (10.678 to NC)	NC (2.595 to NC)	NC (8.969 to NC)	15.08 (5.585 to 15.080)	NC (13.667 to NC)	14.69 (9.298 to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.8 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.595 to NC)	NC (8.969 to NC)	15.08 (NC to NC)	NC (13.667 to NC)	NC (14.686 to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.2543		0.6000		0.8427		0.7112		0.0305	
Hazard ratio (95% CI) vs Pd	-	1.66 (0.69 to 4.01)		0.72 (0.21 to 2.50)		0.76 (0.05 to 12.10)		0.78 (0.21 to 2.94)		0.34 (0.12 to 0.95)	
P-value	-	0.2594		0.6016		0.8432		0.7119		0.0387	
Deterioration probability (95% CI)[b]											

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (18.6)	12 (15.6)	15 (26.8)	22 (28.6)	0.5222
Number (%) of patients censored	79 (81.4)	65 (84.4)	41 (73.2)	55 (71.4)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (3.745 to NC)	NC (6.439 to NC)	6.24 (1.906 to NC)	3.78 (2.168 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4711		0.8981	
Hazard ratio (95% CI) vs Pd	-	0.77 (0.37 to 1.59)		1.04 (0.54 to 2.01)	
P-value	-	0.4724		0.8985	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (36.1)	39 (50.6)	35 (62.5)	44 (57.1)	0.0672
Number (%) of patients censored	62 (63.9)	38 (49.4)	21 (37.5)	33 (42.9)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	3.09 (1.938 to 5.979)	1.91 (1.051 to 2.793)	1.97 (1.084 to 3.253)	1.87 (1.084 to 2.201)	
Median (95% CI)	NC (7.458 to NC)	5.22 (2.990 to NC)	4.70 (3.253 to 6.505)	7.00 (3.318 to 9.495)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.144 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0675		0.4244	
Hazard ratio (95% CI) vs Pd	-	1.53 (0.97 to 2.41)		0.83 (0.53 to 1.30)	
P-value	-	0.0696		0.4250	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (7.2)	6 (7.8)	3 (5.4)	11 (14.3)	0.2789
Number (%) of patients censored	90 (92.8)	71 (92.2)	53 (94.6)	66 (85.7)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.480 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9812		0.1447	
Hazard ratio (95% CI) vs Pd	-	1.01 (0.34 to 3.02)		2.50 (0.70 to 8.98)	
P-value	-	0.9812		0.1589	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (14.4)	14 (18.2)	16 (28.6)	14 (18.2)	0.1908
Number (%) of patients censored	83 (85.6)	63 (81.8)	40 (71.4)	63 (81.8)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (6.571 to NC)	NC (6.899 to NC)	9.56 (4.435 to 15.080)	NC (8.115 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	15.08 (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7343		0.0924	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.54 to 2.39)		0.54 (0.27 to 1.12)	
P-value	-	0.7338		0.0975	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (19.0)	30 (21.7)	7 (43.8)	4 (25.0)	0.2347
Number (%) of patients censored	111 (81.0)	108 (78.3)	9 (56.3)	12 (75.0)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (4.304 to NC)	NC (3.088 to NC)	1.28 (0.953 to 2.825)	6.44 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.150 to NC)	NC (2.628 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.825 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7636		0.2541	
Hazard ratio (95% CI) vs Pd	-	1.08 (0.64 to 1.83)		0.49 (0.14 to 1.70)	
P-value	-	0.7640		0.2636	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	64 (46.7)	75 (54.3)	6 (37.5)	8 (50.0)	0.2601
Number (%) of patients censored	73 (53.3)	63 (45.7)	10 (62.5)	8 (50.0)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	2.60 (1.281 to 3.253)	1.91 (1.150 to 2.530)	4.67 (0.986 to NC)	1.02 (0.953 to 1.906)	
Median (95% CI)	7.56 (5.454 to NC)	7.00 (4.205 to NC)	NC (2.793 to NC)	5.22 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.881 to NC)	NC (5.224 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4295		0.2014	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.82 to 1.60)		1.99 (0.68 to 5.86)	
P-value	-	0.4309		0.2095	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (5.1)	14 (10.1)	3 (18.8)	3 (18.8)	0.3921
Number (%) of patients censored	130 (94.9)	124 (89.9)	13 (81.3)	13 (81.3)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (0.953 to NC)	NC (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.793 to NC)	NC (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1750		0.9661	
Hazard ratio (95% CI) vs Pd	-	1.86 (0.75 to 4.60)		1.04 (0.21 to 5.14)	
P-value	-	0.1819		0.9661	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_imppl_ecog_de_i_t_x.rtf (08APR2021 15:04)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (19.0)	27 (19.6)	4 (25.0)	1 (6.3)	0.1779
Number (%) of patients censored	111 (81.0)	111 (80.4)	12 (75.0)	15 (93.8)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	14.69 (9.298 to NC)	13.67 (8.969 to NC)	5.65 (0.986 to NC)	NC (1.314 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (4.665 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6887		0.1700	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.52 to 1.54)		0.24 (0.03 to 2.18)	
P-value	-	0.6879		0.2059	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detpl_ecog_de_i_t_x.rtf (08APR2021 15:04)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (23.5)	11 (17.2)	12 (21.4)	12 (22.6)	9 (20.9)	11 (32.4)	0.4547
Number (%) of patients censored	39 (76.5)	53 (82.8)	44 (78.6)	41 (77.4)	34 (79.1)	23 (67.6)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	NC (1.938 to NC)	NC (3.745 to NC)	NC (1.150 to NC)	NC (2.924 to NC)	6.24 (1.938 to NC)	1.97 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.242 to NC)	NC (3.088 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4339		0.8992		0.3623	
Hazard ratio (95% CI) vs Pd	-	0.72 (0.32 to 1.64)		0.95 (0.43 to 2.11)		1.50 (0.62 to 3.64)	
P-value	-	0.4359		0.8992		0.3655	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (51.0)	37 (57.8)	26 (46.4)	28 (52.8)	15 (34.9)	15 (44.1)	0.8584
Number (%) of patients censored	25 (49.0)	27 (42.2)	30 (53.6)	25 (47.2)	28 (65.1)	19 (55.9)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	1.97 (1.117 to 3.187)	1.15 (1.018 to 2.168)	3.15 (1.084 to 5.454)	1.91 (1.018 to 2.595)	3.09 (1.018 to 6.505)	4.47 (1.051 to 7.491)	
Median (95% CI)	7.46 (3.023 to NC)	4.83 (2.201 to NC)	7.56 (4.665 to NC)	5.42 (2.595 to NC)	8.38 (5.585 to NC)	8.54 (5.224 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.339 to NC)	NC (9.495 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3934		0.3101		0.8706	
Hazard ratio (95% CI) vs Pd	-	1.24 (0.75 to 2.05)		1.32 (0.77 to 2.25)		0.94 (0.46 to 1.94)	
P-value	-	0.3943		0.3116		0.8705	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (9.8)	5 (7.8)	3 (5.4)	4 (7.5)	2 (4.7)	8 (23.5)	0.2203
Number (%) of patients censored	46 (90.2)	59 (92.2)	53 (94.6)	49 (92.5)	41 (95.3)	26 (76.5)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (NC to NC)	NC (10.283 to NC)	NC (12.057 to NC)	10.48 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.057 to NC)	NC (10.480 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7436		0.7680		0.0296	
Hazard ratio (95% CI) vs Pd	-	0.81 (0.24 to 2.81)		1.25 (0.28 to 5.60)		4.75 (1.01 to 22.40)	
P-value	-	0.7441		0.7684		0.0488	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (23.5)	8 (12.5)	11 (19.6)	11 (20.8)	6 (14.0)	7 (20.6)	0.5917
Number (%) of patients censored	39 (76.5)	56 (87.5)	45 (80.4)	42 (79.2)	37 (86.0)	27 (79.4)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	14.69 (6.571 to NC)	NC (10.678 to NC)	10.68 (4.665 to NC)	NC (6.472 to NC)	NC (4.435 to NC)	13.67 (5.585 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.667 to NC)	
75% quantile (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1780		0.8980		0.9043	
Hazard ratio (95% CI) vs Pd	-	0.55 (0.22 to 1.34)		0.95 (0.41 to 2.18)		1.07 (0.36 to 3.20)	
P-value	-	0.1847		0.8979		0.9045	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (22.6)	8 (20.5)	22 (22.4)	21 (21.2)	4 (16.7)	5 (31.3)	0.6307
Number (%) of patients censored	24 (77.4)	31 (79.5)	76 (77.6)	78 (78.8)	20 (83.3)	11 (68.8)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	NC (1.938 to NC)	NC (1.971 to NC)	NC (1.906 to NC)	NC (3.088 to NC)	5.62 (1.281 to NC)	1.84 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.618 to NC)	NC (1.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8801		0.6837		0.3851	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.34 to 2.55)		0.88 (0.49 to 1.61)		1.78 (0.48 to 6.68)	
P-value	-	0.8797		0.6836		0.3915	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (51.6)	20 (51.3)	50 (51.0)	55 (55.6)	4 (16.7)	8 (50.0)	0.3319
Number (%) of patients censored	15 (48.4)	19 (48.7)	48 (49.0)	44 (44.4)	20 (83.3)	8 (50.0)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	1.94 (1.117 to 3.187)	1.94 (1.018 to 4.797)	2.86 (1.084 to 3.811)	1.91 (1.084 to 2.168)	8.38 (0.986 to NC)	1.31 (0.986 to 8.542)	
Median (95% CI)	7.46 (2.070 to NC)	8.31 (2.891 to NC)	6.51 (5.454 to NC)	4.80 (2.793 to NC)	NC (8.378 to NC)	8.54 (1.117 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.339 to NC)	NC (NC to NC)	NC (NC to NC)	9.49 (6.932 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9554		0.3589		0.0722	
Hazard ratio (95% CI) vs Pd	-	0.98 (0.51 to 1.89)		1.20 (0.82 to 1.76)		2.87 (0.86 to 9.57)	
P-value	-	0.9554		0.3590		0.0857	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (9.7)	4 (10.3)	5 (5.1)	9 (9.1)	2 (8.3)	4 (25.0)	0.7498
Number (%) of patients censored	28 (90.3)	35 (89.7)	93 (94.9)	90 (90.9)	22 (91.7)	12 (75.0)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	NC (3.910 to NC)	NC (11.138 to NC)	NC (NC to NC)	NC (NC to NC)	12.06 (1.281 to NC)	10.48 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.057 to NC)	NC (2.267 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.057 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9874		0.3398		0.2900	
Hazard ratio (95% CI) vs Pd	-	1.01 (0.23 to 4.53)		1.69 (0.57 to 5.05)		2.44 (0.44 to 13.43)	
P-value	-	0.9874		0.3453		0.3054	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (22.6)	5 (12.8)	21 (21.4)	19 (19.2)	2 (8.3)	4 (25.0)	0.3990
Number (%) of patients censored	24 (77.4)	34 (87.2)	77 (78.6)	80 (80.8)	22 (91.7)	12 (75.0)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	14.69 (2.595 to NC)	NC (8.115 to NC)	15.08 (5.585 to NC)	13.67 (8.969 to NC)	NC (1.084 to NC)	6.93 (0.986 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (NC to NC)	NC (4.435 to NC)	NC (5.585 to NC)	
75% quantile (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3268		0.4163		0.3462	
Hazard ratio (95% CI) vs Pd	-	0.57 (0.18 to 1.79)		0.77 (0.42 to 1.44)		2.23 (0.40 to 12.33)	
P-value	-	0.3332		0.4175		0.3584	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detpl_seriss_de_i_t_x.rtf (08APR2021 15:04)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (13.0)	3 (21.4)	18 (18.9)	28 (23.7)	0.7405
Number (%) of patients censored	20 (87.0)	11 (78.6)	77 (81.1)	90 (76.3)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (0.986 to NC)	3.78 (1.840 to NC)	NC (2.793 to NC)	9.86 (2.924 to NC)	
Median (95% CI)	NC (NC to NC)	NC (1.938 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5782		0.5594	
Hazard ratio (95% CI) vs Pd	-	1.57 (0.32 to 7.78)		1.19 (0.66 to 2.16)	
P-value	-	0.5814		0.5599	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (30.4)	5 (35.7)	46 (48.4)	67 (56.8)	0.9871
Number (%) of patients censored	16 (69.6)	9 (64.3)	49 (51.6)	51 (43.2)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	3.81 (1.150 to 6.571)	3.32 (1.051 to NC)	2.00 (1.018 to 3.187)	1.71 (1.051 to 2.168)	
Median (95% CI)	6.57 (3.811 to NC)	NC (1.314 to NC)	6.51 (4.665 to NC)	6.05 (3.417 to 8.542)	
75% quantile (95% CI)	NC (6.571 to NC)	NC (4.698 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8170		0.3669	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.36 to 3.62)		1.19 (0.82 to 1.73)	
P-value	-	0.8171		0.3675	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (8.7)	0 (0.0)	7 (7.4)	15 (12.7)	0.9893
Number (%) of patients censored	21 (91.3)	14 (100.0)	88 (92.6)	103 (87.3)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.634 to NC)	
Median (95% CI)	NC (12.057 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3368		0.3077	
Hazard ratio (95% CI) vs Pd	-			1.59 (0.65 to 3.90)	
P-value	-	0.9980		0.3121	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (17.4)	3 (21.4)	20 (21.1)	23 (19.5)	0.5981
Number (%) of patients censored	19 (82.6)	11 (78.6)	75 (78.9)	95 (80.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	9.56 (2.957 to NC)	6.67 (1.314 to NC)	15.08 (5.585 to NC)	NC (8.739 to NC)	
Median (95% CI)	NC (5.651 to NC)	NC (3.318 to NC)	NC (15.080 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8324		0.4582	
Hazard ratio (95% CI) vs Pd	-	1.18 (0.26 to 5.29)		0.80 (0.44 to 1.45)	
P-value	-	0.8326		0.4591	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (13.9)	5 (20.8)	14 (17.9)	25 (24.3)	0.8604
Number (%) of patients censored	31 (86.1)	19 (79.2)	64 (82.1)	78 (75.7)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (1.281 to NC)	NC (1.018 to NC)	NC (2.793 to NC)	9.86 (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5572		0.4514	
Hazard ratio (95% CI) vs Pd	-	1.45 (0.42 to 5.00)		1.29 (0.67 to 2.47)	
P-value	-	0.5595		0.4526	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (36.1)	11 (45.8)	38 (48.7)	59 (57.3)	0.7802
Number (%) of patients censored	23 (63.9)	13 (54.2)	40 (51.3)	44 (42.7)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	3.15 (1.347 to 6.144)	2.27 (1.018 to 4.205)	1.94 (1.018 to 3.187)	1.51 (1.051 to 2.168)	
Median (95% CI)	6.57 (3.811 to NC)	4.70 (2.267 to NC)	7.56 (4.107 to NC)	6.93 (2.990 to 9.495)	
75% quantile (95% CI)	NC (NC to NC)	NC (4.698 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4863		0.4674	
Hazard ratio (95% CI) vs Pd	-	1.33 (0.60 to 2.97)		1.16 (0.77 to 1.75)	
P-value	-	0.4877		0.4679	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (5.6)	1 (4.2)	6 (7.7)	13 (12.6)	0.6225
Number (%) of patients censored	34 (94.4)	23 (95.8)	72 (92.3)	90 (87.4)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (12.057 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (13.634 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9320		0.3956	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.08 to 10.13)		1.52 (0.58 to 3.99)	
P-value	-	0.9320		0.3991	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (16.7)	4 (16.7)	18 (23.1)	22 (21.4)	0.8359
Number (%) of patients censored	30 (83.3)	20 (83.3)	60 (76.9)	81 (78.6)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	9.56 (3.154 to NC)	NC (1.314 to NC)	11.24 (4.665 to NC)	13.67 (8.345 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	15.08 (15.080 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8548		0.4745	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.25 to 3.16)		0.80 (0.43 to 1.49)	
P-value	-	0.8549		0.4755	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (20.0)	20 (24.1)	15 (23.8)	14 (19.7)	0.2864
Number (%) of patients censored	72 (80.0)	63 (75.9)	48 (76.2)	57 (80.3)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (2.136 to NC)	3.78 (2.168 to NC)	6.24 (2.825 to NC)	NC (3.745 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5516		0.3071	
Hazard ratio (95% CI) vs Pd	-	1.21 (0.64 to 2.29)		0.69 (0.33 to 1.42)	
P-value	-	0.5518		0.3099	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (45.6)	37 (44.6)	29 (46.0)	46 (64.8)	0.1268
Number (%) of patients censored	49 (54.4)	46 (55.4)	34 (54.0)	25 (35.2)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	2.79 (1.216 to 3.745)	2.20 (1.906 to 4.632)	2.86 (1.018 to 5.585)	1.08 (1.018 to 1.873)	
Median (95% CI)	13.34 (4.698 to NC)	9.49 (4.797 to NC)	7.56 (5.585 to NC)	4.21 (1.906 to 6.998)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.115 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8214		0.0753	
Hazard ratio (95% CI) vs Pd	-	0.95 (0.61 to 1.48)		1.52 (0.95 to 2.42)	
P-value	-	0.8215		0.0774	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (7.8)	8 (9.6)	3 (4.8)	9 (12.7)	0.4879
Number (%) of patients censored	83 (92.2)	75 (90.4)	60 (95.2)	62 (87.3)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (NC to NC)	NC (11.138 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6656		0.2262	
Hazard ratio (95% CI) vs Pd	-	1.25 (0.45 to 3.45)		2.20 (0.59 to 8.13)	
P-value	-	0.6660		0.2381	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (20.0)	12 (14.5)	12 (19.0)	16 (22.5)	0.5402
Number (%) of patients censored	72 (80.0)	71 (85.5)	51 (81.0)	55 (77.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	14.69 (6.801 to NC)	NC (8.115 to NC)	11.24 (4.665 to NC)	10.68 (8.739 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2387		0.8361	
Hazard ratio (95% CI) vs Pd	-	0.65 (0.31 to 1.34)		0.92 (0.44 to 1.96)	
P-value	-	0.2424		0.8361	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	33 (21.9)	33 (21.7)	0.9813
Number (%) of patients censored	2 (100.0)	1 (50.0)	118 (78.1)	119 (78.3)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	1.08 (1.084 to NC)	NC (2.990 to NC)	NC (3.351 to NC)	
Median (95% CI)	NC (NC to NC)	NC (1.084 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.084 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.7533	
Hazard ratio (95% CI) vs Pd	-			0.93 (0.57 to 1.50)	
P-value	-	0.9990		0.7531	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	69 (45.7)	83 (54.6)	0.9803
Number (%) of patients censored	1 (50.0)	2 (100.0)	82 (54.3)	69 (45.4)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	3.19 (3.187 to NC)	NC (NC to NC)	2.79 (1.347 to 3.811)	1.91 (1.084 to 2.201)	
Median (95% CI)	NC (3.187 to NC)	NC (NC to NC)	7.56 (5.651 to NC)	6.05 (4.107 to 8.542)	
75% quantile (95% CI)	NC (3.187 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.1958	
Hazard ratio (95% CI) vs Pd	-			1.23 (0.90 to 1.70)	
P-value	-	0.9990		0.1967	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	10 (6.6)	17 (11.2)	0.9998
Number (%) of patients censored	2 (100.0)	2 (100.0)	141 (93.4)	135 (88.8)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.634 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.2566	
Hazard ratio (95% CI) vs Pd	-			1.57 (0.72 to 3.42)	
P-value	-			0.2606	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	30 (19.9)	28 (18.4)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	121 (80.1)	124 (81.6)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	14.69 (6.801 to NC)	NC (9.002 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.3881	
Hazard ratio (95% CI) vs Pd	-			0.80 (0.48 to 1.34)	
P-value	-			0.3891	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (20.8)	24 (23.1)	9 (22.0)	5 (15.2)	0.6461
Number (%) of patients censored	80 (79.2)	80 (76.9)	32 (78.0)	28 (84.8)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (2.990 to NC)	NC (2.825 to NC)	NC (1.117 to NC)	NC (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.3599	
Hazard ratio (95% CI) vs Pd	-	1.08 (0.60 to 1.93)		0.60 (0.20 to 1.80)	
P-value	-	0.8087		0.3650	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (48.5)	53 (51.0)	17 (41.5)	21 (63.6)	0.2841
Number (%) of patients censored	52 (51.5)	51 (49.0)	24 (58.5)	12 (36.4)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	2.83 (1.084 to 3.253)	1.91 (1.084 to 2.891)	3.09 (1.150 to 6.144)	1.91 (1.084 to 2.201)	
Median (95% CI)	7.46 (4.107 to NC)	7.49 (4.632 to NC)	NC (4.665 to NC)	2.79 (1.938 to 8.411)	
75% quantile (95% CI)	NC (13.339 to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.830 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9492		0.0640	
Hazard ratio (95% CI) vs Pd	-	1.01 (0.69 to 1.49)		1.82 (0.96 to 3.45)	
P-value	-	0.9492		0.0680	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (4.0)	12 (11.5)	3 (7.3)	2 (6.1)	0.1957
Number (%) of patients censored	97 (96.0)	92 (88.5)	38 (92.7)	31 (93.9)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.138 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0713		0.7286	
Hazard ratio (95% CI) vs Pd	-	2.72 (0.88 to 8.42)		0.73 (0.12 to 4.37)	
P-value	-	0.0835		0.7297	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (24.8)	17 (16.3)	4 (9.8)	8 (24.2)	0.0832
Number (%) of patients censored	76 (75.2)	87 (83.7)	37 (90.2)	25 (75.8)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	9.56 (5.585 to 15.080)	NC (9.232 to NC)	NC (6.801 to NC)	9.10 (1.906 to NC)	
Median (95% CI)	15.08 (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0486		0.1817	
Hazard ratio (95% CI) vs Pd	-	0.54 (0.29 to 1.01)		2.22 (0.67 to 7.38)	
P-value	-	0.0521		0.1933	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (21.0)	24 (23.5)	12 (23.1)	10 (19.6)	0.4509
Number (%) of patients censored	79 (79.0)	78 (76.5)	40 (76.9)	41 (80.4)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (2.990 to NC)	9.86 (2.825 to NC)	4.30 (1.084 to NC)	NC (2.267 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7809		0.4834	
Hazard ratio (95% CI) vs Pd	-	1.09 (0.60 to 1.95)		0.74 (0.32 to 1.72)	
P-value	-	0.7813		0.4845	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (48.0)	51 (50.0)	21 (40.4)	31 (60.8)	0.1025
Number (%) of patients censored	52 (52.0)	51 (50.0)	31 (59.6)	20 (39.2)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	2.79 (1.084 to 3.745)	1.91 (1.084 to 2.990)	3.09 (1.150 to 5.881)	1.31 (1.051 to 2.168)	
Median (95% CI)	7.46 (4.698 to NC)	7.56 (4.632 to NC)	NC (5.454 to NC)	4.21 (2.037 to 8.411)	
75% quantile (95% CI)	NC (13.339 to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.312 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9895		0.0448	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.68 to 1.49)		1.75 (1.01 to 3.05)	
P-value	-	0.9895		0.0476	
Hazard ratio inverted (95% CI) vs IPd		-		0.57 (0.33 to 0.99)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (4.0)	12 (11.8)	6 (11.5)	5 (9.8)	0.1168
Number (%) of patients censored	96 (96.0)	90 (88.2)	46 (88.5)	46 (90.2)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.138 to NC)	NC (3.910 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0702		0.6507	
Hazard ratio (95% CI) vs Pd	-	2.73 (0.88 to 8.46)		0.76 (0.23 to 2.49)	
P-value	-	0.0823		0.6517	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (24.0)	15 (14.7)	5 (9.6)	12 (23.5)	0.0151
Number (%) of patients censored	76 (76.0)	87 (85.3)	47 (90.4)	39 (76.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	10.68 (4.435 to 15.080)	NC (9.232 to NC)	NC (11.236 to NC)	10.68 (6.932 to NC)	
Median (95% CI)	15.08 (14.686 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0326		0.0985	
Hazard ratio (95% CI) vs Pd	-	0.50 (0.26 to 0.96)		2.35 (0.83 to 6.67)	
P-value	-	0.0361		0.1089	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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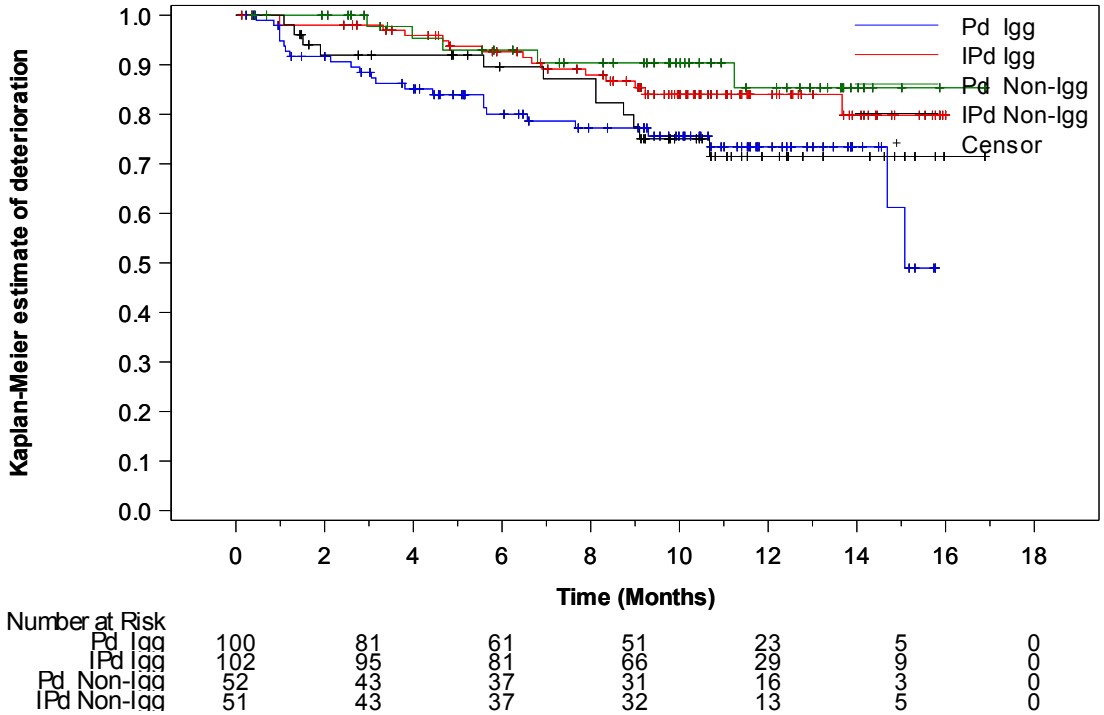
16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to MM type at initial diagnosis (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd Igg	100	81	61	51	23	5	0
IPd Igg	102	95	81	66	29	9	0
Pd Non-Igg	52	43	37	31	16	3	0
IPd Non-Igg	51	43	37	32	13	5	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	3 (21.4)	32 (22.4)	31 (22.1)	0.6052
Number (%) of patients censored	9 (90.0)	11 (78.6)	111 (77.6)	109 (77.9)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (1.741 to NC)	NC (1.840 to NC)	NC (2.825 to NC)	NC (3.088 to NC)	
Median (95% CI)	NC (1.741 to NC)	NC (2.924 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6261		0.8007	
Hazard ratio (95% CI) vs Pd	-	1.74 (0.18 to 16.79)		0.94 (0.57 to 1.54)	
P-value	-	0.6305		0.8007	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	7 (50.0)	69 (48.3)	76 (54.3)	0.1829
Number (%) of patients censored	9 (90.0)	7 (50.0)	74 (51.7)	64 (45.7)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (3.055 to NC)	1.08 (0.986 to 6.932)	2.60 (1.281 to 3.253)	1.91 (1.150 to 2.201)	
Median (95% CI)	NC (3.055 to NC)	6.93 (1.051 to NC)	7.46 (5.585 to NC)	6.05 (4.107 to 9.495)	
75% quantile (95% CI)	NC (NC to NC)	NC (6.932 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0881		0.3689	
Hazard ratio (95% CI) vs Pd	-	5.15 (0.63 to 42.00)		1.16 (0.84 to 1.61)	
P-value	-	0.1259		0.3693	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	1 (7.1)	9 (6.3)	16 (11.4)	0.3360
Number (%) of patients censored	9 (90.0)	13 (92.9)	134 (93.7)	124 (88.6)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (1.741 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (13.634 to NC)	
Median (95% CI)	NC (1.741 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5825		0.1810	
Hazard ratio (95% CI) vs Pd	-	0.46 (0.03 to 7.68)		1.73 (0.77 to 3.92)	
P-value	-	0.5910		0.1865	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	3 (21.4)	29 (20.3)	25 (17.9)	0.8041
Number (%) of patients censored	9 (90.0)	11 (78.6)	114 (79.7)	115 (82.1)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (3.055 to NC)	7.89 (1.314 to NC)	14.69 (6.801 to NC)	NC (9.002 to NC)	
Median (95% CI)	NC (3.055 to NC)	NC (6.932 to NC)	NC (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9329		0.3693	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.11 to 11.44)		0.78 (0.46 to 1.34)	
P-value	-	0.9329		0.3701	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (26.0)	20 (23.0)	7 (14.3)	13 (23.6)	0.2036
Number (%) of patients censored	71 (74.0)	67 (77.0)	42 (85.7)	42 (76.4)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	3.91 (1.906 to NC)	NC (2.924 to NC)	NC (3.745 to NC)	NC (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4451		0.2956	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.44 to 1.43)		1.63 (0.65 to 4.07)	
P-value	-	0.4461		0.3004	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (47.9)	51 (58.6)	21 (42.9)	29 (52.7)	0.7523
Number (%) of patients censored	50 (52.1)	36 (41.4)	28 (57.1)	26 (47.3)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	2.60 (1.150 to 3.253)	1.91 (1.084 to 2.201)	3.06 (1.018 to 5.454)	1.91 (1.051 to 3.417)	
Median (95% CI)	7.56 (4.665 to NC)	4.80 (2.891 to 8.411)	6.57 (4.698 to NC)	7.56 (3.417 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1866		0.6203	
Hazard ratio (95% CI) vs Pd	-	1.31 (0.88 to 1.95)		1.15 (0.66 to 2.02)	
P-value	-	0.1879		0.6206	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (9.4)	9 (10.3)	1 (2.0)	8 (14.5)	0.1064
Number (%) of patients censored	87 (90.6)	78 (89.7)	48 (98.0)	47 (85.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (NC to NC)	NC (9.889 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9764		0.0417	
Hazard ratio (95% CI) vs Pd	-	1.01 (0.40 to 2.56)		6.52 (0.81 to 52.14)	
P-value	-	0.9764		0.0772	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (17.7)	16 (18.4)	12 (24.5)	11 (20.0)	0.4889
Number (%) of patients censored	79 (82.3)	71 (81.6)	37 (75.5)	44 (80.0)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	14.69 (9.561 to NC)	NC (8.115 to NC)	7.66 (3.811 to NC)	13.67 (8.115 to NC)	
Median (95% CI)	NC (14.686 to NC)	NC (NC to NC)	NC (10.678 to NC)	NC (13.667 to NC)	
75% quantile (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7755		0.2721	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.46 to 1.79)		0.63 (0.28 to 1.44)	
P-value	-	0.7756		0.2762	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	32 (21.2)	33 (21.7)	0.9586
Number (%) of patients censored	1 (50.0)	1 (50.0)	119 (78.8)	119 (78.3)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	1.91 (1.906 to NC)	NC (3.745 to NC)	NC (3.351 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (1.906 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (1.906 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.8750	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		0.96 (0.59 to 1.56)	
P-value	-	0.8092		0.8750	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	70 (46.4)	82 (53.9)	0.9747
Number (%) of patients censored	2 (100.0)	1 (50.0)	81 (53.6)	70 (46.1)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	0.99 (0.986 to NC)	2.79 (1.347 to 3.745)	1.91 (1.117 to 2.201)	
Median (95% CI)	NC (NC to NC)	NC (0.986 to NC)	7.56 (5.585 to NC)	6.93 (4.205 to 9.495)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.2816	
Hazard ratio (95% CI) vs Pd	-			1.19 (0.87 to 1.64)	
P-value	-	0.9990		0.2831	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	9 (6.0)	16 (10.5)	0.4405
Number (%) of patients censored	1 (50.0)	1 (50.0)	142 (94.0)	136 (89.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	5.09 (5.092 to NC)	NC (NC to NC)	NC (13.634 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (5.092 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.2252	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		1.65 (0.73 to 3.73)	
P-value	-	0.8092		0.2301	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	30 (19.9)	28 (18.4)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	121 (80.1)	124 (81.6)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	14.69 (6.801 to NC)	NC (9.002 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.4086	
Hazard ratio (95% CI) vs Pd	-			0.80 (0.48 to 1.35)	
P-value	-			0.4095	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (20.0)	29 (24.6)	10 (26.3)	5 (13.9)	0.1767
Number (%) of patients censored	92 (80.0)	89 (75.4)	28 (73.7)	31 (86.1)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (2.825 to NC)	9.86 (2.628 to NC)	4.30 (1.840 to NC)	NC (3.088 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6280		0.2066	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.66 to 1.98)		0.51 (0.17 to 1.48)	
P-value	-	0.6282		0.2154	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (42.6)	63 (53.4)	21 (55.3)	20 (55.6)	0.6775
Number (%) of patients censored	66 (57.4)	55 (46.6)	17 (44.7)	16 (44.4)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	2.83 (1.281 to 4.107)	1.87 (1.084 to 2.530)	2.07 (1.018 to 3.745)	1.91 (1.084 to 2.793)	
Median (95% CI)	9.30 (5.651 to NC)	7.00 (4.632 to NC)	5.65 (3.055 to NC)	3.75 (2.201 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	13.34 (13.339 to NC)	NC (8.246 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2234		0.7031	
Hazard ratio (95% CI) vs Pd	-	1.26 (0.87 to 1.83)		1.13 (0.61 to 2.08)	
P-value	-	0.2244		0.7033	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (6.1)	17 (14.4)	3 (7.9)	0 (0.0)	0.9884
Number (%) of patients censored	108 (93.9)	101 (85.6)	35 (92.1)	36 (100.0)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.138 to NC)	NC (12.057 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0864		0.1025	
Hazard ratio (95% CI) vs Pd	-	2.12 (0.88 to 5.12)			
P-value	-	0.0939		0.9972	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (18.3)	21 (17.8)	9 (23.7)	7 (19.4)	0.9994
Number (%) of patients censored	94 (81.7)	97 (82.2)	29 (76.3)	29 (80.6)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (6.571 to NC)	NC (8.739 to NC)	14.69 (4.435 to NC)	9.23 (6.899 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	15.08 (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5652		0.6878	
Hazard ratio (95% CI) vs Pd	-	0.84 (0.46 to 1.53)		0.82 (0.30 to 2.20)	
P-value	-	0.5657		0.6883	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (20.8)	30 (20.4)	3 (33.3)	4 (57.1)	0.2190
Number (%) of patients censored	114 (79.2)	117 (79.6)	6 (66.7)	3 (42.9)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (3.745 to NC)	NC (3.778 to NC)	2.99 (2.136 to NC)	1.05 (1.018 to 1.971)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.136 to NC)	1.97 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.938 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6856		0.1749	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.54 to 1.49)		2.73 (0.60 to 12.40)	
P-value	-	0.6852		0.1922	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	64 (44.4)	82 (55.8)	6 (66.7)	1 (14.3)	0.0498
Number (%) of patients censored	80 (55.6)	65 (44.2)	3 (33.3)	6 (85.7)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	2.83 (1.938 to 3.811)	1.91 (1.084 to 2.168)	2.07 (0.986 to 3.745)	NC (1.117 to NC)	
Median (95% CI)	8.38 (5.651 to NC)	5.42 (3.745 to 8.411)	3.75 (0.986 to NC)	NC (1.117 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.088 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1013		0.0563	
Hazard ratio (95% CI) vs Pd	-	1.31 (0.95 to 1.82)		0.16 (0.02 to 1.36)	
P-value	-	0.1024		0.0940	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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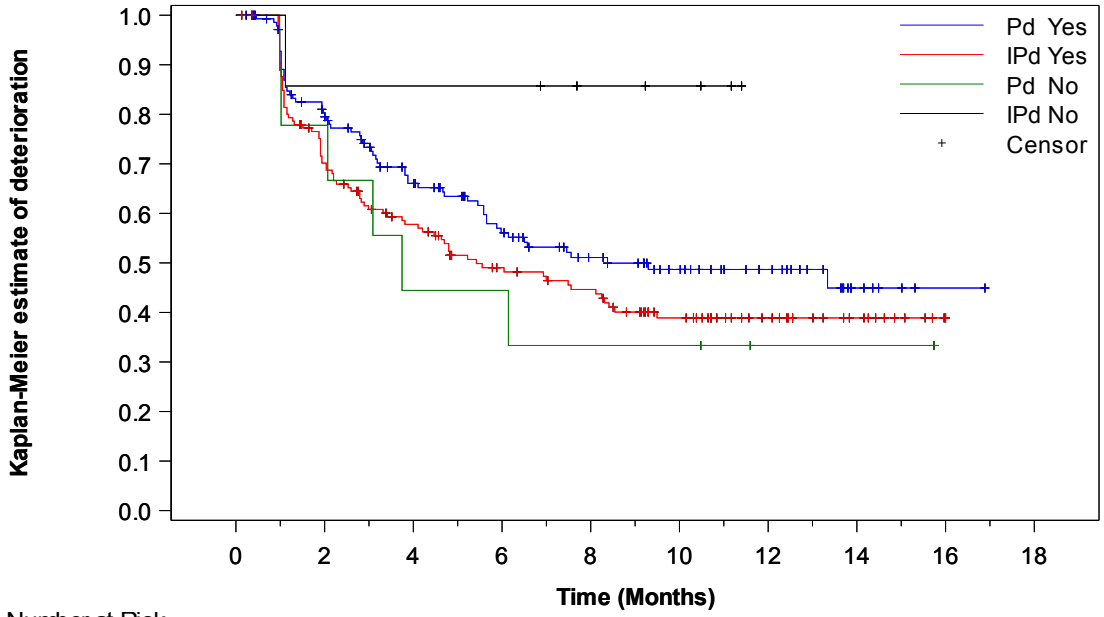
16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to refractory to IMID status (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd Yes	144	94	61	43	22	3	0
IPd Yes	147	83	57	41	20	5	0
Pd No	9	6	4	3	1	1	0
IPd No	7	6	6	4	0	0	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (6.9)	16 (10.9)	0 (0.0)	1 (14.3)	0.9898
Number (%) of patients censored	134 (93.1)	131 (89.1)	9 (100.0)	6 (85.7)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (NC to NC)	NC (3.088 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.088 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3817		0.2568	
Hazard ratio (95% CI) vs Pd	-	1.42 (0.64 to 3.13)			
P-value	-	0.3841		0.9984	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_imppl_refr1_de_i_t_x.rtf (08APR2021 15:04)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (18.8)	28 (19.0)	3 (33.3)	0 (0.0)	0.9876
Number (%) of patients censored	117 (81.3)	119 (81.0)	6 (66.7)	7 (100.0)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	15.08 (6.571 to NC)	NC (8.969 to NC)	14.69 (7.655 to NC)	NC (NC to NC)	
Median (95% CI)	NC (15.080 to NC)	NC (NC to NC)	14.69 (7.655 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5832		0.2967	
Hazard ratio (95% CI) vs Pd	-	0.86 (0.51 to 1.46)			
P-value	-	0.5835		0.9979	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detpl_refr1_de_i_t_x.rtf (08APR2021 15:04)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (23.9)	18 (19.4)	12 (18.5)	16 (26.2)	0.3301
Number (%) of patients censored	67 (76.1)	75 (80.6)	53 (81.5)	45 (73.8)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	7.62 (2.793 to NC)	NC (3.088 to NC)	NC (2.267 to NC)	6.44 (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4498		0.5153	
Hazard ratio (95% CI) vs Pd	-	0.78 (0.42 to 1.47)		1.28 (0.61 to 2.71)	
P-value	-	0.4508		0.5163	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (48.9)	51 (54.8)	27 (41.5)	32 (52.5)	0.9225
Number (%) of patients censored	45 (51.1)	42 (45.2)	38 (58.5)	29 (47.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	2.86 (1.938 to 4.107)	1.91 (1.150 to 2.793)	2.00 (1.084 to 3.877)	1.28 (1.018 to 2.530)	
Median (95% CI)	7.46 (5.224 to NC)	7.00 (3.745 to 9.495)	NC (3.877 to NC)	5.55 (2.825 to NC)	
75% quantile (95% CI)	NC (13.339 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3834		0.4270	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.80 to 1.80)		1.23 (0.74 to 2.05)	
P-value	-	0.3851		0.4285	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detl_llen_de_i_t_x.rtf (08APR2021 15:03)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (10.2)	8 (8.6)	1 (1.5)	9 (14.8)	0.0395
Number (%) of patients censored	79 (89.8)	85 (91.4)	64 (98.5)	52 (85.2)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (12.057 to NC)	NC (11.138 to NC)	NC (NC to NC)	NC (5.815 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6316		0.0119	
Hazard ratio (95% CI) vs Pd	-	0.79 (0.31 to 2.05)		8.92 (1.13 to 70.43)	
P-value	-	0.6324		0.0379	
Hazard ratio inverted (95% CI) vs IPd		-		0.11 (0.01 to 0.88)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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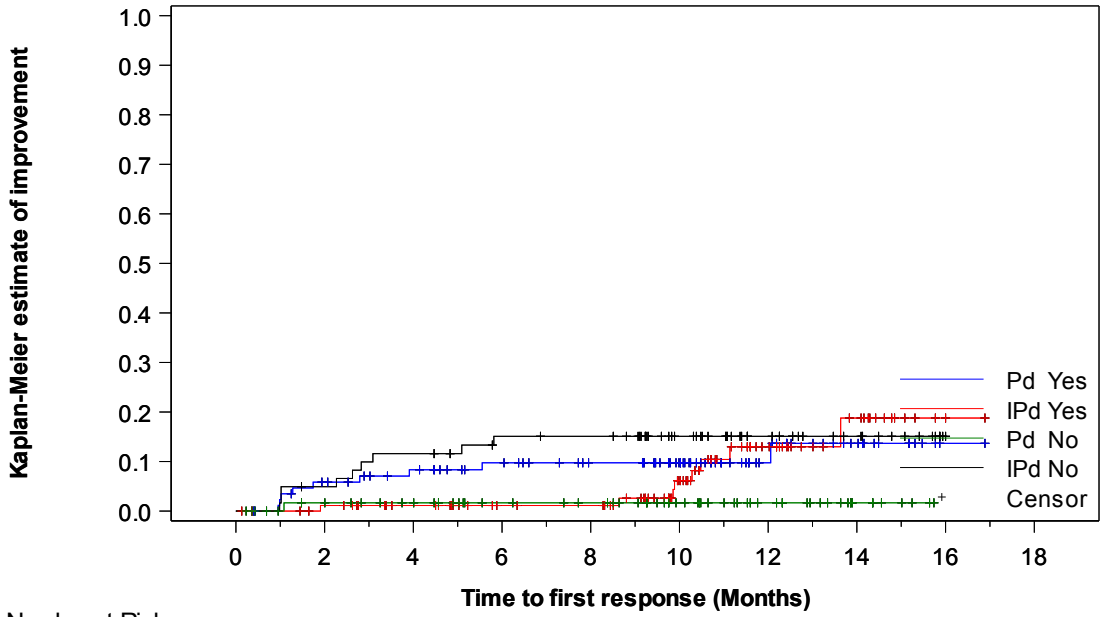
16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to refractory to lenalidomide in last previous regimen (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd Yes	88	75	64	56	23	7	0
IPd Yes	93	84	72	65	26	5	0
Pd No	65	55	45	39	19	4	0
IPd No	61	54	48	45	21	8	0

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Side-effects of treatment
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (21.6)	17 (18.3)	11 (16.9)	11 (18.0)	0.9233
Number (%) of patients censored	69 (78.4)	76 (81.7)	54 (83.1)	50 (82.0)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	15.08 (5.585 to NC)	NC (8.115 to NC)	14.69 (5.651 to NC)	13.67 (8.739 to NC)	
Median (95% CI)	NC (15.080 to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.686 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4820		0.6393	
Hazard ratio (95% CI) vs Pd	-	0.79 (0.41 to 1.52)		0.82 (0.35 to 1.90)	
P-value	-	0.4830		0.6398	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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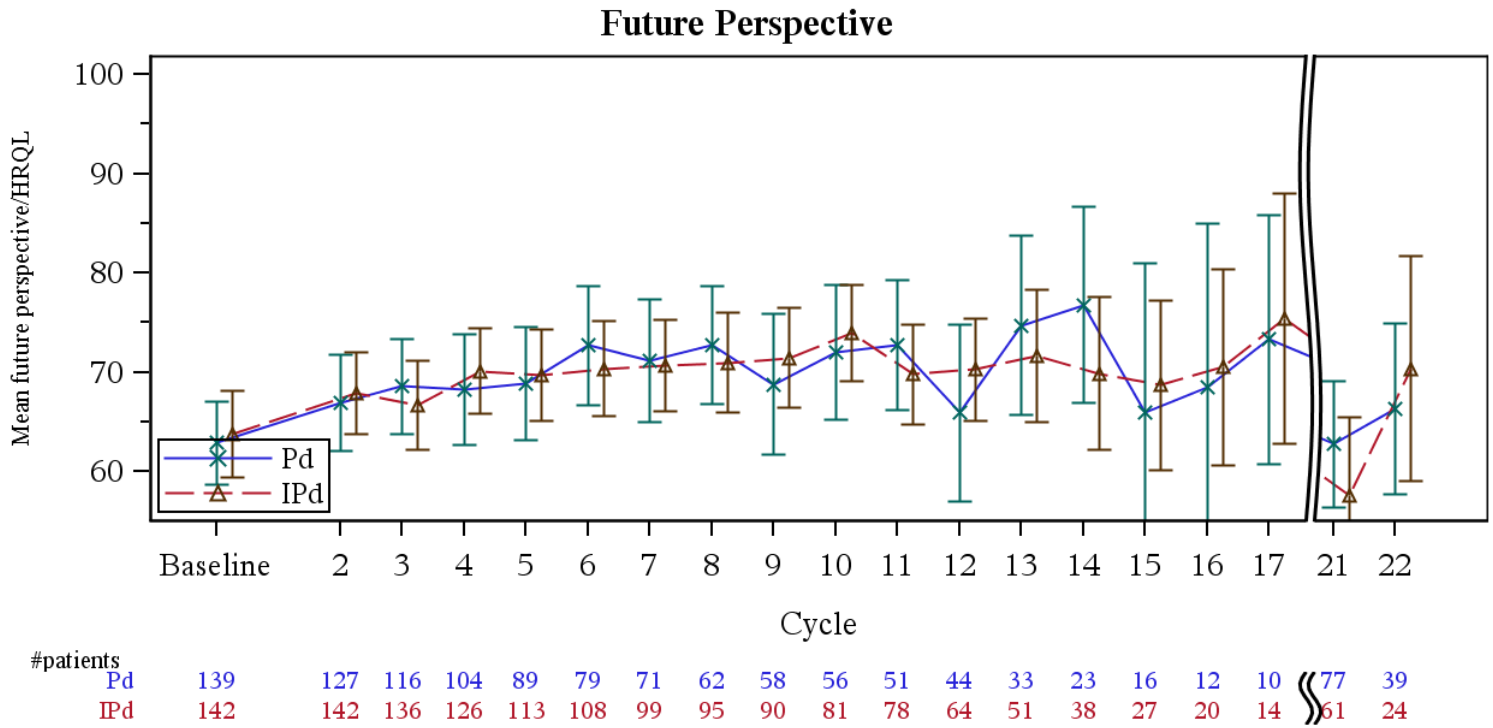
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Future perspective
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 QLQ-MY20 - Mean and 95% CI for future perspective score over time - ITT population



A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Future perspective
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.16 QLQ-MY20 - Time to first improvement by 15 pt in future perspective (LOCF) - ITT population

First improvement 15 points Future perspective (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	55 (35.9)	68 (44.2)
Number (%) of patients censored	98 (64.1)	86 (55.8)
Kaplan-Meier estimates of future perspective in months		
25% quantile (95% CI)	2.27 (1.446 to 3.778)	1.97 (1.150 to 3.581)
Median (95% CI)	NC (NC to NC)	NC (5.815 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4099
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.16 (0.81 to 1.66)
P-value	-	0.4103
Probability (95% CI)[c]		
2 Months	0.23 (0.162 to 0.297)	0.25 (0.185 to 0.322)
4 Months	0.33 (0.253 to 0.407)	0.34 (0.266 to 0.418)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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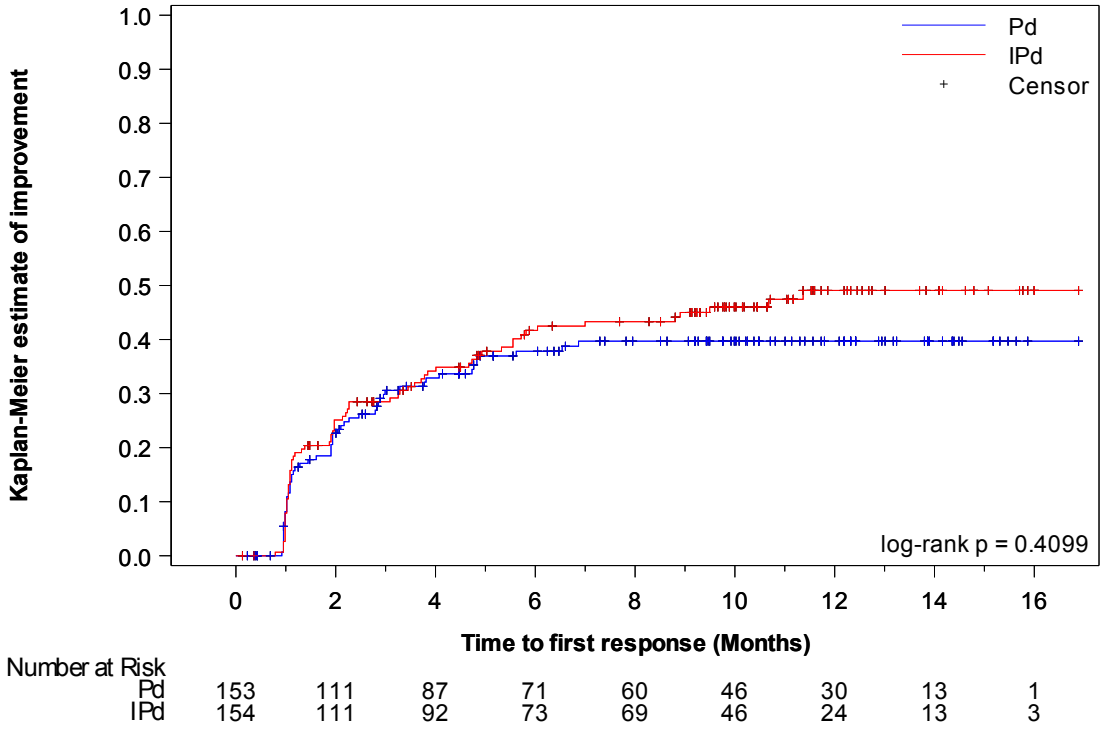
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Future perspective
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.17 QLQ-MY20 - Time to first improvement by 15 pt in future perspective - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_per_imp15l_de_i_f_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Future perspective
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.18 QLQ-MY20 - Time to first deterioration by 15 pt in future perspective (LOCF) - ITT population

First deterioration 15 points Future perspective (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	62 (40.5)	56 (36.4)
Number (%) of patients censored	91 (59.5)	98 (63.6)
Kaplan-Meier estimates of future perspective in months		
25% quantile (95% CI)	2.89 (2.333 to 4.731)	2.86 (2.201 to 7.129)
Median (95% CI)	NC (9.298 to NC)	NC (11.663 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3493
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.84 (0.58 to 1.21)
P-value	-	0.3497
Probability (95% CI)[c]		
2 Months	0.85 (0.780 to 0.898)	0.83 (0.765 to 0.885)
4 Months	0.69 (0.609 to 0.761)	0.72 (0.637 to 0.783)

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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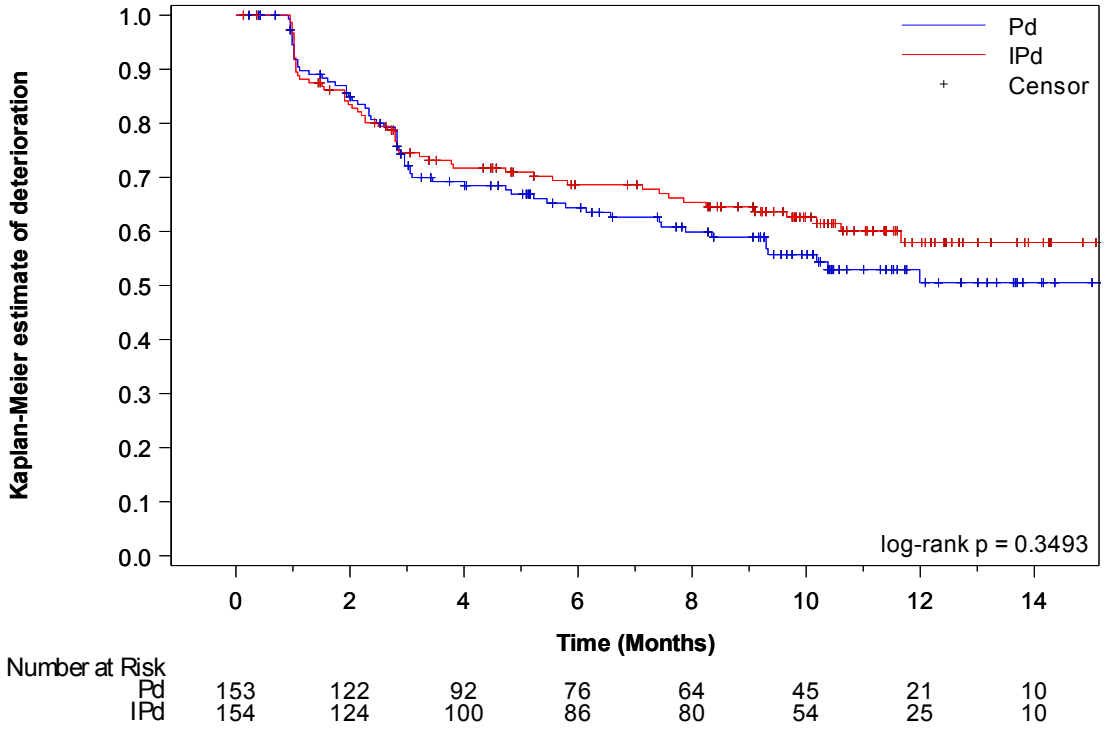
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Future perspective
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.19 QLQ-MY20 - Time to first deterioration by 15 pt in future perspective - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_per_det15l_de_i_f_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Future perspective
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.20 QLQ-MY20 - Time until permanent improvement by 15 pt in future perspective (LOCF) - ITT population

First permanent improvement 15 points Future perspective (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	27 (17.6)	29 (18.8)
Number (%) of patients censored	126 (82.4)	125 (81.2)
Kaplan-Meier estimates of future perspective in months		
25% quantile (95% CI)	NC (8.411 to NC)	14.82 (9.232 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.7884
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.93 (0.55 to 1.57)
P-value	-	0.7880
Probability (95% CI)[c]		
2 Months	0.10 (0.060 to 0.158)	0.03 (0.009 to 0.062)
4 Months	0.13 (0.082 to 0.192)	0.09 (0.050 to 0.141)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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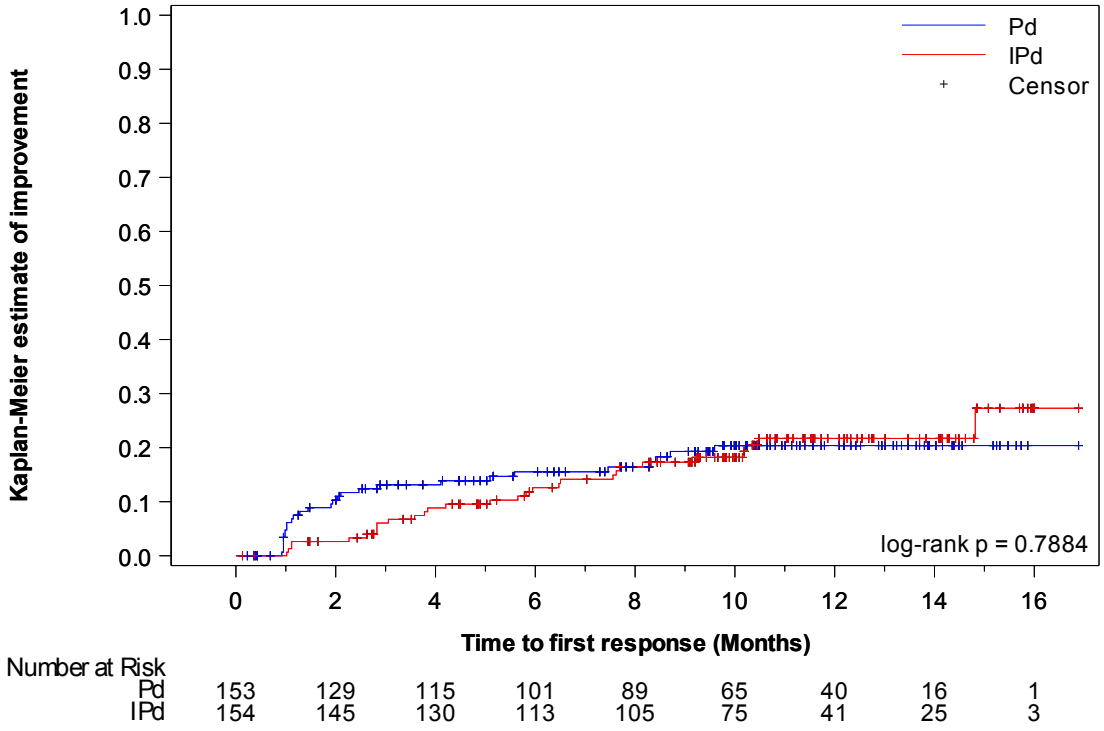
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Future perspective
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.21 QLQ-MY20 - Time until permanent improvement by 15 pt in future perspective - Kaplan-Meier curve (LOCF) - ITT population



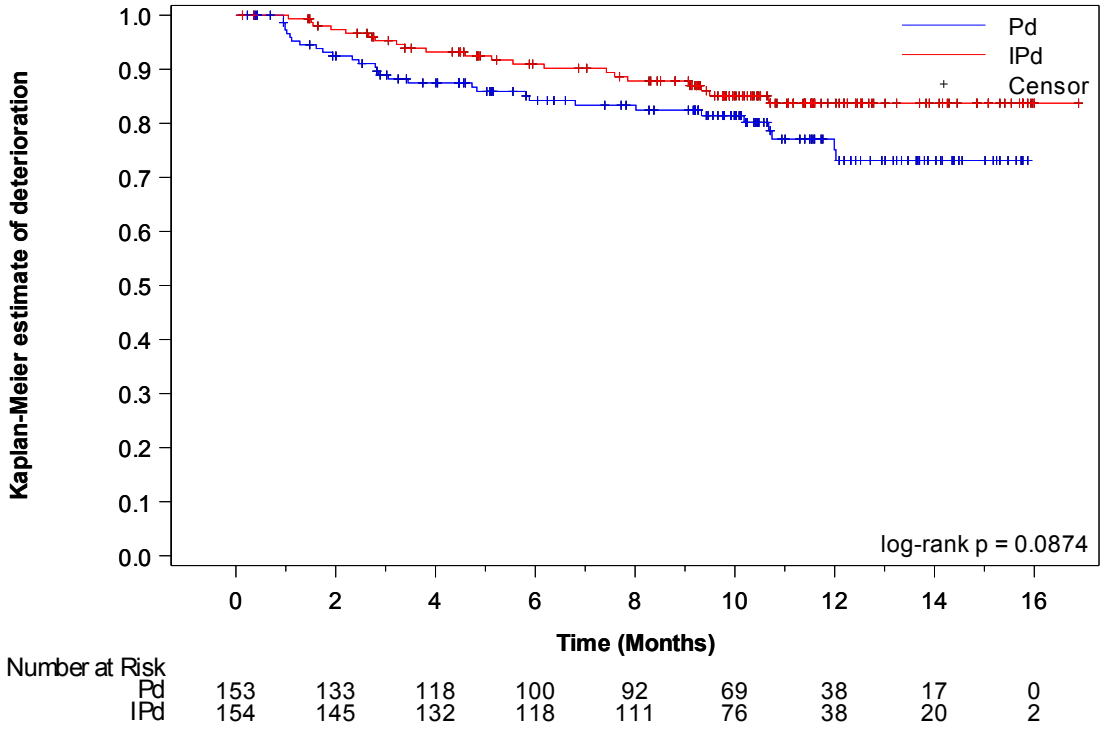
A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_per_imp15pl_de_i_f_x.rtf (08APR2021 15:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Future perspective
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.22 QLQ-MY20 - Time until permanent deterioration by 15 pt in future perspective (LOCF) - ITT population

First permanent deterioration 15 points Future perspective (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	30 (19.6)	21 (13.6)
Number (%) of patients censored	123 (80.4)	133 (86.4)
Kaplan-Meier estimates of future perspective in months		
25% quantile (95% CI)	12.02 (8.016 to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0874
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.62 (0.35 to 1.08)
P-value	-	0.0905
Probability (95% CI)[c]		
2 Months	0.92 (0.868 to 0.958)	0.97 (0.931 to 0.990)
4 Months	0.87 (0.809 to 0.919)	0.93 (0.877 to 0.963)

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_sr_15pts_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_det15pl_de_i_t_x.rtf (08APR2021 15:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.1 Future perspective
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.23 QLQ-MY20 - Time until permanent deterioration by 15 pt in future perspective - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_per_det15pl_de_i_f_x.rtf (08APR2021 15:29)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (55.7)	35 (64.8)	26 (48.1)	44 (64.7)	15 (51.7)	16 (50.0)	0.3691
Number (%) of patients censored	31 (44.3)	19 (35.2)	28 (51.9)	24 (35.3)	14 (48.3)	16 (50.0)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	1.03 (0.986 to 1.150)	1.08 (0.986 to 1.150)	1.12 (0.986 to 1.938)	1.08 (1.018 to 1.314)	1.12 (0.986 to 1.938)	1.18 (0.986 to 3.318)	
Median (95% CI)	2.30 (1.906 to NC)	2.27 (1.150 to 8.378)	7.46 (1.938 to NC)	2.92 (1.380 to 3.745)	3.19 (1.183 to NC)	8.90 (1.873 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (6.078 to NC)	NC (NC to NC)	NC (3.811 to NC)	NC (5.782 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6218		0.1313		0.4801	
Hazard ratio (95% CI) vs Pd	-	1.12 (0.71 to 1.77)		1.45 (0.89 to 2.36)		0.78 (0.38 to 1.57)	
P-value	-	0.6220		0.1335		0.4812	

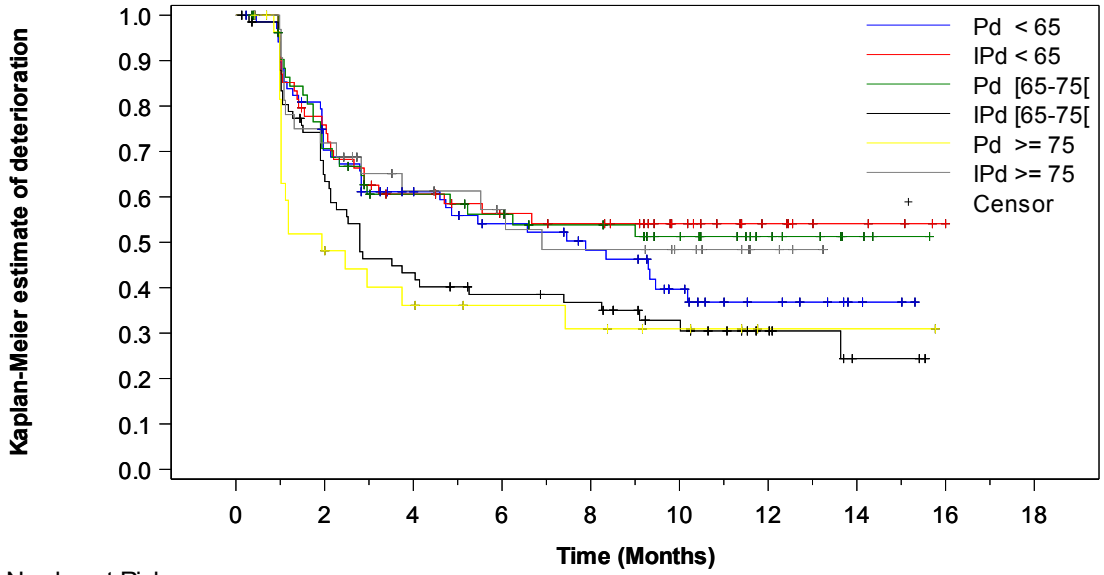
A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_impl_age_de_i_t_x.rtf (08APR2021 15:00)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (54.3)	24 (44.4)	24 (44.4)	45 (66.2)	18 (62.1)	15 (46.9)	0.0118
Number (%) of patients censored	32 (45.7)	30 (55.6)	30 (55.6)	23 (33.8)	11 (37.9)	17 (53.1)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	1.94 (1.084 to 2.825)	2.04 (1.018 to 2.891)	1.91 (1.117 to 2.891)	1.51 (1.018 to 2.004)	1.02 (0.986 to 1.117)	1.61 (1.018 to 5.520)	
Median (95% CI)	7.89 (2.825 to 10.185)	NC (2.891 to NC)	NC (2.825 to NC)	2.79 (2.103 to 7.392)	1.94 (1.018 to 7.425)	6.90 (2.267 to NC)	
75% quantile (95% CI)	NC (10.185 to NC)	NC (NC to NC)	NC (NC to NC)	13.63 (8.246 to NC)	NC (2.957 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2996		0.0386		0.0757	
Hazard ratio (95% CI) vs Pd	-	0.76 (0.46 to 1.27)		1.68 (1.02 to 2.76)		0.54 (0.27 to 1.08)	
P-value	-	0.3011		0.0408		0.0803	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detl_age_de_i_t_x.rtf (08APR2021 14:59)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to age (IRT) (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd < 65	70	39	29	23	8	2	0
IPd < 65	54	33	25	21	8	3	0
Pd [65-75[	54	29	25	21	8	1	0
IPd [65-75[	68	30	23	17	7	2	0
Pd >= 75	29	10	7	5	1	1	0
IPd >= 75	32	18	13	11	3	0	0

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detl_age_de_i_f_x.rtf (08APR2021 14:31)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (27.1)	19 (35.2)	9 (16.7)	24 (35.3)	9 (31.0)	9 (28.1)	0.2186
Number (%) of patients censored	51 (72.9)	35 (64.8)	45 (83.3)	44 (64.7)	20 (69.0)	23 (71.9)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	8.71 (1.906 to NC)	3.58 (1.117 to 10.218)	NC (4.862 to NC)	8.15 (3.515 to 10.251)	5.59 (0.986 to NC)	5.72 (1.117 to NC)	
Median (95% CI)	NC (12.057 to NC)	NC (10.218 to NC)	NC (NC to NC)	15.47 (10.251 to NC)	NC (5.585 to NC)	NC (8.903 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.474 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4397		0.0624		0.5022	
Hazard ratio (95% CI) vs Pd	-	1.28 (0.68 to 2.43)		2.04 (0.95 to 4.39)		0.73 (0.29 to 1.84)	
P-value	-	0.4409		0.0681		0.5039	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_imppl_age_de_i_t_x.rtf (08APR2021 15:00)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (28.6)	12 (22.2)	11 (20.4)	15 (22.1)	11 (37.9)	7 (21.9)	0.4530
Number (%) of patients censored	50 (71.4)	42 (77.8)	43 (79.6)	53 (77.9)	18 (62.1)	25 (78.1)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	6.80 (2.825 to 12.025)	NC (3.220 to NC)	13.24 (1.938 to NC)	NC (5.684 to NC)	2.46 (0.986 to 11.926)	9.76 (5.125 to NC)	
Median (95% CI)	NC (12.025 to NC)	NC (NC to NC)	NC (13.240 to NC)	NC (NC to NC)	11.93 (2.858 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.926 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3535		0.9610		0.0943	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.35 to 1.46)		0.98 (0.45 to 2.14)		0.45 (0.18 to 1.17)	
P-value	-	0.3558		0.9609		0.1030	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	52 (51.5)	62 (60.8)	28 (53.8)	33 (63.5)	0.8316
Number (%) of patients censored	49 (48.5)	40 (39.2)	24 (46.2)	19 (36.5)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.08 (1.018 to 1.347)	1.08 (1.018 to 1.643)	1.08 (0.986 to 1.610)	1.07 (1.018 to 1.117)	
Median (95% CI)	3.91 (2.070 to NC)	3.45 (1.906 to 6.078)	2.89 (1.610 to NC)	2.79 (1.117 to 5.552)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.552 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3939		0.7326	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.81 to 1.70)		1.09 (0.66 to 1.81)	
P-value	-	0.3957		0.7333	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_impl_plne_de_i_t_x.rtf (08APR2021 15:00)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	53 (52.5)	57 (55.9)	27 (51.9)	27 (51.9)	0.6340
Number (%) of patients censored	48 (47.5)	45 (44.1)	25 (48.1)	25 (48.1)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.61 (1.084 to 2.168)	1.91 (1.084 to 2.136)	1.91 (1.018 to 2.136)	1.91 (1.051 to 2.825)	
Median (95% CI)	7.43 (2.825 to NC)	4.70 (2.661 to 13.634)	6.24 (1.971 to NC)	6.90 (2.070 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7322		0.7485	
Hazard ratio (95% CI) vs Pd	-	1.07 (0.73 to 1.55)		0.92 (0.54 to 1.56)	
P-value	-	0.7324		0.7483	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detl_plne_de_i_t_x.rtf (08APR2021 14:59)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	24 (23.8)	32 (31.4)	13 (25.0)	20 (38.5)	0.8664
Number (%) of patients censored	77 (76.2)	70 (68.6)	39 (75.0)	32 (61.5)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	11.70 (4.107 to NC)	8.44 (3.055 to 10.251)	8.71 (1.018 to NC)	3.58 (1.117 to 8.148)	
Median (95% CI)	NC (NC to NC)	15.47 (14.554 to NC)	NC (NC to NC)	NC (8.148 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4081		0.3734	
Hazard ratio (95% CI) vs Pd	-	1.25 (0.74 to 2.12)		1.37 (0.68 to 2.76)	
P-value	-	0.4090		0.3754	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_imppl_plne_de_i_t_x.rtf (08APR2021 15:00)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	27 (26.7)	23 (22.5)	15 (28.8)	11 (21.2)	0.7044
Number (%) of patients censored	74 (73.3)	79 (77.5)	37 (71.2)	41 (78.8)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	6.80 (2.825 to NC)	9.49 (6.078 to NC)	10.68 (1.216 to 13.240)	NC (5.322 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.926 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3319		0.2761	
Hazard ratio (95% CI) vs Pd	-	0.76 (0.44 to 1.32)		0.65 (0.30 to 1.42)	
P-value	-	0.3326		0.2797	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (44.3)	54 (60.7)	49 (59.0)	41 (63.1)	0.1477
Number (%) of patients censored	39 (55.7)	35 (39.3)	34 (41.0)	24 (36.9)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.12 (0.986 to 2.300)	1.08 (1.018 to 1.281)	1.05 (0.986 to 1.150)	1.08 (1.018 to 1.380)	
Median (95% CI)	NC (2.464 to NC)	3.09 (1.873 to 8.378)	2.10 (1.281 to 3.910)	3.29 (1.511 to 4.928)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.782 to NC)	NC (5.717 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0872		0.7652	
Hazard ratio (95% CI) vs Pd	-	1.47 (0.94 to 2.28)		0.94 (0.62 to 1.42)	
P-value	-	0.0891		0.7657	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (55.7)	48 (53.9)	41 (49.4)	36 (55.4)	0.8456
Number (%) of patients censored	31 (44.3)	41 (46.1)	42 (50.6)	29 (44.6)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.94 (1.117 to 2.333)	1.91 (1.051 to 2.201)	1.18 (0.986 to 1.938)	1.49 (1.018 to 2.136)	
Median (95% CI)	6.24 (2.793 to 10.185)	5.26 (2.793 to NC)	7.43 (2.825 to NC)	6.08 (2.267 to NC)	
75% quantile (95% CI)	NC (10.185 to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.634 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8972		0.8481	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.64 to 1.48)		1.04 (0.67 to 1.63)	
P-value	-	0.8971		0.8479	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (18.6)	30 (33.7)	24 (28.9)	22 (33.8)	0.2171
Number (%) of patients censored	57 (81.4)	59 (66.3)	59 (71.1)	43 (66.2)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	NC (4.107 to NC)	5.09 (2.924 to 10.251)	8.71 (1.610 to 12.057)	7.62 (1.938 to 9.955)	
Median (95% CI)	NC (NC to NC)	NC (10.283 to NC)	NC (12.057 to NC)	15.47 (9.955 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.474 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0750		0.8969	
Hazard ratio (95% CI) vs Pd	-	1.79 (0.93 to 3.44)		1.04 (0.58 to 1.85)	
P-value	-	0.0793		0.8967	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (21.4)	20 (22.5)	27 (32.5)	14 (21.5)	0.2082
Number (%) of patients censored	55 (78.6)	69 (77.5)	56 (67.5)	51 (78.5)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	13.24 (2.858 to NC)	10.02 (5.684 to NC)	5.88 (1.938 to 10.743)	NC (5.125 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.743 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9860		0.0676	
Hazard ratio (95% CI) vs Pd	-	0.99 (0.51 to 1.94)		0.55 (0.29 to 1.05)	
P-value	-	0.9860		0.0717	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	64 (50.8)	79 (66.9)	13 (68.4)	11 (45.8)	0.0525
Number (%) of patients censored	62 (49.2)	39 (33.1)	6 (31.6)	13 (54.2)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.08 (1.018 to 1.610)	1.08 (1.018 to 1.281)	1.05 (0.986 to 1.117)	1.12 (0.953 to 2.924)	
Median (95% CI)	3.91 (2.070 to NC)	3.09 (1.873 to 3.778)	1.15 (1.051 to NC)	NC (1.117 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (8.674 to NC)	NC (1.150 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1100		0.1560	
Hazard ratio (95% CI) vs Pd	-	1.31 (0.94 to 1.82)		0.56 (0.25 to 1.26)	
P-value	-	0.1111		0.1616	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	69 (54.8)	67 (56.8)	8 (42.1)	14 (58.3)	0.1958
Number (%) of patients censored	57 (45.2)	51 (43.2)	11 (57.9)	10 (41.7)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.74 (1.084 to 1.938)	1.91 (1.084 to 2.136)	2.89 (0.953 to NC)	1.61 (0.986 to 2.037)	
Median (95% CI)	5.45 (2.825 to 9.331)	4.04 (2.793 to 13.634)	NC (2.891 to NC)	5.26 (1.906 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (NC to NC)	NC (5.552 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8255		0.2396	
Hazard ratio (95% CI) vs Pd	-	0.96 (0.69 to 1.35)		1.68 (0.70 to 4.01)	
P-value	-	0.8255		0.2447	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (23.0)	44 (37.3)	5 (26.3)	6 (25.0)	0.3461
Number (%) of patients censored	97 (77.0)	74 (62.7)	14 (73.7)	18 (75.0)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	11.70 (4.862 to NC)	5.09 (3.055 to 8.903)	2.89 (0.986 to NC)	10.28 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	15.47 (10.251 to NC)	NC (2.891 to NC)	NC (10.283 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0742		0.7374	
Hazard ratio (95% CI) vs Pd	-	1.53 (0.96 to 2.44)		0.82 (0.25 to 2.69)	
P-value	-	0.0764		0.7378	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (27.8)	23 (19.5)	5 (26.3)	8 (33.3)	0.2477
Number (%) of patients censored	91 (72.2)	95 (80.5)	14 (73.7)	16 (66.7)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	9.33 (2.858 to 11.992)	NC (8.345 to NC)	13.24 (0.953 to 13.240)	6.08 (1.314 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	13.24 (NC to NC)	NC (7.425 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	13.24 (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0585		0.6781	
Hazard ratio (95% CI) vs Pd	-	0.60 (0.36 to 1.02)		1.27 (0.41 to 3.89)	
P-value	-	0.0612		0.6788	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (66.7)	2 (50.0)	72 (53.7)	83 (63.8)	0.2827
Number (%) of patients censored	1 (33.3)	2 (50.0)	62 (46.3)	47 (36.2)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.28 (1.281 to 2.267)	1.17 (1.018 to NC)	1.08 (1.018 to 1.150)	1.08 (1.018 to 1.183)	
Median (95% CI)	1.77 (1.281 to 2.267)	NC (1.018 to NC)	3.29 (1.938 to NC)	2.92 (1.906 to 3.811)	
75% quantile (95% CI)	2.27 (1.281 to 2.267)	NC (1.018 to NC)	NC (NC to NC)	NC (9.429 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4643		0.3107	
Hazard ratio (95% CI) vs Pd	-	0.49 (0.07 to 3.50)		1.18 (0.86 to 1.61)	
P-value	-	0.4736		0.3119	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	3 (75.0)	72 (53.7)	73 (56.2)	0.9807
Number (%) of patients censored	3 (100.0)	1 (25.0)	62 (46.3)	57 (43.8)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	NC (NC to NC)	1.58 (1.018 to 2.497)	1.91 (1.117 to 2.136)	1.54 (1.084 to 2.070)	
Median (95% CI)	NC (NC to NC)	2.32 (1.018 to NC)	6.57 (2.957 to 9.462)	5.26 (2.825 to 13.634)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (13.634 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1439		0.9036	
Hazard ratio (95% CI) vs Pd	-			1.02 (0.74 to 1.41)	
P-value	-	0.9983		0.9036	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detl_ethn_de_i_t_x.rtf (08APR2021 14:59)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (66.7)	2 (50.0)	31 (23.1)	46 (35.4)	0.0881
Number (%) of patients censored	1 (33.3)	2 (50.0)	103 (76.9)	84 (64.6)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.28 (1.281 to 4.107)	5.31 (3.055 to NC)	9.59 (4.862 to NC)	5.72 (2.924 to 9.396)	
Median (95% CI)	2.69 (1.281 to 4.107)	NC (3.055 to NC)	NC (NC to NC)	15.47 (14.554 to NC)	
75% quantile (95% CI)	4.11 (1.281 to 4.107)	NC (3.055 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1070		0.1093	
Hazard ratio (95% CI) vs Pd	-	0.17 (0.02 to 1.93)		1.45 (0.92 to 2.28)	
P-value	-	0.1529		0.1113	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_imppl_ethn_de_i_t_x.rtf (08APR2021 15:00)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	37 (27.6)	30 (23.1)	0.9999
Number (%) of patients censored	3 (100.0)	4 (100.0)	97 (72.4)	100 (76.9)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	9.33 (4.600 to 12.025)	9.76 (6.078 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.240 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.2405	
Hazard ratio (95% CI) vs Pd	-			0.75 (0.46 to 1.21)	
P-value	-			0.2427	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detpl_ethn_de_i_t_x.rtf (08APR2021 15:00)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	36 (47.4)	33 (60.0)	10 (50.0)	18 (64.3)	4 (80.0)	6 (85.7)	10 (66.7)	9 (42.9)	20 (54.1)	29 (67.4)	0.6068
Number (%) of patients censored	40 (52.6)	22 (40.0)	10 (50.0)	10 (35.7)	1 (20.0)	1 (14.3)	5 (33.3)	12 (57.1)	17 (45.9)	14 (32.6)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	1.15 (0.986 to 1.938)	1.18 (1.018 to 1.938)	1.02 (0.953 to 3.285)	1.03 (0.986 to 1.873)	0.99 (0.953 to 2.267)	0.95 (0.920 to 1.018)	1.08 (1.018 to 1.150)	1.12 (0.953 to 3.285)	1.03 (0.986 to 1.610)	1.08 (0.986 to 1.150)	
Median (95% CI)	5.78 (2.103 to NC)	3.78 (1.938 to 8.903)	5.09 (1.018 to NC)	2.53 (1.084 to NC)	1.12 (0.953 to NC)	1.02 (0.920 to 3.450)	1.15 (1.051 to NC)	NC (1.117 to NC)	2.30 (1.117 to NC)	2.27 (1.117 to 8.378)	
75% quantile (95% CI)	NC (NC to NC)	NC (8.903 to NC)	NC (5.092 to NC)	NC (3.318 to NC)	2.27 (0.953 to NC)	3.45 (0.953 to NC)	NC (1.150 to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.581 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_impl_greg_de_i_t_x.rtf (08APR2021 15:00)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.4489		0.4427		0.7773		0.1999		0.5751	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.75 to 1.92)		1.35 (0.62 to 2.93)		1.20 (0.34 to 4.28)		0.56 (0.23 to 1.38)		1.18 (0.67 to 2.08)	
P-value	-	0.4495		0.4445		0.7776		0.2061		0.5755	
Improvement probability (95% CI)[b]											
2 Months	0.367 (0.257 to 0.478)	0.391 (0.262 to 0.518)	0.368 (0.165 to 0.575)	0.500 (0.306 to 0.666)	0.600 (0.126 to 0.882)	0.714 (0.258 to 0.920)	0.533 (0.263 to 0.744)	0.337 (0.150 to 0.536)	0.419 (0.258 to 0.573)	0.479 (0.322 to 0.620)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_impl_greg_de_i_t_x.rtf (08APR2021 15:00)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	34 (44.7)	25 (45.5)	13 (65.0)	17 (60.7)	2 (40.0)	5 (71.4)	7 (46.7)	13 (61.9)	24 (64.9)	24 (55.8)	0.4843
Number (%) of patients censored	42 (55.3)	30 (54.5)	7 (35.0)	11 (39.3)	3 (60.0)	2 (28.6)	8 (53.3)	8 (38.1)	13 (35.1)	19 (44.2)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	1.28 (1.018 to 2.333)	2.10 (1.018 to 3.220)	1.02 (0.953 to 1.938)	1.05 (0.953 to 2.793)	9.00 (0.986 to NC)	2.53 (2.136 to 4.698)	2.89 (0.986 to 6.571)	1.31 (0.986 to 1.906)	1.91 (0.986 to 2.168)	1.94 (1.051 to 2.661)	
Median (95% CI)	10.18 (2.793 to NC)	NC (3.220 to NC)	2.96 (1.018 to 9.331)	3.47 (1.084 to NC)	NC (0.986 to NC)	4.70 (2.136 to NC)	NC (1.971 to NC)	2.14 (1.314 to NC)	2.96 (1.938 to 9.298)	7.39 (2.070 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.957 to NC)	13.63 (4.140 to NC)	NC (0.986 to NC)	6.08 (2.793 to NC)	NC (NC to NC)	NC (2.136 to NC)	9.46 (5.454 to NC)	NC (10.021 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detl_greg_de_i_t_x.rtf (08APR2021 14:59)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.7998		0.6117		0.2074		0.2218		0.3160	
Hazard ratio (95% CI) vs Pd	-	0.94 (0.56 to 1.57)		0.83 (0.40 to 1.71)		2.92 (0.52 to 16.41)		1.77 (0.70 to 4.45)		0.75 (0.42 to 1.32)	
P-value	-	0.8007		0.6122		0.2233		0.2278		0.3176	
Deterioration probability (95% CI)[b]											
2 Months	0.663 (0.540 to 0.760)	0.760 (0.622 to 0.853)	0.526 (0.287 to 0.719)	0.643 (0.438 to 0.789)	0.800 (0.204 to 0.969)	1.000 (1.000 to 1.000)	0.800 (0.500 to 0.931)	0.561 (0.325 to 0.743)	0.660 (0.480 to 0.791)	0.688 (0.523 to 0.805)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detl_greg_de_i_t_x.rtf (08APR2021 14:59)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	19 (25.0)	18 (32.7)	2 (10.0)	12 (42.9)	2 (40.0)	2 (28.6)	4 (26.7)	5 (23.8)	10 (27.0)	15 (34.9)	0.3766
Number (%) of patients censored	57 (75.0)	37 (67.3)	18 (90.0)	16 (57.1)	3 (60.0)	5 (71.4)	11 (73.3)	16 (76.2)	27 (73.0)	28 (65.1)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	6.57 (2.103 to NC)	7.56 (1.938 to 10.218)	NC (0.953 to NC)	6.47 (1.084 to 9.232)	4.11 (0.986 to NC)	3.06 (2.628 to NC)	2.89 (1.018 to NC)	10.28 (1.117 to NC)	9.53 (1.018 to NC)	5.06 (1.051 to 14.554)	
Median (95% CI)	NC (NC to NC)	NC (9.955 to NC)	NC (NC to NC)	15.47 (7.491 to 15.474)	NC (0.986 to NC)	NC (2.628 to NC)	NC (1.150 to NC)	NC (10.283 to NC)	NC (11.696 to NC)	NC (10.251 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_imppl_greg_de_i_t_x.rtf (08APR2021 15:00)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	15.47 (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.5092		0.0280		0.7019		0.6549		0.7286	
Hazard ratio (95% CI) vs Pd	-	1.24 (0.65 to 2.37)		4.68 (1.03 to 21.23)		0.68 (0.10 to 4.87)		0.74 (0.20 to 2.78)		1.15 (0.52 to 2.57)	
P-value	-	0.5101		0.0456		0.7036		0.6561		0.7288	
Hazard ratio inverted (95% CI) vs IPd		-		0.21 (0.05 to 0.97)		1.46 (0.21 to 10.43)		1.35 (0.36 to 5.07)		0.87 (0.39 to 1.94)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_imppl_greg_de_i_t_x.rtf (08APR2021 15:00)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=37)	IPd (N=43)	p-value of treatment-by-subgroup interaction[c]
Number (%) of events	18 (23.7)	14 (25.5)	9 (45.0)	5 (17.9)	1 (20.0)	1 (14.3)	4 (26.7)	7 (33.3)	10 (27.0)	7 (16.3)	0.2978
Number (%) of patients censored	58 (76.3)	41 (74.5)	11 (55.0)	23 (82.1)	4 (80.0)	6 (85.7)	11 (73.3)	14 (66.7)	27 (73.0)	36 (83.7)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	10.68 (2.333 to NC)	5.59 (3.220 to NC)	3.45 (0.986 to 11.926)	NC (2.891 to NC)	NC (0.986 to NC)	NC (6.078 to NC)	13.24 (1.084 to 13.240)	7.43 (1.314 to NC)	6.80 (1.938 to NC)	NC (9.101 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	11.99 (3.450 to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (6.078 to NC)	13.24 (7.425 to 13.240)	NC (7.425 to NC)	NC (10.743 to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detpl_greg_de_i_t_x.rtf (08APR2021 15:00)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	13.24 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.9350		0.0465		0.7919		0.6960		0.1089	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.51 to 2.07)		0.34 (0.12 to 1.03)		0.69 (0.04 to 11.04)		1.28 (0.37 to 4.38)		0.46 (0.17 to 1.22)	
P-value	-	0.9349		0.0572		0.7931		0.6967		0.1176	
Deterioration probability (95% CI)[b]											

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detpl_greg_de_i_t_x.rtf (08APR2021 15:00)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (50.5)	50 (64.9)	31 (55.4)	45 (58.4)	0.4978
Number (%) of patients censored	48 (49.5)	27 (35.1)	25 (44.6)	32 (41.6)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.12 (0.986 to 1.906)	1.12 (1.018 to 1.281)	1.05 (1.018 to 1.117)	1.08 (0.986 to 1.873)	
Median (95% CI)	3.91 (2.004 to NC)	2.60 (1.380 to 5.552)	2.83 (1.117 to NC)	3.32 (1.873 to 9.429)	
75% quantile (95% CI)	NC (NC to NC)	NC (6.078 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2464		0.9223	
Hazard ratio (95% CI) vs Pd	-	1.26 (0.85 to 1.87)		1.02 (0.65 to 1.62)	
P-value	-	0.2475		0.9225	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (44.3)	36 (46.8)	37 (66.1)	48 (62.3)	0.9560
Number (%) of patients censored	54 (55.7)	41 (53.2)	19 (33.9)	29 (37.7)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.74 (1.084 to 2.136)	2.20 (1.478 to 2.891)	1.61 (0.986 to 2.168)	1.23 (1.018 to 1.906)	
Median (95% CI)	10.18 (2.825 to NC)	10.02 (3.515 to NC)	4.60 (2.168 to 6.571)	2.86 (1.971 to 7.392)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.571 to NC)	NC (9.101 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8199		0.8568	
Hazard ratio (95% CI) vs Pd	-	0.95 (0.61 to 1.48)		0.96 (0.63 to 1.48)	
P-value	-	0.8203		0.8564	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detl_rreg_de_i_t_x.rtf (08APR2021 14:59)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (27.8)	25 (32.5)	10 (17.9)	27 (35.1)	0.1616
Number (%) of patients censored	70 (72.2)	52 (67.5)	46 (82.1)	50 (64.9)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	5.59 (1.938 to NC)	5.72 (2.267 to 10.251)	NC (2.891 to NC)	7.49 (2.924 to 10.283)	
Median (95% CI)	NC (NC to NC)	NC (10.251 to NC)	NC (NC to NC)	15.47 (10.283 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.474 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8476		0.0579	
Hazard ratio (95% CI) vs Pd	-	1.05 (0.61 to 1.82)		1.99 (0.96 to 4.12)	
P-value	-	0.8473		0.0629	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (21.6)	17 (22.1)	21 (37.5)	17 (22.1)	0.1849
Number (%) of patients censored	76 (78.4)	60 (77.9)	35 (62.5)	60 (77.9)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	12.02 (2.464 to NC)	NC (4.600 to NC)	4.83 (2.825 to 11.926)	9.76 (6.965 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	13.24 (10.743 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.240 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8157		0.0290	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.49 to 1.76)		0.50 (0.26 to 0.94)	
P-value	-	0.8163		0.0323	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	72 (52.6)	86 (62.3)	8 (50.0)	9 (56.3)	0.8123
Number (%) of patients censored	65 (47.4)	52 (37.7)	8 (50.0)	7 (43.8)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.08 (1.018 to 1.183)	1.12 (1.051 to 1.248)	1.02 (0.953 to 2.825)	1.02 (0.953 to 1.084)	
Median (95% CI)	3.29 (2.004 to NC)	3.09 (1.906 to 4.665)	4.76 (0.986 to NC)	3.78 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.764 to NC)	NC (3.778 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4280		0.6881	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.83 to 1.55)		1.22 (0.47 to 3.16)	
P-value	-	0.4297		0.6884	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	71 (51.8)	75 (54.3)	9 (56.3)	9 (56.3)	0.9013
Number (%) of patients censored	66 (48.2)	63 (45.7)	7 (43.8)	7 (43.8)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.91 (1.117 to 1.971)	1.91 (1.183 to 2.136)	0.99 (0.986 to 2.793)	1.08 (0.296 to 1.971)	
Median (95% CI)	7.46 (2.957 to NC)	5.55 (2.858 to NC)	3.75 (0.986 to NC)	2.14 (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.745 to NC)	NC (2.136 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9794		0.8501	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.73 to 1.39)		1.09 (0.43 to 2.77)	
P-value	-	0.9794		0.8500	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (23.4)	45 (32.6)	5 (31.3)	7 (43.8)	0.8052
Number (%) of patients censored	105 (76.6)	93 (67.4)	11 (68.8)	9 (56.3)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	11.70 (2.924 to NC)	7.62 (3.515 to 10.218)	5.09 (0.986 to NC)	2.83 (0.986 to 8.903)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (1.281 to NC)	8.90 (2.628 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.778 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2745		0.4040	
Hazard ratio (95% CI) vs Pd	-	1.29 (0.82 to 2.03)		1.63 (0.51 to 5.17)	
P-value	-	0.2758		0.4084	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (25.5)	30 (21.7)	7 (43.8)	4 (25.0)	0.5490
Number (%) of patients censored	102 (74.5)	108 (78.3)	9 (56.3)	12 (75.0)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	10.68 (4.600 to 13.240)	NC (6.965 to NC)	2.79 (0.986 to 7.425)	4.60 (0.296 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	7.43 (1.413 to NC)	NC (3.515 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.425 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2589		0.3402	
Hazard ratio (95% CI) vs Pd	-	0.76 (0.46 to 1.23)		0.55 (0.16 to 1.90)	
P-value	-	0.2605		0.3471	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (60.8)	39 (60.9)	32 (57.1)	33 (62.3)	16 (37.2)	20 (58.8)	0.2590
Number (%) of patients censored	20 (39.2)	25 (39.1)	24 (42.9)	20 (37.7)	27 (62.8)	14 (41.2)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	1.05 (0.986 to 1.117)	1.08 (0.986 to 1.643)	1.12 (1.018 to 1.906)	1.18 (1.084 to 1.873)	1.45 (0.986 to 4.928)	1.02 (0.986 to 1.051)	
Median (95% CI)	2.07 (1.084 to NC)	2.92 (1.873 to 8.674)	2.30 (1.906 to NC)	3.45 (1.873 to 5.717)	NC (3.285 to NC)	2.27 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.717 to NC)	NC (NC to NC)	NC (3.581 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8395		0.9846		0.1227	
Hazard ratio (95% CI) vs Pd	-	0.95 (0.59 to 1.53)		1.00 (0.62 to 1.63)		1.67 (0.86 to 3.23)	
P-value	-	0.8390		0.9846		0.1267	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_impl_seiss_de_i_t_x.rtf (08APR2021 15:00)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (64.7)	31 (48.4)	27 (48.2)	32 (60.4)	18 (41.9)	19 (55.9)	0.2775
Number (%) of patients censored	18 (35.3)	33 (51.6)	29 (51.8)	21 (39.6)	25 (58.1)	15 (44.1)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	1.22 (0.986 to 1.938)	1.51 (1.018 to 2.136)	1.94 (1.018 to 2.333)	2.00 (0.986 to 2.530)	1.94 (0.986 to 6.242)	1.91 (1.051 to 2.825)	
Median (95% CI)	4.73 (1.938 to 7.885)	8.25 (2.136 to NC)	9.00 (2.168 to NC)	5.55 (2.497 to 13.634)	9.33 (2.825 to NC)	3.52 (1.971 to NC)	
75% quantile (95% CI)	NC (7.885 to NC)	NC (NC to NC)	NC (NC to NC)	13.63 (10.021 to NC)	NC (9.462 to NC)	NC (3.745 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2105		0.4546		0.4649	
Hazard ratio (95% CI) vs Pd	-	0.73 (0.45 to 1.20)		1.22 (0.73 to 2.03)		1.27 (0.67 to 2.42)	
P-value	-	0.2123		0.4562		0.4659	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (25.5)	19 (29.7)	16 (28.6)	20 (37.7)	8 (18.6)	12 (35.3)	0.7846
Number (%) of patients censored	38 (74.5)	45 (70.3)	40 (71.4)	33 (62.3)	35 (81.4)	22 (64.7)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	11.70 (1.938 to NC)	9.40 (2.924 to NC)	4.86 (1.150 to NC)	6.47 (3.055 to 10.218)	12.06 (1.446 to NC)	3.58 (1.051 to 8.903)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	15.47 (9.955 to NC)	NC (12.057 to NC)	NC (7.491 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.474 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6531		0.5758		0.2457	
Hazard ratio (95% CI) vs Pd	-	1.18 (0.58 to 2.38)		1.21 (0.62 to 2.33)		1.69 (0.69 to 4.14)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (37.3)	12 (18.8)	12 (21.4)	13 (24.5)	10 (23.3)	8 (23.5)	0.3792
Number (%) of patients censored	32 (62.7)	52 (81.3)	44 (78.6)	40 (75.5)	33 (76.7)	26 (76.5)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	5.88 (1.610 to 10.743)	NC (7.425 to NC)	11.93 (2.464 to NC)	9.33 (5.552 to NC)	11.99 (1.084 to NC)	6.18 (2.891 to NC)	
Median (95% CI)	NC (10.743 to NC)	NC (NC to NC)	NC (11.926 to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0444		0.9374		0.7013	
Hazard ratio (95% CI) vs Pd	-	0.48 (0.23 to 1.00)		1.03 (0.47 to 2.26)		0.83 (0.33 to 2.12)	
P-value	-	0.0491		0.9374		0.7017	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (64.5)	24 (61.5)	51 (52.0)	64 (64.6)	9 (37.5)	7 (43.8)	0.5373
Number (%) of patients censored	11 (35.5)	15 (38.5)	47 (48.0)	35 (35.4)	15 (62.5)	9 (56.3)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	1.05 (0.986 to 1.117)	1.08 (0.986 to 1.906)	1.12 (1.018 to 1.906)	1.08 (1.018 to 1.183)	1.28 (0.953 to 3.285)	1.02 (0.723 to 2.267)	
Median (95% CI)	1.94 (1.051 to NC)	2.92 (1.643 to NC)	3.78 (2.103 to NC)	3.29 (1.873 to 4.665)	3.29 (1.281 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (2.825 to NC)	NC (8.674 to NC)	NC (NC to NC)	NC (8.903 to NC)	NC (3.285 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6246		0.1993		0.8637	
Hazard ratio (95% CI) vs Pd	-	0.86 (0.48 to 1.56)		1.27 (0.88 to 1.84)		1.09 (0.41 to 2.94)	
P-value	-	0.6249		0.2003		0.8638	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (64.5)	16 (41.0)	53 (54.1)	60 (60.6)	7 (29.2)	8 (50.0)	0.0947
Number (%) of patients censored	11 (35.5)	23 (59.0)	45 (45.9)	39 (39.4)	17 (70.8)	8 (50.0)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	1.22 (0.986 to 1.938)	2.07 (1.018 to 7.392)	1.91 (1.018 to 2.333)	1.48 (1.018 to 2.004)	1.94 (0.953 to NC)	1.38 (1.051 to 3.745)	
Median (95% CI)	2.96 (1.610 to NC)	NC (2.858 to NC)	7.43 (2.825 to NC)	2.89 (2.267 to 6.899)	NC (1.938 to NC)	3.75 (1.314 to NC)	
75% quantile (95% CI)	NC (5.224 to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.634 to NC)	NC (NC to NC)	NC (3.745 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0694		0.3767		0.4112	
Hazard ratio (95% CI) vs Pd	-	0.55 (0.28 to 1.06)		1.18 (0.82 to 1.71)		1.53 (0.55 to 4.22)	
P-value	-	0.0736		0.3775		0.4147	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (29.0)	13 (33.3)	22 (22.4)	36 (36.4)	6 (25.0)	3 (18.8)	0.4125
Number (%) of patients censored	22 (71.0)	26 (66.7)	76 (77.6)	63 (63.6)	18 (75.0)	13 (81.3)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	8.71 (1.117 to NC)	5.09 (1.643 to NC)	9.59 (2.891 to NC)	6.47 (2.825 to 9.232)	2.46 (0.953 to NC)	NC (0.986 to NC)	
Median (95% CI)	NC (11.696 to NC)	NC (10.251 to NC)	NC (NC to NC)	NC (10.218 to NC)	12.06 (2.464 to NC)	NC (2.267 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.057 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7615		0.0992		0.5062	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.49 to 2.68)		1.56 (0.92 to 2.65)		0.63 (0.16 to 2.51)	
P-value	-	0.7617		0.1020		0.5101	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (25.8)	5 (12.8)	29 (29.6)	23 (23.2)	5 (20.8)	6 (37.5)	0.4325
Number (%) of patients censored	23 (74.2)	34 (87.2)	69 (70.4)	76 (76.8)	19 (79.2)	10 (62.5)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	7.43 (1.281 to NC)	NC (5.684 to NC)	10.18 (2.793 to 11.992)	9.76 (6.078 to NC)	NC (0.953 to NC)	3.91 (1.314 to 6.177)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (NC to NC)	NC (2.825 to NC)	6.18 (3.515 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.177 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1972		0.2164		0.6969	
Hazard ratio (95% CI) vs Pd	-	0.49 (0.16 to 1.49)		0.71 (0.41 to 1.23)		1.27 (0.38 to 4.18)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (43.5)	6 (42.9)	48 (50.5)	77 (65.3)	0.4553
Number (%) of patients censored	13 (56.5)	8 (57.1)	47 (49.5)	41 (34.7)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.18 (0.953 to 1.610)	1.51 (0.920 to 3.318)	1.08 (1.018 to 1.906)	1.05 (1.018 to 1.117)	
Median (95% CI)	5.78 (1.183 to NC)	NC (1.150 to NC)	3.38 (2.168 to NC)	2.27 (1.643 to 3.811)	
75% quantile (95% CI)	NC (5.782 to NC)	NC (3.318 to NC)	NC (NC to NC)	NC (9.429 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8294		0.1004	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.32 to 2.47)		1.35 (0.94 to 1.94)	
P-value	-	0.8294		0.1017	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (43.5)	7 (50.0)	49 (51.6)	67 (56.8)	0.9810
Number (%) of patients censored	13 (56.5)	7 (50.0)	46 (48.4)	51 (43.2)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	2.17 (1.018 to 3.745)	1.31 (0.296 to 4.698)	1.74 (1.018 to 1.971)	1.91 (1.051 to 2.136)	
Median (95% CI)	7.43 (2.168 to NC)	4.70 (1.051 to NC)	8.34 (2.957 to NC)	4.14 (2.793 to 10.021)	
75% quantile (95% CI)	NC (7.425 to NC)	NC (4.698 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8964		0.5824	
Hazard ratio (95% CI) vs Pd	-	1.07 (0.40 to 2.82)		1.11 (0.77 to 1.60)	
P-value	-	0.8964		0.5826	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (26.1)	4 (28.6)	20 (21.1)	42 (35.6)	0.6433
Number (%) of patients censored	17 (73.9)	10 (71.4)	75 (78.9)	76 (64.4)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	12.06 (0.953 to NC)	3.32 (1.084 to NC)	NC (2.924 to NC)	6.47 (3.055 to 9.856)	
Median (95% CI)	NC (12.057 to NC)	NC (1.938 to NC)	NC (NC to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9438		0.0755	
Hazard ratio (95% CI) vs Pd	-	1.05 (0.29 to 3.73)		1.61 (0.95 to 2.75)	
P-value	-	0.9435		0.0784	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (21.7)	5 (35.7)	28 (29.5)	26 (22.0)	0.1464
Number (%) of patients censored	18 (78.3)	9 (64.3)	67 (70.5)	92 (78.0)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	10.18 (1.117 to NC)	6.67 (0.296 to NC)	7.43 (2.793 to 12.025)	NC (6.078 to NC)	
Median (95% CI)	NC (10.185 to NC)	NC (3.220 to NC)	NC (12.025 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (8.345 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4125		0.1133	
Hazard ratio (95% CI) vs Pd	-	1.67 (0.48 to 5.81)		0.65 (0.38 to 1.11)	
P-value	-	0.4175		0.1160	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (52.8)	13 (54.2)	37 (47.4)	67 (65.0)	0.2911
Number (%) of patients censored	17 (47.2)	11 (45.8)	41 (52.6)	36 (35.0)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.08 (0.986 to 1.446)	1.15 (0.920 to 3.285)	1.08 (0.986 to 1.938)	1.05 (0.986 to 1.117)	
Median (95% CI)	2.27 (1.150 to NC)	3.32 (1.281 to NC)	NC (2.004 to NC)	2.27 (1.643 to 3.811)	
75% quantile (95% CI)	NC (5.782 to NC)	NC (4.928 to NC)	NC (NC to NC)	NC (9.429 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8422		0.0775	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.46 to 1.89)		1.43 (0.96 to 2.14)	
P-value	-	0.8422		0.0791	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (38.9)	13 (54.2)	42 (53.8)	58 (56.3)	0.3701
Number (%) of patients censored	22 (61.1)	11 (45.8)	36 (46.2)	45 (43.7)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	2.79 (1.183 to 4.731)	1.48 (0.296 to 3.745)	1.51 (1.018 to 1.971)	1.91 (1.051 to 2.136)	
Median (95% CI)	NC (2.825 to NC)	4.70 (2.136 to NC)	7.89 (2.891 to NC)	5.26 (2.793 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (6.669 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2797		0.9285	
Hazard ratio (95% CI) vs Pd	-	1.51 (0.71 to 3.22)		1.02 (0.68 to 1.52)	
P-value	-	0.2831		0.9286	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (36.1)	6 (25.0)	13 (16.7)	38 (36.9)	0.0384
Number (%) of patients censored	23 (63.9)	18 (75.0)	65 (83.3)	65 (63.1)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	2.10 (1.018 to 12.057)	5.72 (1.084 to NC)	NC (5.092 to NC)	6.47 (3.055 to 9.856)	
Median (95% CI)	NC (4.107 to NC)	NC (5.717 to NC)	NC (NC to NC)	NC (10.283 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3385		0.0146	
Hazard ratio (95% CI) vs Pd	-	0.63 (0.24 to 1.65)		2.15 (1.15 to 4.04)	
P-value	-	0.3429		0.0171	
Hazard ratio inverted (95% CI) vs IPd		-		0.46 (0.25 to 0.87)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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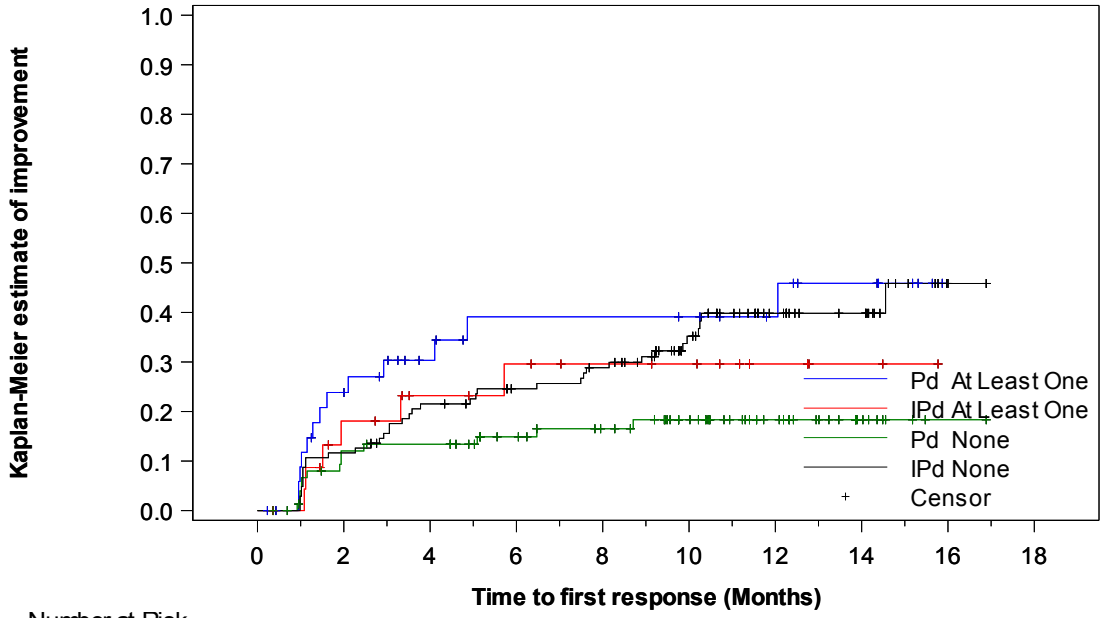
16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to cytogenetic abnormality (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd At Least One	36	21	13	13	9	4	0
IPd At Least One	24	16	11	9	4	1	0
Pd None	78	63	54	45	21	3	0
IPd None	103	85	71	60	25	6	0

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (19.4)	8 (33.3)	24 (30.8)	21 (20.4)	0.0555
Number (%) of patients censored	29 (80.6)	16 (66.7)	54 (69.2)	82 (79.6)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	10.18 (2.793 to NC)	6.67 (0.296 to NC)	7.43 (1.938 to 12.025)	NC (6.177 to NC)	
Median (95% CI)	NC (NC to NC)	NC (6.669 to NC)	NC (12.025 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3082		0.0558	
Hazard ratio (95% CI) vs Pd	-	1.69 (0.61 to 4.66)		0.57 (0.32 to 1.02)	
P-value	-	0.3136		0.0591	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (56.7)	53 (63.9)	29 (46.0)	42 (59.2)	0.7945
Number (%) of patients censored	39 (43.3)	30 (36.1)	34 (54.0)	29 (40.8)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.05 (0.986 to 1.150)	1.12 (1.018 to 1.314)	1.12 (1.018 to 1.610)	1.05 (0.986 to 1.248)	
Median (95% CI)	2.89 (1.938 to NC)	2.92 (1.873 to 4.041)	7.46 (1.610 to NC)	3.45 (1.873 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (6.078 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5519		0.4329	
Hazard ratio (95% CI) vs Pd	-	1.12 (0.77 to 1.65)		1.21 (0.75 to 1.94)	
P-value	-	0.5517		0.4336	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (54.4)	41 (49.4)	31 (49.2)	43 (60.6)	0.3463
Number (%) of patients censored	41 (45.6)	42 (50.6)	32 (50.8)	28 (39.4)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.74 (1.150 to 1.971)	1.97 (1.183 to 2.793)	1.12 (0.986 to 2.464)	1.31 (1.018 to 2.004)	
Median (95% CI)	5.22 (2.793 to NC)	8.25 (2.858 to NC)	7.43 (2.464 to NC)	3.75 (2.136 to 9.101)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5252		0.4891	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.58 to 1.32)		1.18 (0.74 to 1.87)	
P-value	-	0.5267		0.4896	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (26.7)	30 (36.1)	13 (20.6)	22 (31.0)	0.8769
Number (%) of patients censored	66 (73.3)	53 (63.9)	50 (79.4)	49 (69.0)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	9.53 (2.464 to NC)	5.09 (2.267 to 10.218)	NC (1.610 to NC)	8.15 (3.055 to NC)	
Median (95% CI)	NC (NC to NC)	15.47 (10.251 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.474 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2563		0.4694	
Hazard ratio (95% CI) vs Pd	-	1.36 (0.80 to 2.33)		1.29 (0.65 to 2.56)	
P-value	-	0.2588		0.4705	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (28.9)	13 (15.7)	16 (25.4)	21 (29.6)	0.1481
Number (%) of patients censored	64 (71.1)	70 (84.3)	47 (74.6)	50 (70.4)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	9.33 (2.793 to 13.240)	NC (8.345 to NC)	7.43 (1.117 to NC)	7.43 (4.600 to NC)	
Median (95% CI)	NC (13.240 to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0350		0.9776	
Hazard ratio (95% CI) vs Pd	-	0.50 (0.25 to 0.96)		0.99 (0.52 to 1.90)	
P-value	-	0.0389		0.9776	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	1 (50.0)	78 (51.7)	94 (61.8)	0.1359
Number (%) of patients censored	0 (0.0)	1 (50.0)	73 (48.3)	58 (38.2)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.02 (1.018 to 1.084)	1.12 (1.117 to NC)	1.08 (1.018 to 1.281)	1.08 (1.018 to 1.183)	
Median (95% CI)	1.05 (1.018 to 1.084)	NC (1.117 to NC)	3.38 (2.103 to NC)	3.29 (1.906 to 4.665)	
75% quantile (95% CI)	1.08 (1.018 to 1.084)	NC (1.117 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0896		0.2992	
Hazard ratio (95% CI) vs Pd	-			1.17 (0.87 to 1.58)	
P-value	-	0.9985		0.2997	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	80 (53.0)	84 (55.3)	1.0000
Number (%) of patients censored	2 (100.0)	2 (100.0)	71 (47.0)	68 (44.7)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	1.74 (1.084 to 1.938)	1.91 (1.084 to 2.070)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	6.24 (2.891 to 9.462)	5.26 (2.793 to 10.021)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.9608	
Hazard ratio (95% CI) vs Pd	-			1.01 (0.74 to 1.37)	
P-value	-			0.9608	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detl_allt_de_i_t_x.rtf (08APR2021 14:59)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	1 (50.0)	35 (23.2)	51 (33.6)	0.3667
Number (%) of patients censored	0 (0.0)	1 (50.0)	116 (76.8)	101 (66.4)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.02 (1.018 to 8.706)	1.12 (1.117 to NC)	11.70 (4.107 to NC)	7.49 (3.351 to 9.856)	
Median (95% CI)	4.86 (1.018 to 8.706)	NC (1.117 to NC)	NC (NC to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	8.71 (1.018 to 8.706)	NC (1.117 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4328		0.1692	
Hazard ratio (95% CI) vs Pd	-	0.39 (0.03 to 4.44)		1.35 (0.88 to 2.08)	
P-value	-	0.4482		0.1708	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_imppl_allt_de_i_t_x.rtf (08APR2021 15:00)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	42 (27.8)	34 (22.4)	0.9998
Number (%) of patients censored	2 (100.0)	2 (100.0)	109 (72.2)	118 (77.6)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	9.33 (3.450 to 11.992)	10.02 (6.177 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.240 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.1376	
Hazard ratio (95% CI) vs Pd	-			0.71 (0.45 to 1.12)	
P-value	-			0.1390	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detpl_allt_de_i_t_x.rtf (08APR2021 15:00)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (50.5)	66 (63.5)	24 (58.5)	20 (60.6)	0.5746
Number (%) of patients censored	50 (49.5)	38 (36.5)	17 (41.5)	13 (39.4)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.12 (1.018 to 1.906)	1.08 (1.018 to 1.150)	1.05 (0.953 to 1.150)	1.12 (0.986 to 2.267)	
Median (95% CI)	4.76 (2.070 to NC)	2.92 (1.873 to 4.665)	2.30 (1.084 to NC)	3.45 (1.971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (8.903 to NC)	NC (3.384 to NC)	NC (4.928 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1902		0.6476	
Hazard ratio (95% CI) vs Pd	-	1.28 (0.89 to 1.84)		0.87 (0.48 to 1.58)	
P-value	-	0.1913		0.6478	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	55 (54.5)	56 (53.8)	19 (46.3)	19 (57.6)	0.5011
Number (%) of patients censored	46 (45.5)	48 (46.2)	22 (53.7)	14 (42.4)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.22 (1.018 to 1.938)	1.97 (1.281 to 2.267)	1.97 (1.150 to 4.830)	1.18 (0.986 to 2.136)	
Median (95% CI)	4.86 (2.333 to 10.185)	5.55 (2.891 to NC)	9.30 (2.957 to NC)	3.75 (1.478 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (NC to NC)	NC (9.101 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5379		0.3080	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.61 to 1.29)		1.39 (0.74 to 2.63)	
P-value	-	0.5370		0.3102	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (21.8)	39 (37.5)	10 (24.4)	8 (24.2)	0.1413
Number (%) of patients censored	79 (78.2)	65 (62.5)	31 (75.6)	25 (75.8)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	11.70 (2.464 to NC)	5.72 (3.351 to 9.396)	9.53 (1.446 to NC)	7.49 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	15.47 (10.251 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.474 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0615		0.9230	
Hazard ratio (95% CI) vs Pd	-	1.64 (0.97 to 2.77)		0.96 (0.38 to 2.42)	
P-value	-	0.0642		0.9231	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (27.7)	23 (22.1)	10 (24.4)	7 (21.2)	0.9865
Number (%) of patients censored	73 (72.3)	81 (77.9)	31 (75.6)	26 (78.8)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	10.18 (2.825 to 11.992)	10.02 (5.684 to NC)	6.80 (1.741 to NC)	NC (2.201 to NC)	
Median (95% CI)	NC (13.240 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2140		0.5146	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.41 to 1.23)		0.73 (0.28 to 1.91)	
P-value	-	0.2163		0.5164	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (51.0)	64 (62.7)	29 (55.8)	30 (58.8)	0.3679
Number (%) of patients censored	49 (49.0)	38 (37.3)	23 (44.2)	21 (41.2)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.12 (1.018 to 1.906)	1.08 (1.018 to 1.150)	1.05 (0.986 to 1.150)	1.12 (0.986 to 1.971)	
Median (95% CI)	4.76 (1.938 to NC)	2.79 (1.511 to 5.552)	2.79 (1.150 to NC)	3.29 (1.971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.928 to NC)	NC (9.429 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2383		0.7911	
Hazard ratio (95% CI) vs Pd	-	1.25 (0.86 to 1.80)		0.93 (0.56 to 1.56)	
P-value	-	0.2392		0.7908	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	54 (54.0)	54 (52.9)	25 (48.1)	29 (56.9)	0.1993
Number (%) of patients censored	46 (46.0)	48 (47.1)	27 (51.9)	22 (43.1)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.22 (1.018 to 1.938)	1.99 (1.314 to 2.661)	1.97 (1.117 to 4.600)	1.12 (1.018 to 1.906)	
Median (95% CI)	6.24 (2.333 to NC)	6.08 (2.891 to NC)	9.00 (2.957 to NC)	2.83 (1.511 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4907		0.3004	
Hazard ratio (95% CI) vs Pd	-	0.88 (0.60 to 1.28)		1.33 (0.78 to 2.27)	
P-value	-	0.4897		0.3020	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detl_dghc_de_i_t_x.rtf (08APR2021 14:59)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (22.0)	39 (38.2)	15 (28.8)	13 (25.5)	0.1029
Number (%) of patients censored	78 (78.0)	63 (61.8)	37 (71.2)	38 (74.5)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	11.70 (2.464 to NC)	5.72 (3.351 to 9.232)	4.86 (1.150 to NC)	10.22 (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	15.47 (10.251 to NC)	NC (9.528 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.474 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0562		0.5632	
Hazard ratio (95% CI) vs Pd	-	1.66 (0.98 to 2.80)		0.80 (0.38 to 1.69)	
P-value	-	0.0588		0.5639	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_imppl_dghc_de_i_t_x.rtf (08APR2021 15:00)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (28.0)	22 (21.6)	14 (26.9)	12 (23.5)	0.7738
Number (%) of patients censored	72 (72.0)	80 (78.4)	38 (73.1)	39 (76.5)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	10.18 (2.825 to 11.992)	NC (5.684 to NC)	6.80 (1.610 to NC)	9.76 (4.238 to NC)	
Median (95% CI)	NC (11.992 to NC)	NC (NC to NC)	NC (12.025 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1683		0.5150	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.39 to 1.18)		0.77 (0.36 to 1.68)	
P-value	-	0.1710		0.5156	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (40.0)	6 (42.9)	76 (53.1)	89 (63.6)	0.5908
Number (%) of patients censored	6 (60.0)	8 (57.1)	67 (46.9)	51 (36.4)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.94 (0.920 to NC)	1.12 (0.986 to NC)	1.08 (1.018 to 1.150)	1.08 (1.018 to 1.183)	
Median (95% CI)	NC (0.920 to NC)	NC (1.084 to NC)	3.19 (2.004 to NC)	3.09 (1.873 to 3.811)	
75% quantile (95% CI)	NC (3.384 to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.429 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8241		0.2737	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.24 to 3.08)		1.19 (0.87 to 1.61)	
P-value	-	0.8243		0.2752	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (60.0)	8 (57.1)	74 (51.7)	76 (54.3)	0.5211
Number (%) of patients censored	4 (40.0)	6 (42.9)	69 (48.3)	64 (45.7)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.74 (0.953 to 2.333)	1.05 (0.986 to 2.661)	1.61 (1.084 to 1.971)	1.91 (1.183 to 2.136)	
Median (95% CI)	2.33 (0.953 to NC)	2.94 (0.986 to NC)	7.46 (2.957 to NC)	5.55 (2.858 to 13.634)	
75% quantile (95% CI)	NC (1.938 to NC)	NC (2.661 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7498		0.8747	
Hazard ratio (95% CI) vs Pd	-	0.84 (0.29 to 2.46)		1.03 (0.74 to 1.41)	
P-value	-	0.7501		0.8747	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	4 (28.6)	36 (25.2)	48 (34.3)	0.6960
Number (%) of patients censored	9 (90.0)	10 (71.4)	107 (74.8)	92 (65.7)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	NC (1.938 to NC)	5.09 (1.084 to NC)	9.53 (2.891 to NC)	7.49 (3.055 to 9.856)	
Median (95% CI)	NC (1.938 to NC)	NC (3.581 to NC)	NC (NC to NC)	15.47 (14.554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4393		0.2419	
Hazard ratio (95% CI) vs Pd	-	2.33 (0.26 to 21.02)		1.29 (0.84 to 1.99)	
P-value	-	0.4523		0.2432	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (40.0)	6 (42.9)	38 (26.6)	28 (20.0)	0.7543
Number (%) of patients censored	6 (60.0)	8 (57.1)	105 (73.4)	112 (80.0)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.94 (0.953 to NC)	3.91 (1.051 to NC)	10.18 (4.665 to 12.025)	NC (6.965 to NC)	
Median (95% CI)	NC (0.953 to NC)	NC (3.220 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (2.333 to NC)	NC (9.495 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3273		0.1198	
Hazard ratio (95% CI) vs Pd	-	0.50 (0.12 to 2.04)		0.68 (0.42 to 1.11)	
P-value	-	0.3363		0.1220	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	55 (57.3)	58 (66.7)	22 (44.9)	32 (58.2)	0.5311
Number (%) of patients censored	41 (42.7)	29 (33.3)	27 (55.1)	23 (41.8)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.05 (0.986 to 1.117)	1.12 (1.018 to 1.873)	1.15 (0.986 to 1.938)	1.05 (0.986 to 1.281)	
Median (95% CI)	2.83 (1.347 to 7.458)	3.32 (1.906 to 5.552)	NC (1.938 to NC)	3.09 (1.281 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (8.378 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6770		0.3116	
Hazard ratio (95% CI) vs Pd	-	1.08 (0.75 to 1.56)		1.32 (0.77 to 2.28)	
P-value	-	0.6771		0.3132	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	54 (56.3)	49 (56.3)	23 (46.9)	32 (58.2)	0.5811
Number (%) of patients censored	42 (43.8)	38 (43.7)	26 (53.1)	23 (41.8)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.61 (1.018 to 1.938)	1.91 (1.051 to 2.103)	1.97 (1.018 to 3.745)	1.41 (1.051 to 2.661)	
Median (95% CI)	4.83 (2.333 to 10.185)	4.14 (2.201 to NC)	7.89 (2.957 to NC)	4.04 (2.661 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (NC to NC)	NC (10.021 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9456		0.5304	
Hazard ratio (95% CI) vs Pd	-	0.99 (0.67 to 1.45)		1.19 (0.69 to 2.03)	
P-value	-	0.9456		0.5309	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (24.0)	36 (41.4)	11 (22.4)	14 (25.5)	0.3107
Number (%) of patients censored	73 (76.0)	51 (58.6)	38 (77.6)	41 (74.5)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	9.59 (4.862 to NC)	5.72 (3.055 to 9.396)	5.59 (1.446 to NC)	8.44 (1.643 to NC)	
Median (95% CI)	NC (NC to NC)	15.47 (9.955 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.474 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0567		0.9262	
Hazard ratio (95% CI) vs Pd	-	1.65 (0.98 to 2.79)		1.04 (0.47 to 2.29)	
P-value	-	0.0593		0.9263	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (27.1)	17 (19.5)	14 (28.6)	14 (25.5)	0.7758
Number (%) of patients censored	70 (72.9)	70 (80.5)	35 (71.4)	41 (74.5)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	9.33 (3.450 to NC)	NC (5.552 to NC)	10.68 (1.938 to 12.025)	9.76 (5.585 to NC)	
Median (95% CI)	NC (13.240 to NC)	NC (NC to NC)	NC (10.743 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.4483	
Hazard ratio (95% CI) vs Pd	-	0.65 (0.35 to 1.19)		0.75 (0.36 to 1.58)	
P-value	-	0.1606		0.4499	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	2 (100.0)	79 (52.3)	93 (61.2)	0.5242
Number (%) of patients censored	1 (50.0)	0 (0.0)	72 (47.7)	59 (38.8)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	1.91 (1.906 to 1.971)	1.08 (1.018 to 1.150)	1.08 (1.018 to 1.150)	
Median (95% CI)	NC (1.281 to NC)	1.94 (1.906 to 1.971)	3.38 (2.070 to NC)	3.32 (1.906 to 4.928)	
75% quantile (95% CI)	NC (1.281 to NC)	1.97 (1.906 to 1.971)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6949		0.4218	
Hazard ratio (95% CI) vs Pd	-	1.62 (0.14 to 18.31)		1.13 (0.84 to 1.53)	
P-value	-	0.6975		0.4232	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	80 (53.0)	83 (54.6)	0.9820
Number (%) of patients censored	2 (100.0)	1 (50.0)	71 (47.0)	69 (45.4)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	NC (NC to NC)	0.99 (0.986 to NC)	1.74 (1.084 to 1.938)	1.91 (1.117 to 2.103)	
Median (95% CI)	NC (NC to NC)	NC (0.986 to NC)	6.24 (2.891 to 9.462)	5.52 (2.825 to 13.634)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.9550	
Hazard ratio (95% CI) vs Pd	-			0.99 (0.73 to 1.35)	
P-value	-	0.9990		0.9550	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	2 (100.0)	36 (23.8)	50 (32.9)	0.7374
Number (%) of patients censored	1 (50.0)	0 (0.0)	115 (76.2)	102 (67.1)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	1.97 (1.971 to 5.092)	9.59 (4.107 to NC)	7.56 (3.351 to 9.955)	
Median (95% CI)	NC (1.281 to NC)	3.53 (1.971 to 5.092)	NC (NC to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	5.09 (1.971 to 5.092)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6949		0.2485	
Hazard ratio (95% CI) vs Pd	-	1.62 (0.14 to 18.31)		1.29 (0.84 to 1.97)	
P-value	-	0.6975		0.2497	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	42 (27.8)	34 (22.4)	0.9998
Number (%) of patients censored	2 (100.0)	2 (100.0)	109 (72.2)	118 (77.6)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	9.33 (3.450 to 11.992)	10.02 (6.177 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.240 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.1490	
Hazard ratio (95% CI) vs Pd	-			0.72 (0.46 to 1.13)	
P-value	-			0.1506	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	60 (52.2)	74 (62.7)	20 (52.6)	21 (58.3)	0.9055
Number (%) of patients censored	55 (47.8)	44 (37.3)	18 (47.4)	15 (41.7)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.08 (0.986 to 1.150)	1.08 (1.018 to 1.150)	1.12 (1.018 to 2.825)	1.10 (1.018 to 1.873)	
Median (95% CI)	2.83 (1.906 to NC)	3.09 (1.906 to 4.041)	4.93 (2.070 to NC)	3.58 (1.281 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.674 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4723		0.6107	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.81 to 1.59)		1.17 (0.64 to 2.16)	
P-value	-	0.4726		0.6103	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	55 (47.8)	61 (51.7)	25 (65.8)	23 (63.9)	0.2787
Number (%) of patients censored	60 (52.2)	57 (48.3)	13 (34.2)	13 (36.1)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.94 (1.183 to 2.825)	1.51 (1.051 to 1.971)	1.12 (0.986 to 1.938)	2.04 (0.986 to 2.497)	
Median (95% CI)	9.30 (5.224 to NC)	5.55 (2.793 to NC)	1.97 (1.610 to 4.731)	4.70 (2.201 to 10.021)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.891 to NC)	NC (6.899 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5987		0.3307	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.77 to 1.59)		0.75 (0.43 to 1.33)	
P-value	-	0.5992		0.3323	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (24.3)	40 (33.9)	9 (23.7)	12 (33.3)	0.6093
Number (%) of patients censored	87 (75.7)	78 (66.1)	29 (76.3)	24 (66.7)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	6.47 (1.938 to NC)	6.47 (3.055 to 9.955)	11.70 (1.938 to NC)	7.56 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (12.057 to NC)	NC (8.444 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4272		0.2854	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.75 to 1.98)		1.60 (0.67 to 3.80)	
P-value	-	0.4279		0.2897	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (26.1)	27 (22.9)	12 (31.6)	7 (19.4)	0.5780
Number (%) of patients censored	85 (73.9)	91 (77.1)	26 (68.4)	29 (80.6)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	10.68 (2.825 to 12.025)	9.76 (5.684 to NC)	5.88 (1.610 to NC)	NC (5.585 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.425 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3138		0.2249	
Hazard ratio (95% CI) vs Pd	-	0.77 (0.46 to 1.29)		0.57 (0.22 to 1.44)	
P-value	-	0.3152		0.2311	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	73 (50.7)	91 (61.9)	7 (77.8)	4 (57.1)	0.3183
Number (%) of patients censored	71 (49.3)	56 (38.1)	2 (22.2)	3 (42.9)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.08 (1.018 to 1.183)	1.08 (1.018 to 1.183)	0.99 (0.986 to 2.168)	1.02 (1.018 to 3.515)	
Median (95% CI)	3.78 (2.004 to NC)	3.09 (1.906 to 4.665)	2.17 (0.986 to NC)	3.52 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	4.93 (2.070 to NC)	NC (1.938 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2628		0.4445	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.88 to 1.62)		0.62 (0.18 to 2.13)	
P-value	-	0.2634		0.4487	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	76 (52.8)	81 (55.1)	4 (44.4)	3 (42.9)	0.9617
Number (%) of patients censored	68 (47.2)	66 (44.9)	5 (55.6)	4 (57.1)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.74 (1.117 to 1.971)	1.91 (1.183 to 2.136)	1.91 (0.986 to NC)	1.05 (0.986 to NC)	
Median (95% CI)	6.57 (2.891 to 9.462)	5.26 (2.825 to 13.634)	NC (0.986 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.906 to NC)	NC (1.117 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9898		0.9442	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.73 to 1.37)		1.06 (0.24 to 4.73)	
P-value	-	0.9898		0.9440	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (23.6)	48 (32.7)	3 (33.3)	4 (57.1)	0.3171
Number (%) of patients censored	110 (76.4)	99 (67.3)	6 (66.7)	3 (42.9)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	9.59 (2.891 to NC)	7.56 (3.581 to 9.955)	11.70 (0.986 to NC)	1.02 (1.018 to 3.515)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (0.986 to NC)	3.52 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.696 to NC)	NC (1.938 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3197		0.2406	
Hazard ratio (95% CI) vs Pd	-	1.25 (0.80 to 1.94)		2.44 (0.53 to 11.34)	
P-value	-	0.3207		0.2542	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (27.8)	32 (21.8)	2 (22.2)	2 (28.6)	0.4039
Number (%) of patients censored	104 (72.2)	115 (78.2)	7 (77.8)	5 (71.4)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	7.43 (2.825 to 11.992)	NC (6.669 to NC)	10.68 (3.450 to NC)	6.18 (4.731 to NC)	
Median (95% CI)	NC (13.240 to NC)	NC (NC to NC)	NC (3.450 to NC)	NC (4.731 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1013		0.5723	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.43 to 1.08)		1.80 (0.23 to 14.16)	
P-value	-	0.1034		0.5767	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (48.9)	55 (59.1)	37 (56.9)	40 (65.6)	0.4138
Number (%) of patients censored	45 (51.1)	38 (40.9)	28 (43.1)	21 (34.4)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.05 (1.018 to 1.610)	1.08 (1.018 to 1.183)	1.08 (0.986 to 1.150)	1.12 (1.018 to 1.511)	
Median (95% CI)	5.78 (2.103 to NC)	3.58 (1.873 to 8.674)	2.27 (1.150 to 5.092)	3.09 (1.873 to 3.745)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.092 to NC)	NC (3.745 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2464		0.9656	
Hazard ratio (95% CI) vs Pd	-	1.27 (0.85 to 1.89)		0.99 (0.63 to 1.55)	
P-value	-	0.2474		0.9656	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	56 (63.6)	52 (55.9)	24 (36.9)	32 (52.5)	0.0953
Number (%) of patients censored	32 (36.4)	41 (44.1)	41 (63.1)	29 (47.5)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.18 (1.018 to 1.938)	1.91 (1.183 to 2.103)	1.94 (1.216 to 6.242)	1.91 (1.018 to 2.793)	
Median (95% CI)	2.89 (2.136 to 7.425)	4.70 (2.267 to 10.021)	NC (6.242 to NC)	6.08 (2.825 to NC)	
75% quantile (95% CI)	NC (9.298 to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.634 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3000		0.1952	
Hazard ratio (95% CI) vs Pd	-	0.82 (0.56 to 1.20)		1.42 (0.83 to 2.40)	
P-value	-	0.3008		0.1975	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detl_llen_de_i_t_x.rtf (08APR2021 14:59)

16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (20.5)	30 (32.3)	19 (29.2)	22 (36.1)	0.2666
Number (%) of patients censored	70 (79.5)	63 (67.7)	46 (70.8)	39 (63.9)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	NC (4.862 to NC)	7.56 (3.055 to 10.218)	4.11 (1.150 to 11.696)	4.93 (2.825 to 10.251)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (11.696 to NC)	NC (10.251 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1060		0.9863	
Hazard ratio (95% CI) vs Pd	-	1.61 (0.90 to 2.89)		1.01 (0.54 to 1.86)	
P-value	-	0.1094		0.9863	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (36.4)	17 (18.3)	10 (15.4)	17 (27.9)	0.0082
Number (%) of patients censored	56 (63.6)	76 (81.7)	55 (84.6)	44 (72.1)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	4.60 (1.610 to 9.331)	NC (9.101 to NC)	12.02 (10.678 to NC)	6.97 (4.731 to NC)	
Median (95% CI)	NC (10.743 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0051		0.2123	
Hazard ratio (95% CI) vs Pd	-	0.44 (0.25 to 0.80)		1.64 (0.75 to 3.58)	
P-value	-	0.0065		0.2169	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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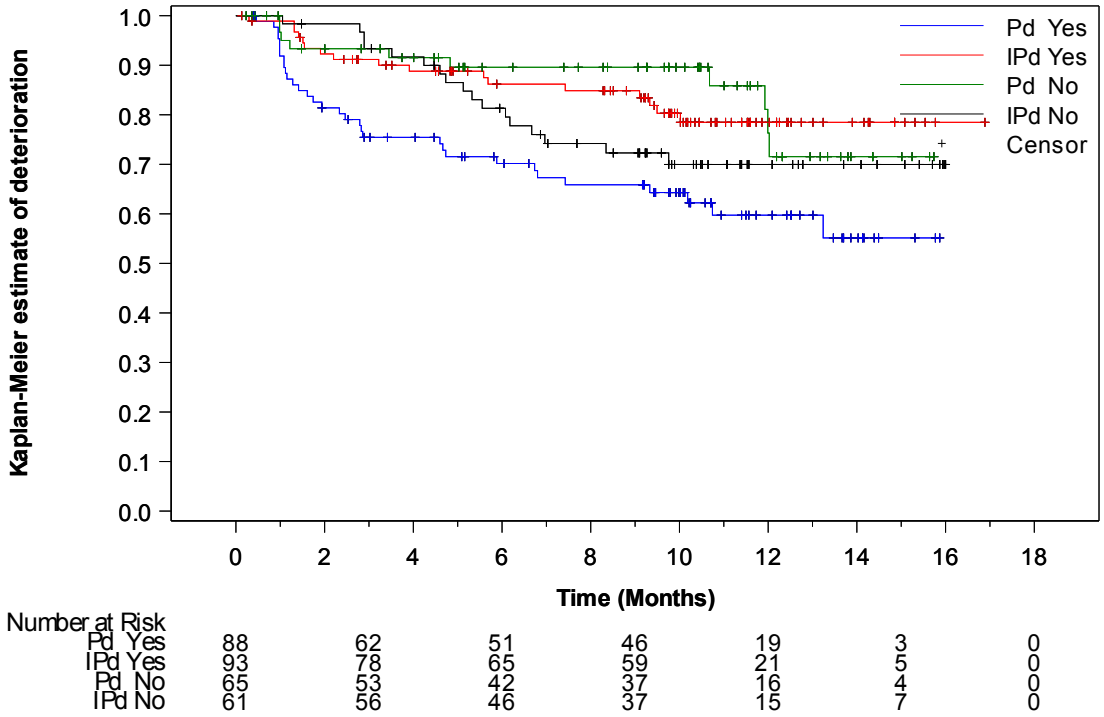
16.2.6.3 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.3.1 Future perspective
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to refractory to lenalidomide in last previous regimen (LOCF) - Kaplan-Meier curve - ITT population



A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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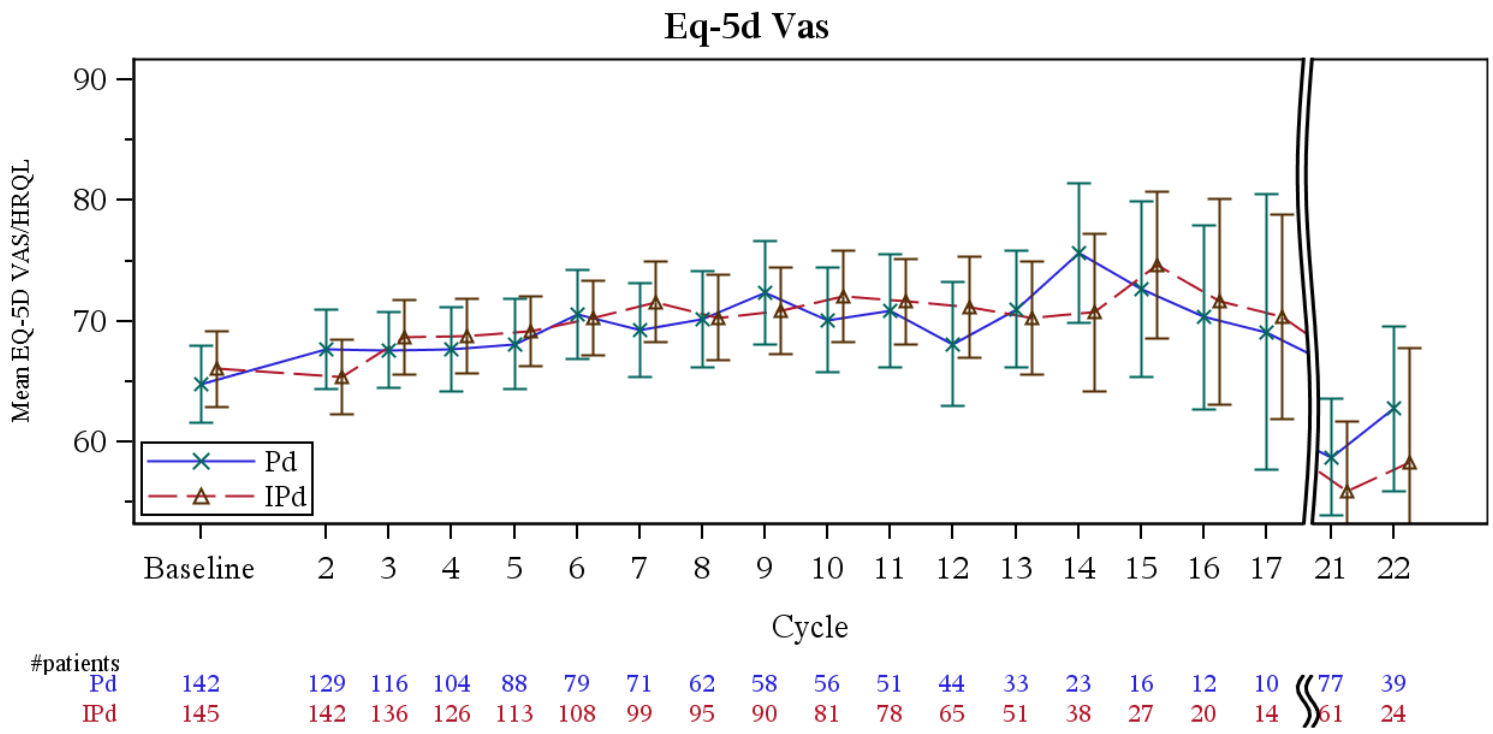
16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.1 EQ-5D VAS
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.1 EQ-5D - Mean and 95% CI for EQ-5D VAS score over time (LOCF) - ITT population



A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.1 EQ-5D VAS
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.28 EQ-5D - Time to first improvement by 15 pt in EQ-5D VAS (LOCF) - ITT population

First improvement 15 points EQ VAS Score	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	46 (30.1)	57 (37.0)
Number (%) of patients censored	107 (69.9)	97 (63.0)
Kaplan-Meier estimates of EQ-5D VAS score in months		
25% quantile (95% CI)	4.80 (2.136 to 8.969)	2.96 (1.906 to 4.895)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3430
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.21 (0.82 to 1.79)
P-value	-	0.3437
Probability (95% CI)[c]		
2 Months	0.17 (0.116 to 0.237)	0.19 (0.135 to 0.260)
4 Months	0.24 (0.172 to 0.311)	0.30 (0.232 to 0.380)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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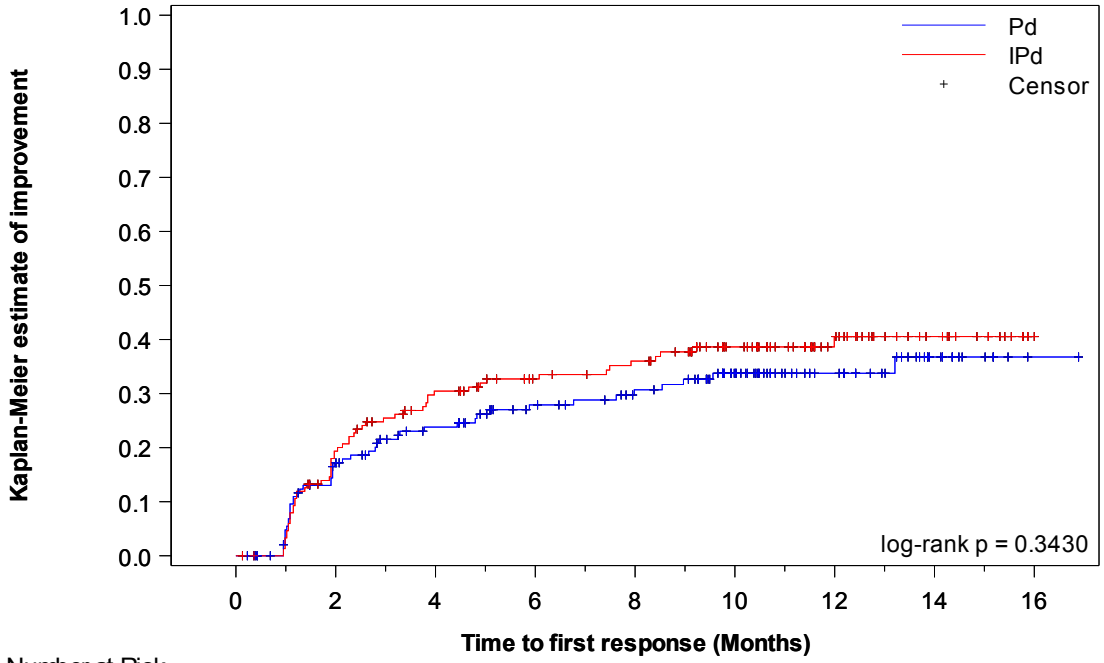
16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.1 EQ-5D VAS
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.29 EQ-5D - Time to first improvement by 15 pt in EQ-5D VAS - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Pd	153	118	99	82	72	52	30	12	1
IPd	153	119	97	83	77	57	31	15	1

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.1 EQ-5D VAS
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.30 EQ-5D - Time to first deterioration by 15 pt in EQ-5D VAS (LOCF) - ITT population

First deterioration 15 points EQ VAS Score	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	59 (38.6)	74 (48.1)
Number (%) of patients censored	94 (61.4)	80 (51.9)
Kaplan-Meier estimates of EQ-5D VAS score in months		
25% quantile (95% CI)	3.15 (2.004 to 4.862)	2.83 (1.938 to 3.811)
Median (95% CI)	15.08 (11.105 to NC)	10.45 (6.965 to 15.474)
75% quantile (95% CI)	NC (15.080 to NC)	NC (14.817 to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3369
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.18 (0.84 to 1.67)
P-value	-	0.3374
Probability (95% CI)[c]		
2 Months	0.83 (0.757 to 0.881)	0.79 (0.713 to 0.845)
4 Months	0.70 (0.614 to 0.766)	0.67 (0.589 to 0.740)

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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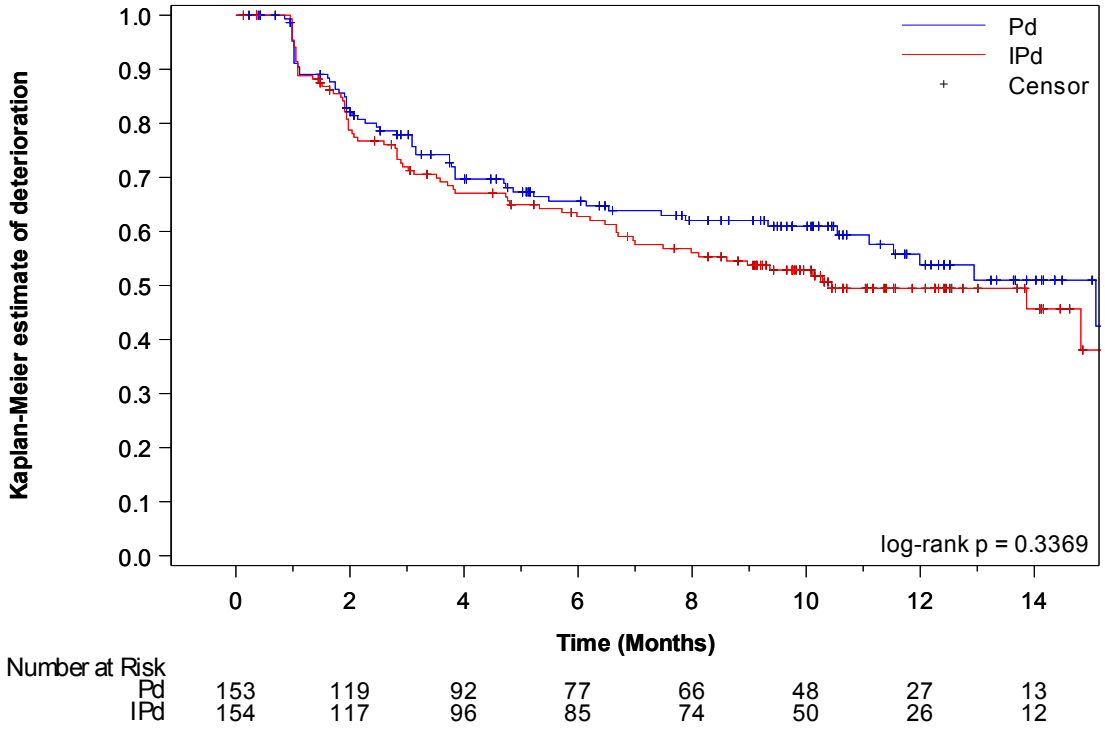
16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.1 EQ-5D VAS
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.31 EQ-5D - Time to first deterioration by 15 pt in EQ-5D VAS - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_15pts_i_f.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_det15l_de_i_f_x.rtf (08APR2021 15:33)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.1 EQ-5D VAS
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.32 EQ-5D - Time until permanent improvement by 15 pt in EQ-5D VAS (LOCF) - ITT population

First permanent improvement 15 points EQ VAS Score (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	21 (13.7)	20 (13.0)
Number (%) of patients censored	132 (86.3)	134 (87.0)
Kaplan-Meier estimates of EQ-5D VAS score in months		
25% quantile (95% CI)	NC (11.072 to NC)	NC (12.945 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5843
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.84 (0.46 to 1.56)
P-value	-	0.5847
Probability (95% CI)[c]		
2 Months	0.05 (0.026 to 0.100)	0.03 (0.012 to 0.071)
4 Months	0.08 (0.041 to 0.128)	0.05 (0.025 to 0.098)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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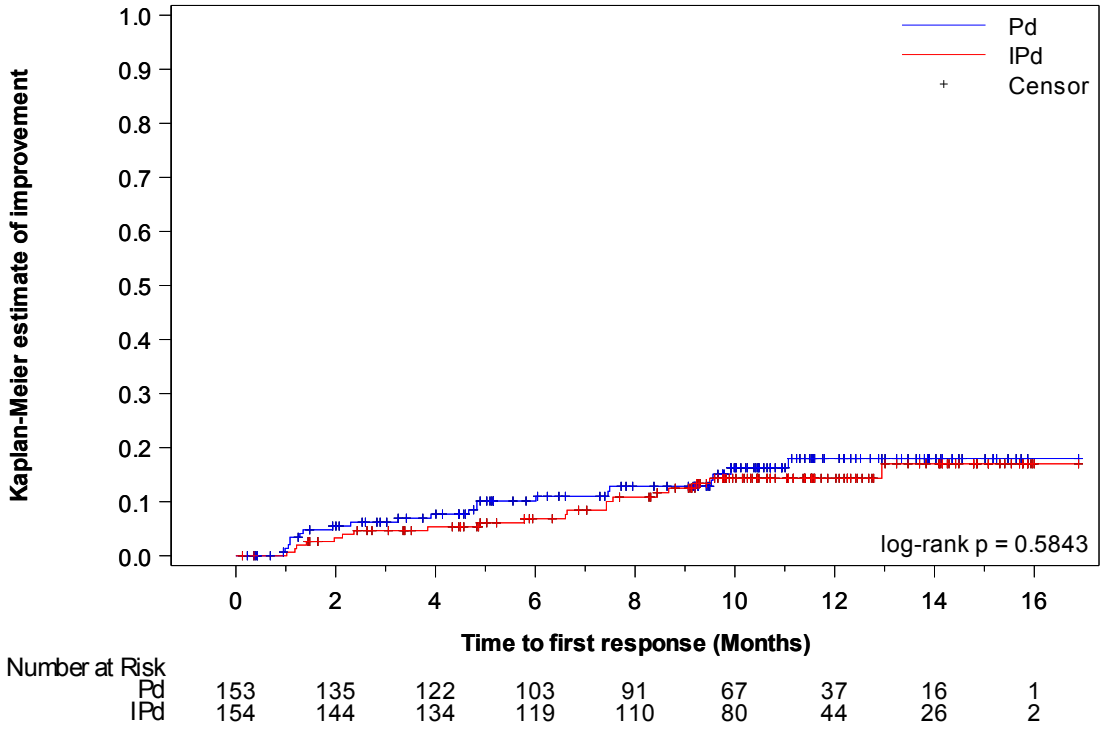
16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.1 EQ-5D VAS
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.33 EQ-5D - Time until permanent improvement by 15 pt in EQ-5D VAS - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.1 EQ-5D VAS
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.34 EQ-5D - Time until permanent deterioration by 15 pt in EQ-5D VAS (LOCF) - ITT population

First permanent deterioration 15 points EQ VAS Score (%)	**Pd (N=153)**	**IPd (N=154)**
Number (%) of events	32 (20.9)	29 (18.8)
Number (%) of patients censored	121 (79.1)	125 (81.2)
Kaplan-Meier estimates of EQ-5D VAS score in months		
25% quantile (95% CI)	11.99 (5.290 to NC)	13.67 (11.170 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3506
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.79 (0.48 to 1.30)
P-value	-	0.3517
Probability (95% CI)[c]		
2 Months	0.90 (0.835 to 0.937)	0.95 (0.905 to 0.978)
4 Months	0.85 (0.776 to 0.896)	0.91 (0.853 to 0.948)

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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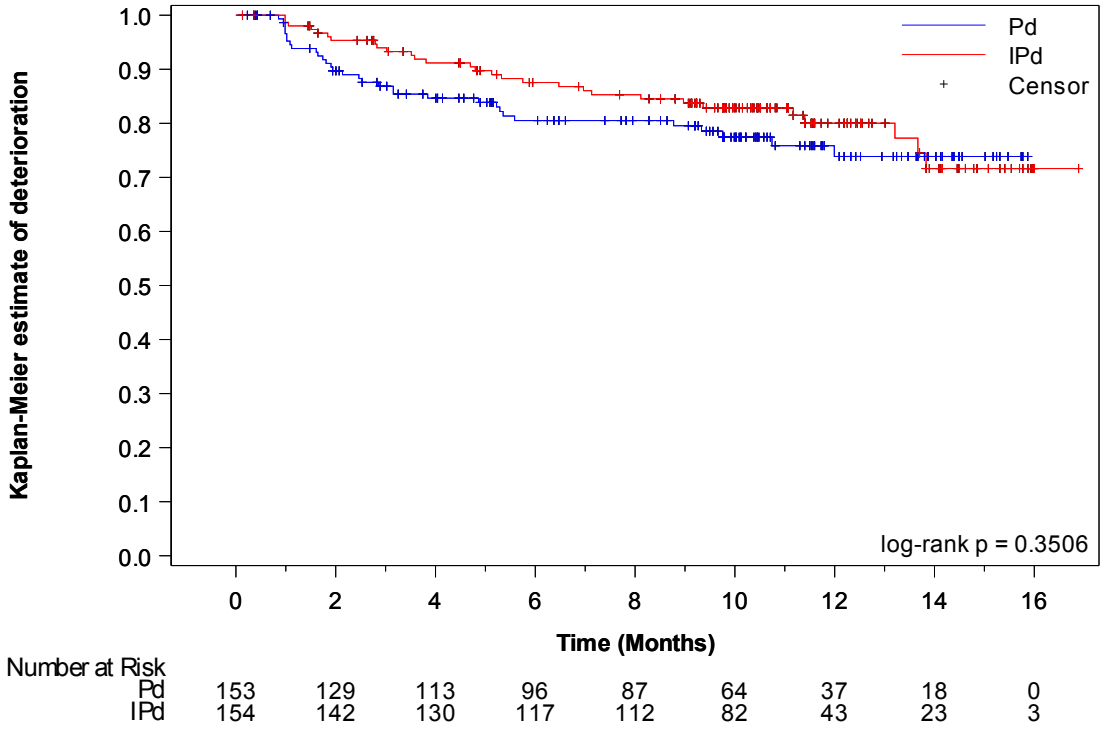
16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.1 EQ-5D VAS
16.2.6.1.1.1 Efficacy response data
16.2.6.1.1.1.35 EQ-5D - Time until permanent deterioration by 15 pt in EQ-5D VAS - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (32.9)	28 (51.9)	27 (50.0)	34 (50.0)	13 (44.8)	13 (40.6)	0.0760
Number (%) of patients censored	47 (67.1)	26 (48.1)	27 (50.0)	34 (50.0)	16 (55.2)	19 (59.4)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	2.30 (1.084 to NC)	1.15 (1.018 to 1.906)	1.15 (0.986 to 1.873)	2.79 (1.873 to 3.680)	1.94 (1.084 to 3.285)	2.22 (0.986 to 9.823)	
Median (95% CI)	NC (NC to NC)	5.16 (1.906 to NC)	7.98 (1.873 to NC)	7.49 (3.680 to NC)	8.97 (1.971 to NC)	NC (3.055 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.969 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0430		0.4105		0.5182	
Hazard ratio (95% CI) vs Pd	-	1.76 (1.01 to 3.05)		0.81 (0.49 to 1.34)		0.78 (0.36 to 1.68)	
P-value	-	0.0458		0.4114		0.5193	
Hazard ratio inverted (95% CI) vs IPd		-		1.24 (0.74 to 2.06)		1.29 (0.60 to 2.79)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_age_de_i_t_x.rtf (08APR2021 15:05)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to age (IRT) (LOCF) - ITT population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (57.1)	29 (53.7)	24 (44.4)	44 (64.7)	16 (55.2)	21 (65.6)	0.1597
Number (%) of patients censored	30 (42.9)	25 (46.3)	30 (55.6)	24 (35.3)	13 (44.8)	11 (34.4)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	2.00 (1.084 to 2.825)	1.91 (1.018 to 2.825)	2.04 (1.117 to 3.318)	1.08 (0.986 to 1.906)	1.94 (0.986 to 3.745)	1.94 (0.986 to 2.825)	
Median (95% CI)	6.51 (2.858 to 10.546)	4.80 (2.825 to NC)	14.26 (3.318 to NC)	3.75 (1.906 to 8.115)	4.70 (1.938 to NC)	5.13 (1.971 to 12.485)	
75% quantile (95% CI)	NC (10.546 to NC)	NC (13.864 to NC)	NC (14.259 to NC)	NC (9.758 to NC)	NC (8.115 to NC)	12.48 (6.604 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6435		0.0330		0.7413	
Hazard ratio (95% CI) vs Pd	-	0.89 (0.55 to 1.44)		1.71 (1.04 to 2.81)		1.12 (0.58 to 2.14)	
P-value	-	0.6436		0.0351		0.7414	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detl_age_de_i_t_x.rtf (08APR2021 15:05)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (15.7)	9 (16.7)	13 (24.1)	12 (17.6)	2 (6.9)	5 (15.6)	0.4058
Number (%) of patients censored	59 (84.3)	45 (83.3)	41 (75.9)	56 (82.4)	27 (93.1)	27 (84.4)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	NC (4.830 to NC)	NC (2.628 to NC)	9.56 (1.347 to NC)	14.55 (9.232 to NC)	NC (7.458 to NC)	NC (4.895 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9840		0.2129		0.3799	
Hazard ratio (95% CI) vs Pd	-	1.01 (0.42 to 2.44)		0.61 (0.28 to 1.34)		2.05 (0.40 to 10.58)	
P-value	-	0.9840		0.2175		0.3901	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.1 Subgroup analyses by age (IRT)
16.2.6.3.1.1.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to age (IRT) (LOCF) - ITT population

	< 65		[65-75[		>= 75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (31.4)	15 (27.8)	11 (20.4)	18 (26.5)	12 (41.4)	11 (34.4)	0.4988
Number (%) of patients censored	48 (68.6)	39 (72.2)	43 (79.6)	50 (73.5)	17 (58.6)	21 (65.6)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	5.29 (2.136 to 11.006)	8.48 (3.811 to NC)	11.99 (2.037 to NC)	9.33 (6.472 to NC)	2.53 (0.986 to 5.914)	7.49 (2.661 to NC)	
Median (95% CI)	NC (11.006 to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (15.474 to NC)	8.11 (3.844 to NC)	NC (7.688 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.474 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4058		0.7272		0.2345	
Hazard ratio (95% CI) vs Pd	-	0.76 (0.39 to 1.46)		1.14 (0.54 to 2.43)		0.61 (0.27 to 1.39)	
P-value	-	0.4073		0.7274		0.2391	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detpl_age_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	IPd (N=102)	Pd (N=52)	IPd (N=52)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	43 (42.6)	46 (45.1)	20 (38.5)	29 (55.8)	0.3162
Number (%) of patients censored	58 (57.4)	56 (54.9)	32 (61.5)	23 (44.2)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.87 (1.084 to 2.793)	1.97 (1.216 to 2.858)	1.94 (1.084 to 4.698)	1.91 (1.084 to 2.267)	
Median (95% CI)	NC (3.253 to NC)	NC (3.680 to NC)	NC (2.793 to NC)	5.65 (2.168 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9591		0.2247	
Hazard ratio (95% CI) vs Pd	-	0.99 (0.65 to 1.50)		1.42 (0.80 to 2.53)	
P-value	-	0.9591		0.2271	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_plne_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (47.5)	65 (63.7)	32 (61.5)	29 (55.8)	0.0160
Number (%) of patients censored	53 (52.5)	37 (36.3)	20 (38.5)	23 (44.2)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.04 (1.610 to 2.858)	1.08 (0.986 to 1.643)	1.94 (1.018 to 2.366)	2.07 (1.906 to 3.515)	
Median (95% CI)	11.53 (3.844 to NC)	3.02 (1.906 to 6.308)	4.44 (2.168 to 9.331)	6.70 (3.088 to 13.864)	
75% quantile (95% CI)	NC (NC to NC)	NC (9.758 to NC)	14.26 (7.885 to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0158		0.2282	
Hazard ratio (95% CI) vs Pd	-	1.58 (1.09 to 2.29)		0.73 (0.44 to 1.22)	
P-value	-	0.0167		0.2301	
Hazard ratio inverted (95% CI) vs IPd		-		1.36 (0.82 to 2.25)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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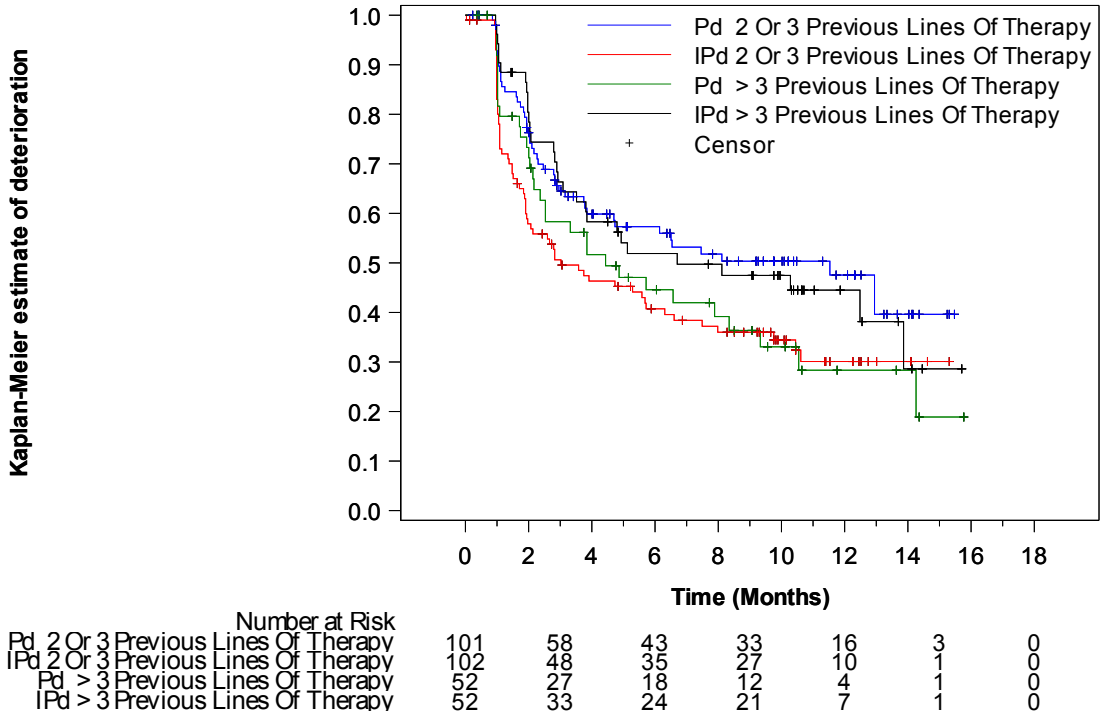
16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.5 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to nb of prior lines (IRT) (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk							
Pd 2 Or 3 Previous Lines Of Therapy	101	58	43	33	16	3	0
IPd 2 Or 3 Previous Lines Of Therapy	102	48	35	27	10	1	0
Pd > 3 Previous Lines Of Therapy	52	27	18	12	4	1	0
IPd > 3 Previous Lines Of Therapy	52	33	24	21	7	1	0

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detl_plne_de_i_f_x.rtf (08APR2021 14:32)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.6 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (18.8)	18 (17.6)	7 (13.5)	8 (15.4)	0.8061
Number (%) of patients censored	82 (81.2)	84 (82.4)	45 (86.5)	44 (84.6)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (4.698 to NC)	14.55 (9.232 to NC)	NC (4.830 to NC)	NC (5.815 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6191		0.9551	
Hazard ratio (95% CI) vs Pd	-	0.85 (0.44 to 1.62)		0.97 (0.35 to 2.68)	
P-value	-	0.6187		0.9551	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_imppl_plne_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.2 Subgroup analyses by nb of prior lines (IRT)
16.2.6.3.1.2.7 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to nb of prior lines (IRT) (LOCF) - ITT population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (26.7)	30 (29.4)	18 (34.6)	14 (26.9)	0.2787
Number (%) of patients censored	74 (73.3)	72 (70.6)	34 (65.4)	38 (73.1)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	5.91 (2.825 to NC)	8.67 (4.205 to 15.474)	4.44 (1.084 to 11.466)	8.11 (5.125 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.474 to NC)	NC (6.998 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9452		0.1566	
Hazard ratio (95% CI) vs Pd	-	0.98 (0.58 to 1.65)		0.61 (0.30 to 1.22)	
P-value	-	0.9452		0.1609	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detpl_plne_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (38.6)	44 (49.4)	36 (43.4)	31 (47.7)	0.3852
Number (%) of patients censored	43 (61.4)	45 (50.6)	47 (56.6)	34 (52.3)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.14 (1.150 to 4.698)	1.91 (1.084 to 2.858)	1.25 (1.051 to 1.938)	1.91 (1.117 to 2.858)	
Median (95% CI)	NC (5.092 to NC)	7.92 (3.811 to NC)	NC (2.793 to NC)	NC (2.858 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2679		0.8987	
Hazard ratio (95% CI) vs Pd	-	1.31 (0.81 to 2.12)		0.97 (0.60 to 1.57)	
P-value	-	0.2694		0.8988	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_sex_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (54.3)	55 (61.8)	42 (50.6)	39 (60.0)	0.7508
Number (%) of patients censored	32 (45.7)	34 (38.2)	41 (49.4)	26 (40.0)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.94 (1.084 to 2.858)	1.87 (1.051 to 2.037)	2.04 (1.150 to 2.530)	1.35 (0.986 to 1.938)	
Median (95% CI)	6.54 (2.957 to 14.259)	4.93 (2.825 to 9.758)	6.57 (3.318 to 12.945)	3.52 (2.004 to 10.448)	
75% quantile (95% CI)	NC (12.945 to NC)	13.86 (10.612 to NC)	NC (12.945 to NC)	NC (10.448 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4496		0.2544	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.77 to 1.78)		1.29 (0.83 to 1.99)	
P-value	-	0.4501		0.2556	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detl_sex_de_i_t_x.rtf (08APR2021 15:05)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (17.1)	16 (18.0)	14 (16.9)	10 (15.4)	0.7196
Number (%) of patients censored	58 (82.9)	73 (82.0)	69 (83.1)	55 (84.6)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (4.830 to NC)	14.55 (8.444 to NC)	NC (4.830 to NC)	NC (8.575 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9179		0.5606	
Hazard ratio (95% CI) vs Pd	-	0.96 (0.45 to 2.03)		0.79 (0.35 to 1.77)	
P-value	-	0.9176		0.5615	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.3 Subgroup analyses by gender
16.2.6.3.1.3.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to gender (LOCF) - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (27.1)	20 (22.5)	26 (31.3)	24 (36.9)	0.3777
Number (%) of patients censored	51 (72.9)	69 (77.5)	57 (68.7)	41 (63.1)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	5.59 (1.741 to NC)	11.40 (6.965 to NC)	5.88 (2.530 to 10.743)	7.06 (3.515 to 10.185)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.743 to NC)	15.47 (10.185 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.474 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2925		0.9637	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.38 to 1.34)		1.01 (0.58 to 1.77)	
P-value	-	0.2948		0.9637	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	55 (43.7)	60 (50.8)	6 (31.6)	13 (54.2)	0.1678
Number (%) of patients censored	71 (56.3)	58 (49.2)	13 (68.4)	11 (45.8)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.87 (1.150 to 1.971)	1.97 (1.216 to 2.825)	1.15 (0.986 to NC)	1.08 (0.986 to 1.906)	
Median (95% CI)	NC (3.285 to NC)	7.92 (3.811 to NC)	NC (1.150 to NC)	3.38 (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.975 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8173		0.1686	
Hazard ratio (95% CI) vs Pd	-	1.04 (0.72 to 1.51)		1.95 (0.74 to 5.15)	
P-value	-	0.8174		0.1765	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	69 (54.8)	73 (61.9)	9 (47.4)	17 (70.8)	0.4320
Number (%) of patients censored	57 (45.2)	45 (38.1)	10 (52.6)	7 (29.2)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.04 (1.643 to 2.464)	1.48 (1.051 to 1.938)	1.15 (0.986 to 9.331)	1.51 (0.033 to 2.661)	
Median (95% CI)	6.14 (3.778 to 10.546)	3.84 (2.793 to 7.984)	9.33 (1.150 to NC)	3.09 (1.906 to 8.115)	
75% quantile (95% CI)	NC (12.945 to NC)	NC (12.485 to NC)	NC (9.331 to NC)	10.28 (4.797 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4111		0.2411	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.83 to 1.60)		1.63 (0.72 to 3.69)	
P-value	-	0.4109		0.2457	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (15.1)	20 (16.9)	5 (26.3)	6 (25.0)	0.8785
Number (%) of patients censored	107 (84.9)	98 (83.1)	14 (73.7)	18 (75.0)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (11.072 to NC)	14.55 (9.659 to NC)	4.83 (0.986 to NC)	8.57 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.830 to NC)	NC (8.575 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9850		0.8993	
Hazard ratio (95% CI) vs Pd	-	0.99 (0.53 to 1.86)		0.93 (0.28 to 3.03)	
P-value	-	0.9850		0.8988	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.4 Subgroup analyses by race
16.2.6.3.1.4.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to race (LOCF) - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (29.4)	33 (28.0)	6 (31.6)	7 (29.2)	0.9003
Number (%) of patients censored	89 (70.6)	85 (72.0)	13 (68.4)	17 (70.8)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	5.88 (3.154 to 11.006)	8.97 (5.322 to NC)	1.71 (0.986 to 11.466)	8.11 (2.661 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.474 to NC)	11.47 (1.708 to 11.466)	NC (8.115 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	11.47 (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3384		0.5992	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.50 to 1.27)		0.74 (0.25 to 2.25)	
P-value	-	0.3395		0.6005	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	3 (75.0)	55 (41.0)	69 (53.1)	0.7990
Number (%) of patients censored	2 (66.7)	1 (25.0)	79 (59.0)	61 (46.9)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	1.02 (1.018 to 9.396)	1.91 (1.150 to 2.661)	1.91 (1.183 to 2.398)	
Median (95% CI)	NC (1.281 to NC)	5.21 (1.018 to NC)	NC (6.867 to NC)	5.82 (3.187 to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8415		0.2106	
Hazard ratio (95% CI) vs Pd	-	1.28 (0.11 to 14.56)		1.25 (0.88 to 1.79)	
P-value	-	0.8419		0.2116	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	0 (0.0)	73 (54.5)	86 (66.2)	0.9788
Number (%) of patients censored	2 (66.7)	4 (100.0)	61 (45.5)	44 (33.8)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.27 (2.267 to NC)	NC (NC to NC)	1.97 (1.610 to 2.366)	1.48 (1.051 to 1.906)	
Median (95% CI)	NC (2.267 to NC)	NC (NC to NC)	6.54 (3.778 to 11.532)	3.58 (2.661 to 5.717)	
75% quantile (95% CI)	NC (2.267 to NC)	NC (NC to NC)	NC (12.945 to NC)	13.86 (10.448 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.1124	
Hazard ratio (95% CI) vs Pd	-			1.29 (0.94 to 1.76)	
P-value	-	0.9990		0.1133	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	1 (25.0)	21 (15.7)	24 (18.5)	0.4613
Number (%) of patients censored	2 (66.7)	3 (75.0)	113 (84.3)	106 (81.5)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (1.018 to NC)	NC (11.072 to NC)	14.55 (9.232 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (1.018 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6949		0.8363	
Hazard ratio (95% CI) vs Pd	-	0.58 (0.04 to 9.30)		1.06 (0.59 to 1.91)	
P-value	-	0.6985		0.8366	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to ethnic origin (LOCF) - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	0 (0.0)	40 (29.9)	39 (30.0)	0.9787
Number (%) of patients censored	2 (66.7)	4 (100.0)	94 (70.1)	91 (70.0)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	5.03 (NC to NC)	NC (NC to NC)	5.59 (2.825 to 11.466)	8.11 (5.322 to 11.400)	
Median (95% CI)	5.03 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.474 to NC)	
75% quantile (95% CI)	5.03 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0455		0.4701	
Hazard ratio (95% CI) vs Pd	-			0.85 (0.55 to 1.32)	
P-value	-	1.0000		0.4706	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	29 (38.2)	20 (36.4)	9 (45.0)	15 (53.6)	3 (60.0)	5 (71.4)	6 (40.0)	11 (52.4)	16 (43.2)	24 (55.8)	0.7475
Number (%) of patients censored	47 (61.8)	35 (63.6)	11 (55.0)	13 (46.4)	2 (40.0)	2 (28.6)	9 (60.0)	10 (47.6)	21 (56.8)	19 (44.2)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	1.87 (1.117 to 2.793)	3.09 (1.183 to 9.823)	1.08 (0.953 to 7.984)	1.48 (0.986 to 2.793)	0.99 (0.953 to NC)	1.94 (1.018 to 2.628)	1.08 (0.986 to NC)	1.08 (0.986 to 2.168)	1.94 (1.248 to 4.698)	1.91 (1.150 to 3.055)	
Median (95% CI)	NC (3.285 to NC)	NC (9.396 to NC)	NC (1.084 to NC)	5.13 (1.906 to NC)	2.83 (0.953 to NC)	2.63 (1.018 to NC)	NC (1.051 to NC)	3.98 (1.084 to NC)	9.56 (2.990 to NC)	4.90 (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (2.530 to NC)	NC (NC to NC)	NC (3.975 to NC)	NC (NC to NC)	NC (7.491 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_greg_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.4595		0.7401		0.9318		0.5286		0.3750	
Hazard ratio (95% CI) vs Pd	-	0.80 (0.45 to 1.43)		1.15 (0.50 to 2.63)		1.06 (0.25 to 4.50)		1.38 (0.51 to 3.73)		1.33 (0.71 to 2.50)	
P-value	-	0.4604		0.7403		0.9318		0.5303		0.3767	
Improvement probability (95% CI)[b]											
2 Months	0.326 (0.220 to 0.435)	0.189 (0.097 to 0.303)	0.263 (0.096 to 0.468)	0.357 (0.189 to 0.530)	0.400 (0.052 to 0.753)	0.286 (0.041 to 0.612)	0.333 (0.122 to 0.564)	0.388 (0.186 to 0.587)	0.283 (0.148 to 0.435)	0.289 (0.161 to 0.429)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	35 (46.1)	33 (60.0)	14 (70.0)	17 (60.7)	2 (40.0)	4 (57.1)	7 (46.7)	16 (76.2)	22 (59.5)	24 (55.8)	0.2926
Number (%) of patients censored	41 (53.9)	22 (40.0)	6 (30.0)	11 (39.3)	3 (60.0)	3 (42.9)	8 (53.3)	5 (23.8)	15 (40.5)	19 (44.2)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	2.10 (1.840 to 3.844)	1.51 (1.018 to 2.595)	0.99 (0.953 to 1.938)	1.00 (0.953 to 1.938)	2.27 (0.986 to NC)	1.71 (1.084 to 9.758)	1.15 (0.986 to 9.331)	1.91 (0.953 to 2.661)	2.14 (1.248 to 2.825)	1.91 (1.051 to 2.825)	
Median (95% CI)	10.55 (4.698 to NC)	4.93 (2.595 to 6.702)	2.37 (0.986 to 6.505)	2.79 (1.051 to NC)	NC (0.986 to NC)	9.76 (1.084 to NC)	NC (1.018 to NC)	3.09 (1.906 to 8.115)	3.84 (2.300 to 7.885)	10.45 (1.971 to 13.864)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (12.945 to NC)	NC (6.702 to NC)	6.51 (2.366 to NC)	NC (3.844 to NC)	NC (0.986 to NC)	NC (5.290 to NC)	NC (9.331 to NC)	10.28 (3.088 to NC)	14.26 (6.571 to NC)	NC (12.485 to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.0748		0.5328		0.7387		0.1598		0.6123	
Hazard ratio (95% CI) vs Pd	-	1.54 (0.95 to 2.50)		0.80 (0.39 to 1.62)		1.33 (0.24 to 7.30)		1.89 (0.77 to 4.66)		0.86 (0.48 to 1.54)	
P-value	-	0.0770		0.5337		0.7395		0.1667		0.6126	
Deterioration probability (95% CI)[b]											

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	12 (15.8)	6 (10.9)	2 (10.0)	7 (25.0)	1 (20.0)	2 (28.6)	5 (33.3)	5 (23.8)	6 (16.2)	6 (14.0)	0.6242
Number (%) of patients censored	64 (84.2)	49 (89.1)	18 (90.0)	21 (75.0)	4 (80.0)	5 (71.4)	10 (66.7)	16 (76.2)	31 (83.8)	37 (86.0)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (5.552 to NC)	NC (9.659 to NC)	NC (0.953 to NC)	9.23 (1.018 to NC)	NC (0.953 to NC)	2.63 (1.018 to NC)	2.30 (0.986 to NC)	8.57 (0.986 to NC)	NC (3.253 to NC)	14.55 (5.815 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (1.018 to NC)	NC (1.084 to NC)	NC (8.575 to NC)	NC (NC to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.3462		0.2747		0.8311		0.5084		0.5200	
Hazard ratio (95% CI) vs Pd	-	0.63 (0.24 to 1.67)		2.34 (0.49 to 11.28)		1.30 (0.12 to 14.35)		0.66 (0.19 to 2.28)		0.69 (0.22 to 2.15)	
P-value	-	0.3506		0.2891		0.8316		0.5114		0.5223	
Improvement probability (95% CI)[b]											
2 Months	0.099 (0.043 to 0.181)	0.056 (0.015 to 0.139)	0.105 (0.018 to 0.284)	0.107 (0.027 to 0.251)	0.200 (0.008 to 0.582)	0.143 (0.007 to 0.465)	0.200 (0.049 to 0.424)	0.095 (0.016 to 0.261)	0.086 (0.022 to 0.206)	0.024 (0.002 to 0.108)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	19 (25.0)	17 (30.9)	10 (50.0)	9 (32.1)	1 (20.0)	2 (28.6)	4 (26.7)	7 (33.3)	11 (29.7)	9 (20.9)	0.4857
Number (%) of patients censored	57 (75.0)	38 (69.1)	10 (50.0)	19 (67.9)	4 (80.0)	5 (71.4)	11 (73.3)	14 (66.7)	26 (70.3)	34 (79.1)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	7.00 (3.154 to NC)	7.49 (2.825 to 11.400)	1.12 (0.953 to 9.331)	7.06 (1.971 to NC)	NC (5.027 to NC)	8.97 (8.674 to NC)	11.47 (0.986 to 11.466)	7.90 (2.661 to NC)	5.29 (1.938 to NC)	NC (3.811 to NC)	
Median (95% CI)	NC (NC to NC)	NC (11.170 to NC)	11.99 (1.117 to NC)	15.47 (8.312 to NC)	NC (5.027 to NC)	NC (8.674 to NC)	11.47 (1.018 to 11.466)	NC (7.688 to NC)	NC (6.571 to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detpl_greg_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to geographical region (LOCF) - ITT population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=37)**	**IPd (N=43)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (15.474 to NC)	NC (5.027 to NC)	NC (8.969 to NC)	11.47 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.6724		0.0857		0.7115		0.8712		0.1880	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.60 to 2.22)		0.45 (0.18 to 1.15)		1.57 (0.14 to 17.46)		1.11 (0.32 to 3.85)		0.56 (0.23 to 1.35)	
P-value	-	0.6727		0.0941		0.7138		0.8712		0.1942	
Deterioration probability (95% CI)[b]											

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detpl_greg_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (40.2)	33 (42.9)	24 (42.9)	42 (54.5)	0.2985
Number (%) of patients censored	58 (59.8)	44 (57.1)	32 (57.1)	35 (45.5)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.87 (1.150 to 2.661)	2.27 (1.216 to 3.844)	1.91 (1.051 to 3.253)	1.87 (1.084 to 2.168)	
Median (95% CI)	NC (3.285 to NC)	NC (5.651 to NC)	NC (3.253 to NC)	3.98 (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7678		0.2508	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.58 to 1.49)		1.34 (0.81 to 2.21)	
P-value	-	0.7685		0.2525	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_rreg_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (49.5)	45 (58.4)	32 (57.1)	49 (63.6)	0.7034
Number (%) of patients censored	49 (50.5)	32 (41.6)	24 (42.9)	28 (36.4)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.14 (1.840 to 3.154)	1.64 (1.051 to 2.595)	1.25 (1.018 to 2.300)	1.23 (0.986 to 1.971)	
Median (95% CI)	8.11 (3.844 to 12.945)	5.29 (2.825 to 12.485)	4.73 (2.300 to 14.259)	3.09 (2.004 to 10.283)	
75% quantile (95% CI)	NC (12.945 to NC)	NC (12.485 to NC)	NC (14.259 to NC)	NC (10.448 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2784		0.6459	
Hazard ratio (95% CI) vs Pd	-	1.25 (0.83 to 1.88)		1.11 (0.71 to 1.73)	
P-value	-	0.2794		0.6461	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detl_rreg_de_i_t_x.rtf (08APR2021 15:05)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (17.5)	9 (11.7)	9 (16.1)	17 (22.1)	0.1658
Number (%) of patients censored	80 (82.5)	68 (88.3)	47 (83.9)	60 (77.9)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (4.830 to NC)	NC (NC to NC)	NC (3.253 to NC)	12.94 (7.425 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1931		0.5311	
Hazard ratio (95% CI) vs Pd	-	0.59 (0.26 to 1.32)		1.29 (0.58 to 2.90)	
P-value	-	0.1983		0.5322	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_imppl_rreg_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to regulatory region (LOCF) - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (25.8)	21 (27.3)	20 (35.7)	23 (29.9)	0.4848
Number (%) of patients censored	72 (74.2)	56 (72.7)	36 (64.3)	54 (70.1)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	6.57 (3.844 to NC)	8.97 (4.698 to NC)	3.32 (1.018 to 11.466)	7.69 (4.797 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.743 to NC)	NC (15.474 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8049		0.2344	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.52 to 1.66)		0.70 (0.38 to 1.27)	
P-value	-	0.8054		0.2369	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detpl_rreg_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	55 (40.1)	67 (48.6)	8 (50.0)	8 (50.0)	0.4846
Number (%) of patients censored	82 (59.9)	71 (51.4)	8 (50.0)	8 (50.0)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.91 (1.150 to 2.793)	1.91 (1.183 to 2.366)	1.15 (0.953 to 1.971)	2.86 (1.018 to 6.505)	
Median (95% CI)	NC (6.867 to NC)	9.40 (3.811 to NC)	2.79 (1.084 to NC)	6.51 (2.628 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.793 to NC)	NC (3.680 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4001		0.5864	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.82 to 1.66)		0.75 (0.27 to 2.10)	
P-value	-	0.4005		0.5876	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_ecog_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	75 (54.7)	87 (63.0)	5 (31.3)	7 (43.8)	0.5185
Number (%) of patients censored	62 (45.3)	51 (37.0)	11 (68.8)	9 (56.3)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.97 (1.610 to 2.267)	1.48 (1.051 to 1.938)	2.53 (0.986 to NC)	1.71 (0.986 to 7.984)	
Median (95% CI)	6.51 (3.778 to 10.546)	3.91 (2.825 to 6.702)	NC (1.084 to NC)	7.98 (1.084 to NC)	
75% quantile (95% CI)	NC (12.945 to NC)	NC (12.485 to NC)	NC (NC to NC)	NC (7.984 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3047		0.4233	
Hazard ratio (95% CI) vs Pd	-	1.18 (0.86 to 1.60)		1.59 (0.50 to 5.03)	
P-value	-	0.3061		0.4274	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (14.6)	24 (17.4)	6 (37.5)	2 (12.5)	0.1206
Number (%) of patients censored	117 (85.4)	114 (82.6)	10 (62.5)	14 (87.5)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (NC to NC)	14.55 (9.659 to NC)	1.28 (0.953 to 11.072)	NC (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	11.07 (1.084 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.072 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8300		0.1144	
Hazard ratio (95% CI) vs Pd	-	1.07 (0.59 to 1.93)		0.30 (0.06 to 1.47)	
P-value	-	0.8304		0.1372	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (29.9)	41 (29.7)	4 (25.0)	3 (18.8)	0.8152
Number (%) of patients censored	96 (70.1)	97 (70.3)	12 (75.0)	13 (81.3)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	5.88 (3.154 to 11.006)	8.31 (6.472 to 11.400)	2.79 (0.986 to NC)	10.18 (2.661 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.474 to NC)	NC (2.530 to NC)	NC (3.515 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4220		0.6074	
Hazard ratio (95% CI) vs Pd	-	0.84 (0.54 to 1.29)		0.68 (0.15 to 3.04)	
P-value	-	0.4226		0.6096	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (43.1)	31 (48.4)	20 (35.7)	26 (49.1)	20 (46.5)	18 (52.9)	0.5279
Number (%) of patients censored	29 (56.9)	33 (51.6)	36 (64.3)	27 (50.9)	23 (53.5)	16 (47.1)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	1.15 (1.018 to 2.891)	1.15 (1.018 to 2.398)	1.97 (1.150 to 9.561)	2.27 (1.216 to 2.924)	1.28 (0.986 to 2.661)	1.97 (1.018 to 4.895)	
Median (95% CI)	NC (2.793 to NC)	7.92 (2.628 to NC)	NC (6.867 to NC)	9.40 (2.924 to NC)	5.09 (1.938 to NC)	6.51 (3.055 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.768 to NC)	NC (7.491 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5826		0.2730		0.4833	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.67 to 2.01)		1.38 (0.77 to 2.48)		0.79 (0.41 to 1.52)	
P-value	-	0.5830		0.2751		0.4846	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (60.8)	36 (56.3)	30 (53.6)	34 (64.2)	16 (37.2)	21 (61.8)	0.4121
Number (%) of patients censored	20 (39.2)	28 (43.8)	26 (46.4)	19 (35.8)	27 (62.8)	13 (38.2)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	2.04 (1.610 to 4.731)	1.48 (1.084 to 2.037)	1.15 (1.018 to 2.136)	1.91 (0.986 to 2.595)	2.86 (1.741 to 4.435)	1.48 (0.986 to 2.004)	
Median (95% CI)	8.34 (3.844 to 12.945)	5.68 (2.136 to NC)	3.84 (2.037 to NC)	5.13 (2.070 to 10.283)	12.94 (3.745 to NC)	3.09 (1.906 to 12.485)	
75% quantile (95% CI)	14.26 (11.532 to NC)	NC (NC to NC)	NC (NC to NC)	13.86 (9.758 to NC)	NC (12.945 to NC)	12.48 (6.702 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7447		0.6856		0.0570	
Hazard ratio (95% CI) vs Pd	-	1.08 (0.67 to 1.75)		1.11 (0.68 to 1.81)		1.87 (0.97 to 3.60)	
P-value	-	0.7452		0.6861		0.0609	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (19.6)	14 (21.9)	9 (16.1)	8 (15.1)	7 (16.3)	4 (11.8)	0.6346
Number (%) of patients censored	41 (80.4)	50 (78.1)	47 (83.9)	45 (84.9)	36 (83.7)	30 (88.2)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	NC (4.830 to NC)	12.94 (8.444 to NC)	NC (2.300 to NC)	NC (6.637 to NC)	NC (1.938 to NC)	NC (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7504		0.7205		0.4005	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.51 to 2.57)		0.84 (0.32 to 2.18)		0.59 (0.17 to 2.03)	
P-value	-	0.7506		0.7209		0.4058	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.9 Subgroup analyses by ISS staging
16.2.6.3.1.9.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to ISS staging (LOCF) - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=64)**	**Pd (N=56)**	**IPd (N=53)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (33.3)	15 (23.4)	17 (30.4)	16 (30.2)	9 (20.9)	12 (35.3)	0.3510
Number (%) of patients censored	34 (66.7)	49 (76.6)	39 (69.6)	37 (69.8)	34 (79.1)	22 (64.7)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	6.57 (1.938 to NC)	10.45 (5.322 to NC)	4.86 (1.018 to NC)	8.97 (6.472 to 15.474)	9.33 (3.318 to NC)	3.58 (1.840 to 7.688)	
Median (95% CI)	NC (11.006 to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.400 to NC)	NC (11.992 to NC)	NC (6.604 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.474 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2701		0.4816		0.3657	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.34 to 1.36)		0.78 (0.39 to 1.55)		1.49 (0.63 to 3.54)	
P-value	-	0.2731		0.4827		0.3688	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detpl_seiss_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (41.9)	19 (48.7)	42 (42.9)	49 (49.5)	8 (33.3)	7 (43.8)	0.8101
Number (%) of patients censored	18 (58.1)	20 (51.3)	56 (57.1)	50 (50.5)	16 (66.7)	9 (56.3)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	1.05 (0.986 to 4.698)	1.08 (0.986 to 1.906)	1.91 (1.248 to 2.793)	1.97 (1.216 to 2.793)	1.51 (0.986 to NC)	3.84 (0.953 to 6.505)	
Median (95% CI)	NC (1.150 to NC)	NC (1.906 to NC)	NC (5.092 to NC)	7.92 (3.088 to NC)	NC (1.511 to NC)	6.51 (3.055 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.505 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6239		0.5462		0.6055	
Hazard ratio (95% CI) vs Pd	-	1.19 (0.59 to 2.42)		1.13 (0.75 to 1.71)		0.75 (0.25 to 2.23)	
P-value	-	0.6243		0.5473		0.6066	

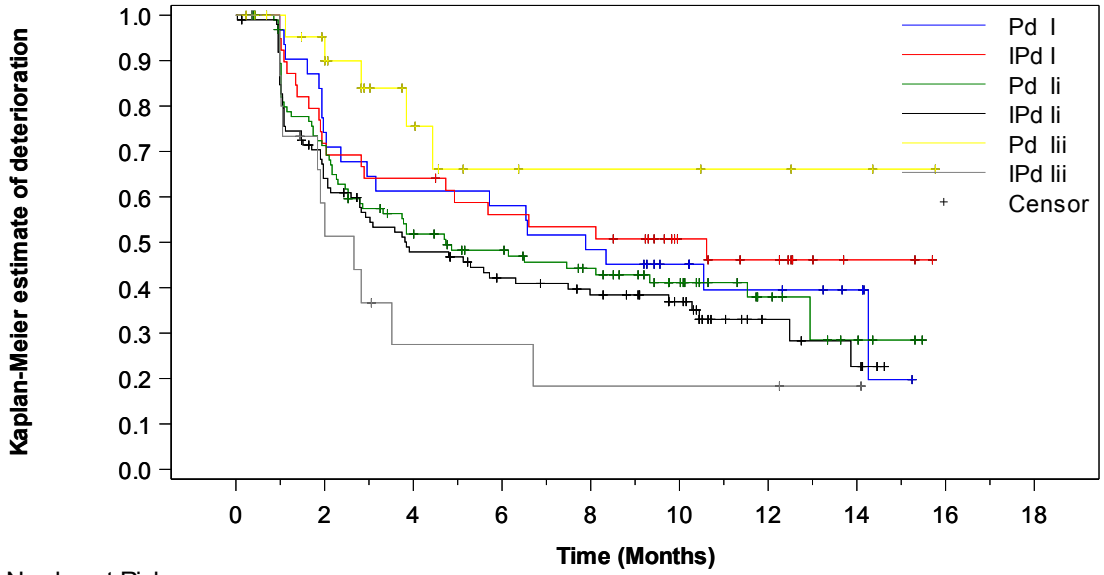
A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_seriss_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (61.3)	20 (51.3)	56 (57.1)	63 (63.6)	5 (20.8)	11 (68.8)	0.0358
Number (%) of patients censored	12 (38.7)	19 (48.7)	42 (42.9)	36 (36.4)	19 (79.2)	5 (31.3)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	1.97 (1.117 to 5.717)	1.91 (1.084 to 4.731)	1.74 (1.018 to 2.168)	1.12 (1.018 to 1.971)	4.44 (1.117 to NC)	1.05 (0.986 to 2.004)	
Median (95% CI)	7.89 (2.366 to NC)	10.61 (2.825 to NC)	4.73 (2.530 to 11.532)	3.84 (2.595 to 7.491)	NC (3.844 to NC)	2.66 (1.018 to 6.702)	
75% quantile (95% CI)	14.26 (10.546 to NC)	NC (NC to NC)	NC (12.945 to NC)	13.86 (10.448 to NC)	NC (NC to NC)	6.70 (2.004 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6585		0.4459		0.0023	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.46 to 1.63)		1.15 (0.80 to 1.65)		4.56 (1.57 to 13.21)	
P-value	-	0.6588		0.4466		0.0052	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detl_seriss_de_i_t_x.rtf (08APR2021 15:05)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.5 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to R-ISS stage (LOCF) - Kaplan-Meier curve - ITT population



Number at Risk

Pd I	31	20	18	14	7	1	0
IPd I	39	25	21	18	8	2	0
Pd Ii	98	53	38	27	10	2	0
IPd Ii	99	51	35	28	7	0	0
Pd Iii	24	12	5	4	3	1	0
IPd Iii	16	5	3	2	2	0	0

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detl_seriss_de_i_f_x.rtf (08APR2021 14:35)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.6 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (19.4)	8 (20.5)	15 (15.3)	18 (18.2)	5 (20.8)	0 (0.0)	0.9997
Number (%) of patients censored	25 (80.6)	31 (79.5)	83 (84.7)	81 (81.8)	19 (79.2)	16 (100.0)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	NC (0.986 to NC)	14.55 (1.018 to NC)	NC (9.561 to NC)	NC (8.575 to NC)	4.70 (1.084 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.698 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.458 to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9569		0.8139		0.0271	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.36 to 2.97)		1.09 (0.55 to 2.15)			
P-value	-	0.9570		0.8144		0.9964	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_imppl_seriss_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.10 Subgroup analyses by R-ISS stage
16.2.6.3.1.10.7 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to R-ISS stage (LOCF) - ITT population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=98)**	**IPd (N=99)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (25.8)	7 (17.9)	33 (33.7)	29 (29.3)	4 (16.7)	8 (50.0)	0.1544
Number (%) of patients censored	23 (74.2)	32 (82.1)	65 (66.3)	70 (70.7)	20 (83.3)	8 (50.0)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	6.57 (1.873 to NC)	NC (7.491 to NC)	5.03 (1.741 to 10.743)	8.48 (5.322 to 15.474)	4.44 (1.117 to NC)	2.83 (1.840 to 6.604)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.466 to NC)	NC (15.474 to NC)	NC (4.435 to NC)	6.60 (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.604 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3895		0.2453		0.1416	
Hazard ratio (95% CI) vs Pd	-	0.64 (0.23 to 1.77)		0.74 (0.45 to 1.23)		2.40 (0.72 to 8.00)	
P-value	-	0.3933		0.2470		0.1542	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (52.2)	5 (35.7)	36 (37.9)	61 (51.7)	0.1150
Number (%) of patients censored	11 (47.8)	9 (64.3)	59 (62.1)	57 (48.3)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.87 (0.953 to 1.938)	2.86 (1.084 to NC)	1.91 (1.117 to 2.825)	1.91 (1.117 to 2.398)	
Median (95% CI)	8.97 (1.873 to NC)	NC (1.938 to NC)	NC (7.984 to NC)	6.51 (3.384 to NC)	
75% quantile (95% CI)	9.56 (8.969 to NC)	NC (3.844 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2900		0.1393	
Hazard ratio (95% CI) vs Pd	-	0.57 (0.20 to 1.63)		1.36 (0.90 to 2.06)	
P-value	-	0.2963		0.1409	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (39.1)	9 (64.3)	50 (52.6)	74 (62.7)	0.2610
Number (%) of patients censored	14 (60.9)	5 (35.7)	45 (47.4)	44 (37.3)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.83 (1.117 to 11.532)	1.97 (0.953 to 2.825)	1.84 (1.084 to 2.366)	1.35 (1.018 to 1.906)	
Median (95% CI)	11.53 (2.825 to NC)	2.83 (1.840 to 3.910)	7.46 (3.844 to NC)	4.73 (2.793 to 8.115)	
75% quantile (95% CI)	NC (8.115 to NC)	3.91 (2.825 to NC)	NC (NC to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0397		0.2298	
Hazard ratio (95% CI) vs Pd	-	2.64 (1.01 to 6.92)		1.25 (0.87 to 1.78)	
P-value	-	0.0476		0.2307	
Hazard ratio inverted (95% CI) vs IPd		-		0.80 (0.56 to 1.15)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (21.7)	1 (7.1)	14 (14.7)	22 (18.6)	0.2351
Number (%) of patients censored	18 (78.3)	13 (92.9)	81 (85.3)	96 (81.4)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	9.56 (0.953 to NC)	NC (8.674 to NC)	NC (11.072 to NC)	14.55 (9.232 to NC)	
Median (95% CI)	NC (4.698 to NC)	NC (8.674 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2508		0.6927	
Hazard ratio (95% CI) vs Pd	-	0.30 (0.04 to 2.62)		1.14 (0.59 to 2.24)	
P-value	-	0.2783		0.6929	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_imppl_cyto_de_i_t_x.rtf (20APR2021 10:52)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.11 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.6.3.1.11.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to cytogenetic abnormality (del17p) (LOCF) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (21.7)	6 (42.9)	29 (30.5)	33 (28.0)	0.1378
Number (%) of patients censored	18 (78.3)	8 (57.1)	66 (69.5)	85 (72.0)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	8.11 (1.117 to NC)	2.74 (1.840 to 11.170)	5.29 (2.037 to 11.466)	8.11 (5.749 to NC)	
Median (95% CI)	NC (4.862 to NC)	11.17 (1.971 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (8.476 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1612		0.3586	
Hazard ratio (95% CI) vs Pd	-	2.30 (0.69 to 7.64)		0.79 (0.48 to 1.30)	
P-value	-	0.1729		0.3596	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (47.2)	9 (37.5)	29 (37.2)	56 (54.4)	0.1181
Number (%) of patients censored	19 (52.8)	15 (62.5)	49 (62.8)	47 (45.6)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.91 (1.117 to 2.300)	2.40 (1.084 to 5.651)	1.91 (1.084 to 2.825)	1.71 (1.084 to 2.267)	
Median (95% CI)	8.97 (1.938 to NC)	NC (2.398 to NC)	NC (6.768 to NC)	6.08 (3.055 to NC)	
75% quantile (95% CI)	NC (9.561 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3519		0.1035	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.30 to 1.53)		1.45 (0.92 to 2.27)	
P-value	-	0.3548		0.1055	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_care_de_i_t_x.rtf (20APR2021 10:52)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (47.2)	16 (66.7)	40 (51.3)	64 (62.1)	0.2545
Number (%) of patients censored	19 (52.8)	8 (33.3)	38 (48.7)	39 (37.9)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.79 (1.248 to 4.862)	1.05 (0.953 to 2.136)	1.74 (1.018 to 2.366)	1.38 (1.018 to 1.938)	
Median (95% CI)	6.14 (3.844 to 12.945)	2.66 (1.478 to 3.910)	8.34 (3.844 to NC)	4.93 (2.793 to 10.283)	
75% quantile (95% CI)	NC (8.115 to NC)	5.72 (2.825 to NC)	NC (12.945 to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0268		0.2967	
Hazard ratio (95% CI) vs Pd	-	2.16 (1.07 to 4.34)		1.23 (0.83 to 1.83)	
P-value	-	0.0306		0.2976	
Hazard ratio inverted (95% CI) vs IPd		-		0.81 (0.55 to 1.20)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (16.7)	3 (12.5)	13 (16.7)	20 (19.4)	0.6357
Number (%) of patients censored	30 (83.3)	21 (87.5)	65 (83.3)	83 (80.6)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (1.281 to NC)	NC (5.717 to NC)	NC (4.830 to NC)	14.55 (8.575 to NC)	
Median (95% CI)	NC (NC to NC)	NC (8.674 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5564		0.9272	
Hazard ratio (95% CI) vs Pd	-	0.66 (0.17 to 2.65)		1.03 (0.51 to 2.08)	
P-value	-	0.5592		0.9275	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (30.6)	11 (45.8)	21 (26.9)	28 (27.2)	0.3191
Number (%) of patients censored	25 (69.4)	13 (54.2)	57 (73.1)	75 (72.8)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	4.86 (2.037 to 11.006)	4.21 (1.840 to 7.129)	9.33 (1.708 to NC)	8.67 (6.604 to NC)	
Median (95% CI)	NC (5.027 to NC)	8.48 (4.205 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (11.170 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3016		0.7097	
Hazard ratio (95% CI) vs Pd	-	1.55 (0.67 to 3.60)		0.90 (0.51 to 1.58)	
P-value	-	0.3053		0.7098	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (36.7)	42 (50.6)	30 (47.6)	33 (46.5)	0.0555
Number (%) of patients censored	57 (63.3)	41 (49.4)	33 (52.4)	38 (53.5)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.94 (1.084 to 2.990)	1.41 (1.084 to 2.366)	1.35 (1.051 to 1.906)	2.27 (1.380 to 3.055)	
Median (95% CI)	NC (8.969 to NC)	6.51 (2.924 to NC)	6.77 (1.906 to NC)	NC (3.680 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0932		0.2758	
Hazard ratio (95% CI) vs Pd	-	1.47 (0.93 to 2.33)		0.76 (0.46 to 1.25)	
P-value	-	0.0953		0.2773	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (53.3)	48 (57.8)	32 (50.8)	46 (64.8)	0.5166
Number (%) of patients censored	42 (46.7)	35 (42.2)	31 (49.2)	25 (35.2)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.97 (1.643 to 2.267)	1.94 (1.051 to 2.595)	2.10 (1.018 to 3.318)	1.35 (0.986 to 1.906)	
Median (95% CI)	6.57 (2.825 to 12.945)	4.93 (2.825 to 12.485)	6.54 (3.318 to 14.259)	3.09 (1.906 to 6.702)	
75% quantile (95% CI)	NC (12.945 to NC)	NC (12.485 to NC)	14.26 (12.945 to NC)	NC (7.984 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6066		0.2021	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.74 to 1.66)		1.34 (0.85 to 2.11)	
P-value	-	0.6061		0.2037	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (17.8)	12 (14.5)	10 (15.9)	14 (19.7)	0.6503
Number (%) of patients censored	74 (82.2)	71 (85.5)	53 (84.1)	57 (80.3)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (4.698 to NC)	NC (14.554 to NC)	NC (5.552 to NC)	12.94 (8.444 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5148		0.9465	
Hazard ratio (95% CI) vs Pd	-	0.78 (0.37 to 1.65)		0.97 (0.43 to 2.19)	
P-value	-	0.5159		0.9464	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.13.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (31.1)	23 (27.7)	17 (27.0)	21 (29.6)	0.8144
Number (%) of patients censored	62 (68.9)	60 (72.3)	46 (73.0)	50 (70.4)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	5.91 (2.136 to 11.006)	10.18 (4.698 to NC)	5.88 (1.117 to NC)	8.31 (5.125 to NC)	
Median (95% CI)	NC (11.466 to NC)	NC (15.474 to NC)	NC (11.992 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.474 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3841		0.7110	
Hazard ratio (95% CI) vs Pd	-	0.78 (0.45 to 1.36)		0.89 (0.47 to 1.68)	
P-value	-	0.3853		0.7112	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	2 (100.0)	61 (40.4)	73 (48.0)	0.8404
Number (%) of patients censored	0 (0.0)	0 (0.0)	90 (59.6)	79 (52.0)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.08 (1.084 to 1.938)	1.08 (1.084 to 2.267)	1.91 (1.150 to 2.661)	1.91 (1.216 to 2.793)	
Median (95% CI)	1.51 (1.084 to 1.938)	1.68 (1.084 to 2.267)	NC (6.867 to NC)	9.40 (3.975 to NC)	
75% quantile (95% CI)	1.94 (1.084 to 1.938)	2.27 (1.084 to 2.267)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5637		0.4959	
Hazard ratio (95% CI) vs Pd	-	0.50 (0.05 to 5.51)		1.13 (0.80 to 1.58)	
P-value	-	0.5715		0.4973	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	79 (52.3)	93 (61.2)	0.9332
Number (%) of patients censored	1 (50.0)	1 (50.0)	72 (47.7)	59 (38.8)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	10.55 (NC to NC)	2.04 (2.037 to NC)	1.97 (1.610 to 2.300)	1.48 (1.051 to 1.938)	
Median (95% CI)	10.55 (NC to NC)	NC (2.037 to NC)	6.54 (3.844 to 12.945)	4.73 (2.825 to 7.491)	
75% quantile (95% CI)	10.55 (NC to NC)	NC (2.037 to NC)	NC (14.259 to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.2115	
Hazard ratio (95% CI) vs Pd	-			1.21 (0.90 to 1.63)	
P-value	-	0.9990		0.2130	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	25 (16.6)	26 (17.1)	0.9837
Number (%) of patients censored	1 (50.0)	2 (100.0)	126 (83.4)	126 (82.9)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.94 (1.938 to NC)	NC (NC to NC)	NC (9.561 to NC)	NC (9.659 to NC)	
Median (95% CI)	NC (1.938 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.938 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.7749	
Hazard ratio (95% CI) vs Pd	-			0.92 (0.53 to 1.60)	
P-value	-	0.9990		0.7746	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_imppl_allt_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.14 Subgroup analyses by previous allogenic transplantation
16.2.6.3.1.14.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to previous allogenic transplantation (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	45 (29.8)	44 (28.9)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	106 (70.2)	108 (71.1)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	5.59 (2.825 to 11.006)	8.31 (6.472 to 11.400)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.474 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.3638	
Hazard ratio (95% CI) vs Pd	-			0.82 (0.54 to 1.25)	
P-value	-			0.3645	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detpl_allt_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (43.6)	53 (51.0)	16 (39.0)	14 (42.4)	0.6750
Number (%) of patients censored	57 (56.4)	51 (49.0)	25 (61.0)	19 (57.6)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.94 (1.150 to 2.825)	1.87 (1.084 to 2.793)	1.15 (0.986 to 2.661)	2.40 (1.183 to 6.078)	
Median (95% CI)	NC (4.698 to NC)	7.49 (3.384 to NC)	NC (1.873 to NC)	NC (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5072		0.7605	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.77 to 1.71)		0.89 (0.44 to 1.83)	
P-value	-	0.5086		0.7610	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_semm_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	54 (53.5)	62 (59.6)	21 (51.2)	20 (60.6)	0.3913
Number (%) of patients censored	47 (46.5)	42 (40.4)	20 (48.8)	13 (39.4)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.97 (1.084 to 2.793)	1.91 (1.084 to 2.595)	2.04 (1.610 to 2.464)	1.38 (0.986 to 2.037)	
Median (95% CI)	7.46 (3.745 to 11.532)	5.13 (3.023 to 10.283)	6.14 (2.267 to NC)	2.92 (1.938 to NC)	
75% quantile (95% CI)	NC (14.259 to NC)	NC (13.864 to NC)	NC (12.945 to NC)	NC (9.758 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5931		0.3876	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.77 to 1.59)		1.31 (0.71 to 2.42)	
P-value	-	0.5940		0.3890	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detl_semm_de_i_t_x.rtf (08APR2021 15:05)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (17.8)	19 (18.3)	6 (14.6)	4 (12.1)	0.9169
Number (%) of patients censored	83 (82.2)	85 (81.7)	35 (85.4)	29 (87.9)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (5.552 to NC)	14.55 (9.232 to NC)	NC (1.084 to NC)	NC (5.717 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8245		0.5651	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.49 to 1.77)		0.69 (0.19 to 2.45)	
P-value	-	0.8242		0.5673	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.15 Subgroup analyses by MM type at SE
16.2.6.3.1.15.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to MM type at SE (LOCF) - ITT population

	Ig G		Ig A		
	Pd (N=101)	**IPd (N=104)**	**Pd (N=41)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (29.7)	30 (28.8)	12 (29.3)	9 (27.3)	0.9480
Number (%) of patients censored	71 (70.3)	74 (71.2)	29 (70.7)	24 (72.7)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	5.91 (2.825 to 11.992)	8.48 (5.749 to 15.474)	5.29 (1.741 to NC)	8.97 (2.825 to NC)	
Median (95% CI)	NC (11.992 to NC)	NC (15.474 to NC)	NC (11.006 to NC)	NC (11.400 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4245		0.5277	
Hazard ratio (95% CI) vs Pd	-	0.81 (0.49 to 1.35)		0.76 (0.32 to 1.80)	
P-value	-	0.4253		0.5290	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (43.0)	51 (50.0)	19 (36.5)	23 (45.1)	0.8988
Number (%) of patients censored	57 (57.0)	51 (50.0)	33 (63.5)	28 (54.9)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.91 (1.150 to 2.793)	1.87 (1.084 to 2.793)	1.25 (1.018 to 2.661)	2.37 (1.216 to 3.811)	
Median (95% CI)	NC (4.698 to NC)	7.49 (3.384 to NC)	NC (2.661 to NC)	NC (3.055 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5563		0.8280	
Hazard ratio (95% CI) vs Pd	-	1.13 (0.75 to 1.70)		1.07 (0.58 to 1.96)	
P-value	-	0.5573		0.8284	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	53 (53.0)	62 (60.8)	26 (50.0)	32 (62.7)	0.4921
Number (%) of patients censored	47 (47.0)	40 (39.2)	26 (50.0)	19 (37.3)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.97 (1.084 to 2.793)	1.91 (1.084 to 2.595)	2.04 (1.610 to 2.530)	1.08 (0.986 to 1.643)	
Median (95% CI)	7.46 (3.844 to 11.532)	4.93 (2.891 to 7.984)	6.51 (2.464 to NC)	2.66 (1.511 to 10.448)	
75% quantile (95% CI)	NC (14.259 to NC)	NC (10.612 to NC)	NC (12.945 to NC)	NC (9.758 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4281		0.1190	
Hazard ratio (95% CI) vs Pd	-	1.16 (0.80 to 1.67)		1.51 (0.90 to 2.54)	
P-value	-	0.4295		0.1216	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (17.0)	18 (17.6)	8 (15.4)	7 (13.7)	0.7125
Number (%) of patients censored	83 (83.0)	84 (82.4)	44 (84.6)	44 (86.3)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (5.552 to NC)	14.55 (9.232 to NC)	NC (1.150 to NC)	NC (7.425 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8440		0.5904	
Hazard ratio (95% CI) vs Pd	-	0.94 (0.48 to 1.82)		0.76 (0.27 to 2.09)	
P-value	-	0.8438		0.5916	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_imppl_dghc_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.16 Subgroup analyses by MM type at initial diagnosis
16.2.6.3.1.16.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to MM type at initial diagnosis (LOCF) - ITT population

	IGG		NON-IGG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (30.0)	30 (29.4)	15 (28.8)	14 (27.5)	0.9820
Number (%) of patients censored	70 (70.0)	72 (70.6)	37 (71.2)	37 (72.5)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	5.91 (2.825 to 11.466)	8.31 (5.749 to 15.474)	5.03 (1.741 to NC)	8.67 (3.121 to NC)	
Median (95% CI)	NC (11.992 to NC)	NC (15.474 to NC)	NC (11.006 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4415		0.5925	
Hazard ratio (95% CI) vs Pd	-	0.82 (0.49 to 1.36)		0.82 (0.40 to 1.70)	
P-value	-	0.4422		0.5931	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detpl_dghc_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (20.0)	8 (57.1)	61 (42.7)	67 (47.9)	0.1710
Number (%) of patients censored	8 (80.0)	6 (42.9)	82 (57.3)	73 (52.1)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (0.920 to NC)	1.38 (0.986 to 2.267)	1.87 (1.150 to 1.971)	1.97 (1.216 to 2.825)	
Median (95% CI)	NC (0.920 to NC)	2.60 (1.084 to NC)	NC (5.092 to NC)	9.40 (3.975 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (2.267 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1447		0.7933	
Hazard ratio (95% CI) vs Pd	-	3.01 (0.64 to 14.20)		1.05 (0.74 to 1.48)	
P-value	-	0.1649		0.7934	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_mri_de_i_t_x.rtf (08APR2021 15:06)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (50.0)	9 (64.3)	75 (52.4)	85 (60.7)	0.1069
Number (%) of patients censored	5 (50.0)	5 (35.7)	68 (47.6)	55 (39.3)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.02 (0.986 to 1.741)	2.83 (1.840 to 6.604)	2.04 (1.708 to 2.530)	1.35 (1.051 to 1.906)	
Median (95% CI)	1.74 (0.986 to NC)	6.60 (2.661 to NC)	7.46 (3.844 to 12.945)	3.91 (2.793 to 6.702)	
75% quantile (95% CI)	NC (1.741 to NC)	NC (6.604 to NC)	NC (14.259 to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0900		0.1155	
Hazard ratio (95% CI) vs Pd	-	0.35 (0.10 to 1.23)		1.28 (0.94 to 1.75)	
P-value	-	0.1020		0.1164	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detl_mri_de_i_t_x.rtf (08APR2021 15:05)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	4 (28.6)	26 (18.2)	22 (15.7)	0.9879
Number (%) of patients censored	10 (100.0)	10 (71.4)	117 (81.8)	118 (84.3)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (NC to NC)	8.57 (2.924 to NC)	NC (5.552 to NC)	NC (12.945 to NC)	
Median (95% CI)	NC (NC to NC)	NC (8.444 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2639		0.3981	
Hazard ratio (95% CI) vs Pd	-			0.78 (0.44 to 1.38)	
P-value	-	0.9961		0.3994	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.17 Subgroup analyses by existing plasmacytoma
16.2.6.3.1.17.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to existing plasmacytoma (LOCF) - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (20.0)	3 (21.4)	43 (30.1)	41 (29.3)	0.5794
Number (%) of patients censored	8 (80.0)	11 (78.6)	100 (69.9)	99 (70.7)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (0.986 to NC)	NC (1.840 to NC)	5.88 (2.825 to 11.006)	8.31 (6.472 to 11.400)	
Median (95% CI)	NC (0.986 to NC)	NC (3.581 to NC)	NC (NC to NC)	NC (15.474 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7118		0.4836	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.12 to 4.32)		0.86 (0.56 to 1.32)	
P-value	-	0.7130		0.4831	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (44.8)	42 (48.3)	18 (36.7)	31 (56.4)	0.2726
Number (%) of patients censored	53 (55.2)	45 (51.7)	31 (63.3)	24 (43.6)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.25 (1.051 to 1.938)	1.91 (1.084 to 2.793)	2.14 (1.511 to 5.092)	1.97 (1.051 to 2.858)	
Median (95% CI)	NC (2.891 to NC)	9.82 (3.187 to NC)	NC (4.698 to NC)	6.08 (2.858 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9964		0.1690	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.65 to 1.53)		1.50 (0.84 to 2.70)	
P-value	-	0.9964		0.1720	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (53.1)	55 (63.2)	27 (55.1)	35 (63.6)	0.7157
Number (%) of patients censored	45 (46.9)	32 (36.8)	22 (44.9)	20 (36.4)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.97 (1.248 to 2.825)	1.51 (1.051 to 2.070)	2.00 (1.018 to 2.530)	1.35 (0.986 to 1.906)	
Median (95% CI)	8.11 (3.844 to 12.945)	4.93 (2.825 to 7.984)	3.84 (2.530 to 12.945)	3.09 (1.906 to 10.448)	
75% quantile (95% CI)	14.26 (12.945 to NC)	13.86 (10.612 to NC)	NC (7.885 to NC)	NC (10.448 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2384		0.6097	
Hazard ratio (95% CI) vs Pd	-	1.26 (0.86 to 1.84)		1.14 (0.69 to 1.89)	
P-value	-	0.2394		0.6100	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (22.9)	17 (19.5)	2 (4.1)	9 (16.4)	0.0617
Number (%) of patients censored	74 (77.1)	70 (80.5)	47 (95.9)	46 (83.6)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	11.07 (3.253 to NC)	14.55 (8.575 to NC)	NC (NC to NC)	NC (5.717 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3731		0.0707	
Hazard ratio (95% CI) vs Pd	-	0.75 (0.40 to 1.41)		3.73 (0.81 to 17.27)	
P-value	-	0.3747		0.0923	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.18 Subgroup analyses by baseline creatinine clearance
16.2.6.3.1.18.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to baseline creatinine clearance (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (29.2)	22 (25.3)	15 (30.6)	18 (32.7)	0.6439
Number (%) of patients censored	68 (70.8)	65 (74.7)	34 (69.4)	37 (67.3)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	5.91 (2.037 to NC)	10.45 (6.965 to NC)	4.44 (2.464 to 11.992)	7.49 (3.121 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.474 to NC)	NC (10.743 to NC)	NC (11.400 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2376		0.7475	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.41 to 1.25)		0.89 (0.45 to 1.77)	
P-value	-	0.2397		0.7477	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	62 (41.1)	74 (48.7)	0.8413
Number (%) of patients censored	1 (50.0)	1 (50.0)	89 (58.9)	78 (51.3)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	1.91 (1.906 to NC)	1.91 (1.150 to 2.300)	1.91 (1.183 to 2.628)	
Median (95% CI)	NC (1.281 to NC)	NC (1.906 to NC)	NC (6.768 to NC)	7.92 (3.844 to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (1.906 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		0.4965	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		1.12 (0.80 to 1.58)	
P-value	-	0.8092		0.4978	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	2 (100.0)	79 (52.3)	92 (60.5)	0.5673
Number (%) of patients censored	1 (50.0)	0 (0.0)	72 (47.7)	60 (39.5)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.10 (2.103 to NC)	1.97 (1.971 to 2.825)	1.97 (1.610 to 2.366)	1.48 (1.051 to 1.938)	
Median (95% CI)	NC (2.103 to NC)	2.40 (1.971 to 2.825)	6.57 (3.844 to 12.945)	4.80 (2.825 to 7.984)	
75% quantile (95% CI)	NC (2.103 to NC)	2.83 (1.971 to 2.825)	NC (14.259 to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4328		0.2326	
Hazard ratio (95% CI) vs Pd	-	2.56 (0.23 to 29.12)		1.20 (0.89 to 1.62)	
P-value	-	0.4482		0.2339	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	0 (0.0)	25 (16.6)	26 (17.1)	0.9872
Number (%) of patients censored	1 (50.0)	2 (100.0)	126 (83.4)	126 (82.9)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.28 (1.281 to NC)	NC (NC to NC)	NC (9.561 to NC)	14.55 (9.659 to NC)	
Median (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.7897	
Hazard ratio (95% CI) vs Pd	-			0.93 (0.54 to 1.61)	
P-value	-	0.9990		0.7894	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.19 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.6.3.1.19.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to previous therapy with anti-CD38 mAB (LOCF) - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	1 (50.0)	45 (29.8)	43 (28.3)	0.9839
Number (%) of patients censored	2 (100.0)	1 (50.0)	106 (70.2)	109 (71.7)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (NC to NC)	11.40 (11.400 to NC)	5.59 (2.825 to 11.006)	8.31 (6.472 to 15.474)	
Median (95% CI)	NC (NC to NC)	NC (11.400 to NC)	NC (NC to NC)	NC (15.474 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (11.400 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.3326	
Hazard ratio (95% CI) vs Pd	-			0.81 (0.54 to 1.24)	
P-value	-			0.3334	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (38.3)	58 (49.2)	19 (50.0)	17 (47.2)	0.3214
Number (%) of patients censored	71 (61.7)	60 (50.8)	19 (50.0)	19 (52.8)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.94 (1.183 to 2.793)	1.91 (1.150 to 2.628)	1.15 (0.986 to 2.793)	1.97 (1.084 to 5.158)	
Median (95% CI)	NC (7.984 to NC)	7.92 (3.384 to NC)	3.25 (1.906 to NC)	9.40 (3.055 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2865		0.5922	
Hazard ratio (95% CI) vs Pd	-	1.24 (0.84 to 1.83)		0.84 (0.43 to 1.61)	
P-value	-	0.2875		0.5926	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	60 (52.2)	76 (64.4)	20 (52.6)	18 (50.0)	0.3766
Number (%) of patients censored	55 (47.8)	42 (35.6)	18 (47.4)	18 (50.0)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.04 (1.150 to 2.530)	1.48 (1.051 to 1.938)	1.97 (1.018 to 3.778)	1.84 (0.986 to 3.581)	
Median (95% CI)	7.46 (3.745 to 12.945)	3.84 (2.661 to 6.604)	6.14 (2.464 to NC)	10.45 (2.070 to NC)	
75% quantile (95% CI)	NC (12.945 to NC)	13.86 (10.283 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1218		0.8603	
Hazard ratio (95% CI) vs Pd	-	1.31 (0.93 to 1.83)		0.94 (0.50 to 1.79)	
P-value	-	0.1229		0.8604	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (15.7)	19 (16.1)	8 (21.1)	7 (19.4)	0.9248
Number (%) of patients censored	97 (84.3)	99 (83.9)	30 (78.9)	29 (80.6)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (9.561 to NC)	NC (12.945 to NC)	NC (1.281 to NC)	NC (1.183 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6643		0.8650	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.45 to 1.66)		0.92 (0.33 to 2.53)	
P-value	-	0.6646		0.8652	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.20 Subgroup analyses by refractory to PI status
16.2.6.3.1.20.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to refractory to PI status (LOCF) - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (28.7)	38 (32.2)	12 (31.6)	6 (16.7)	0.2351
Number (%) of patients censored	82 (71.3)	80 (67.8)	26 (68.4)	30 (83.3)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	5.59 (2.136 to 11.992)	7.49 (5.125 to 11.170)	5.88 (1.938 to NC)	NC (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.474 to NC)	NC (11.006 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7656		0.1322	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.58 to 1.49)		0.48 (0.18 to 1.28)	
P-value	-	0.7649		0.1410	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	57 (39.6)	71 (48.3)	6 (66.7)	4 (57.1)	0.7553
Number (%) of patients censored	87 (60.4)	76 (51.7)	3 (33.3)	3 (42.9)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.91 (1.150 to 2.300)	1.91 (1.216 to 2.628)	1.25 (0.986 to 2.990)	1.02 (1.018 to 3.055)	
Median (95% CI)	NC (6.867 to NC)	9.40 (3.975 to NC)	2.99 (0.986 to NC)	3.06 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.825 to NC)	NC (1.051 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4382		0.7843	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.81 to 1.63)		0.84 (0.24 to 2.98)	
P-value	-	0.4386		0.7846	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	75 (52.1)	91 (61.9)	5 (55.6)	3 (42.9)	0.5582
Number (%) of patients censored	69 (47.9)	56 (38.1)	4 (44.4)	4 (57.1)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.00 (1.643 to 2.464)	1.48 (1.051 to 1.938)	2.17 (0.986 to 14.259)	2.83 (0.986 to NC)	
Median (95% CI)	6.54 (3.844 to 11.532)	3.91 (2.793 to 6.702)	14.26 (0.986 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (12.945 to NC)	NC (12.485 to NC)	NC (2.168 to NC)	NC (4.928 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1812		0.8310	
Hazard ratio (95% CI) vs Pd	-	1.23 (0.91 to 1.67)		0.85 (0.19 to 3.81)	
P-value	-	0.1819		0.8311	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (17.4)	25 (17.0)	1 (11.1)	1 (14.3)	0.6769
Number (%) of patients censored	119 (82.6)	122 (83.0)	8 (88.9)	6 (85.7)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (7.458 to NC)	NC (9.659 to NC)	NC (4.008 to NC)	NC (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.008 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5760		0.8157	
Hazard ratio (95% CI) vs Pd	-	0.85 (0.49 to 1.49)		1.39 (0.09 to 22.25)	
P-value	-	0.5763		0.8165	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.21 Subgroup analyses by refractory to IMID status
16.2.6.3.1.21.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to refractory to IMID status (LOCF) - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (29.9)	41 (27.9)	2 (22.2)	3 (42.9)	0.3240
Number (%) of patients censored	101 (70.1)	106 (72.1)	7 (77.8)	4 (57.1)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	5.29 (2.793 to 11.006)	8.11 (5.749 to NC)	NC (0.986 to NC)	9.89 (9.331 to 11.170)	
Median (95% CI)	NC (NC to NC)	NC (15.474 to NC)	NC (0.986 to NC)	10.81 (9.331 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.331 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2656		0.2828	
Hazard ratio (95% CI) vs Pd	-	0.78 (0.51 to 1.20)		2.59 (0.43 to 15.73)	
P-value	-	0.2667		0.3002	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (39.8)	41 (44.1)	28 (43.1)	34 (55.7)	0.7360
Number (%) of patients censored	53 (60.2)	52 (55.9)	37 (56.9)	27 (44.3)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.91 (1.117 to 2.891)	2.37 (1.380 to 3.811)	1.87 (1.084 to 2.136)	1.18 (1.018 to 2.168)	
Median (95% CI)	NC (6.768 to NC)	NC (5.125 to NC)	NC (2.136 to NC)	3.68 (2.168 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7482		0.4810	
Hazard ratio (95% CI) vs Pd	-	1.08 (0.69 to 1.69)		1.20 (0.72 to 1.98)	
P-value	-	0.7488		0.4825	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (58.0)	58 (62.4)	29 (44.6)	36 (59.0)	0.7546
Number (%) of patients censored	37 (42.0)	35 (37.6)	36 (55.4)	25 (41.0)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.94 (1.150 to 2.464)	1.48 (1.018 to 1.938)	2.17 (1.018 to 3.844)	1.71 (1.051 to 2.825)	
Median (95% CI)	4.86 (2.858 to 8.115)	3.58 (2.070 to 7.984)	12.94 (3.844 to NC)	5.29 (2.825 to 13.864)	
75% quantile (95% CI)	NC (11.532 to NC)	NC (10.283 to NC)	NC (12.945 to NC)	NC (12.485 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4722		0.3013	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.79 to 1.67)		1.29 (0.79 to 2.11)	
P-value	-	0.4731		0.3027	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detl_llen_de_i_t_x.rtf (08APR2021 15:05)

16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (17.0)	15 (16.1)	11 (16.9)	11 (18.0)	0.9724
Number (%) of patients censored	73 (83.0)	78 (83.9)	54 (83.1)	50 (82.0)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (7.458 to NC)	14.55 (9.232 to NC)	NC (1.938 to NC)	NC (5.717 to NC)	
Median (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7186		0.7856	
Hazard ratio (95% CI) vs Pd	-	0.88 (0.43 to 1.79)		0.89 (0.39 to 2.05)	
P-value	-	0.7181		0.7852	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.3 Health-related quality-of-life endpoints - EQ-5D
16.2.6.3.1 EQ-5D VAS
16.2.6.3.1.22 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.6.3.1.22.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to refractory to lenalidomide in last previous regimen (LOCF) - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (36.4)	23 (24.7)	13 (20.0)	21 (34.4)	0.0527
Number (%) of patients censored	56 (63.6)	70 (75.3)	52 (80.0)	40 (65.6)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	4.73 (1.938 to 8.115)	10.18 (4.797 to NC)	11.99 (2.530 to NC)	8.48 (4.698 to 11.170)	
Median (95% CI)	NC (10.743 to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.170 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0586		0.3594	
Hazard ratio (95% CI) vs Pd	-	0.60 (0.35 to 1.02)		1.38 (0.69 to 2.77)	
P-value	-	0.0614		0.3615	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.1 Treatment emergent adverse event by treatment group - Safety population

Any treatment emergent adverse event	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	146 (98.0)	151 (99.3)
Number (%) of patients censored	3 (2.0)	1 (0.7)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.1314 (0.1314 to 0.1643)	0.0986 (0.0657 to 0.1314)
Median (95% CI)	0.3285 (0.2628 to 0.4928)	0.1971 (0.1643 to 0.2300)
75% quantile (95% CI)	0.8871 (0.7228 to 1.3470)	0.5585 (0.3943 to 0.7556)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0038
Hazard ratio (95% CI) vs Pd	-	1.4069 (1.1156 to 1.7742)
P-value	-	0.0039
Hazard ratio inverted (95% CI) vs IPd	0.7108 (0.5636 to 0.8964)	-
probability (95% CI)[b]		
2 Months	0.1111 (0.0664 to 0.1685)	0.0600 (0.0295 to 0.1058)
4 Months	0.0486 (0.0215 to 0.0924)	0.0200 (0.0055 to 0.0530)
6 Months	0.0405 (0.0162 to 0.0826)	0.0133 (0.0026 to 0.0433)

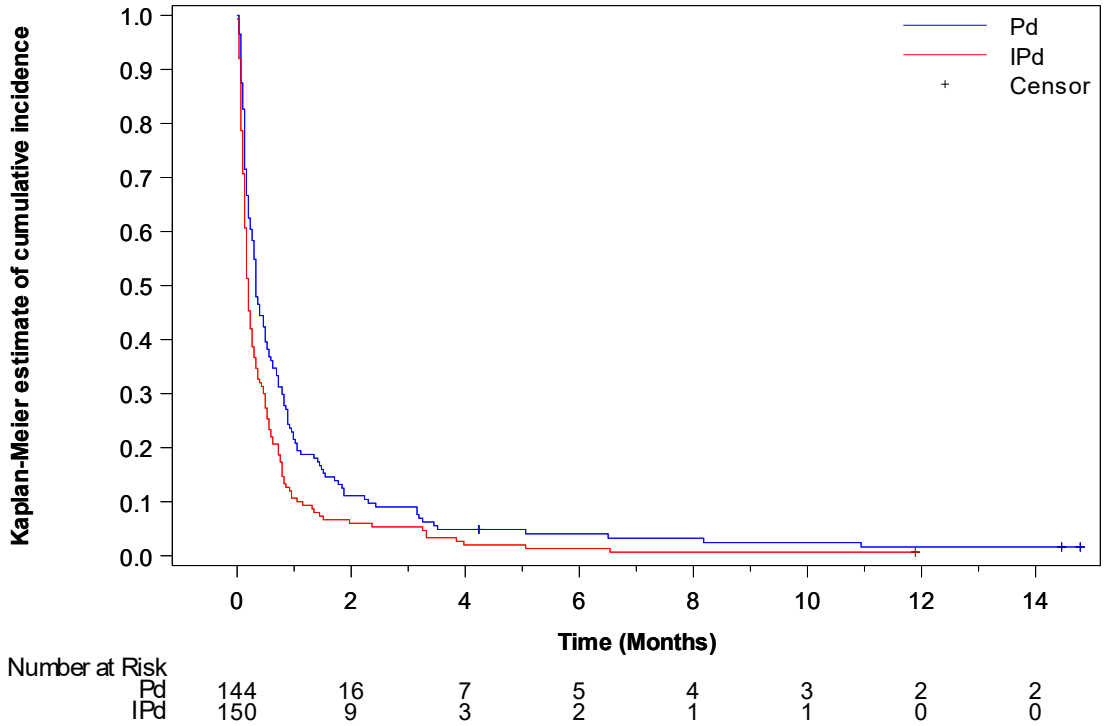
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.1 Treatment emergent adverse event by treatment group - Safety population

Any treatment emergent adverse event	**Pd (N=149)**	**IPd (N=152)**
8 Months	0.0324 (0.0113 to 0.0725)	0.0067 (0.0006 to 0.0336)
10 Months	0.0243 (0.0070 to 0.0620)	0.0067 (0.0006 to 0.0336)
12 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
14 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
16 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
Number of patients at risk[b]		
2 Months	16	9
4 Months	7	3
6 Months	5	2
8 Months	4	1
10 Months	3	1
12 Months	2	0
14 Months	2	0
16 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.3 Non-progression treatment emergent adverse event by treatment group - Safety population

Any treatment emergent adverse event without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	146 (98.0)	151 (99.3)
Number (%) of patients censored	3 (2.0)	1 (0.7)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.1314 (0.1314 to 0.1643)	0.0986 (0.0657 to 0.1314)
Median (95% CI)	0.3285 (0.2628 to 0.4928)	0.1971 (0.1643 to 0.2300)
75% quantile (95% CI)	0.8871 (0.7228 to 1.3470)	0.5585 (0.3943 to 0.7556)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0038
Hazard ratio (95% CI) vs Pd	-	1.4069 (1.1156 to 1.7742)
P-value	-	0.0039
Hazard ratio inverted (95% CI) vs IPd	0.7108 (0.5636 to 0.8964)	-
probability (95% CI)[b]		
2 Months	0.1111 (0.0664 to 0.1685)	0.0600 (0.0295 to 0.1058)
4 Months	0.0486 (0.0215 to 0.0924)	0.0200 (0.0055 to 0.0530)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.3 Non-progression treatment emergent adverse event by treatment group - Safety population

Any treatment emergent adverse event without progression events	**Pd (N=149)**	**IPd (N=152)**
6 Months	0.0405 (0.0162 to 0.0826)	0.0133 (0.0026 to 0.0433)
8 Months	0.0324 (0.0113 to 0.0725)	0.0067 (0.0006 to 0.0336)
10 Months	0.0243 (0.0070 to 0.0620)	0.0067 (0.0006 to 0.0336)
12 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
14 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
16 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
Number of patients at risk[b]		
2 Months	16	9
4 Months	7	3
6 Months	5	2
8 Months	4	1
10 Months	3	1
12 Months	2	0
14 Months	2	0
16 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.4 Treatment emergent serious adverse event by treatment group - Safety population

Treatment emergent serious adverse event	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	80 (53.7)	94 (61.8)
Number (%) of patients censored	69 (46.3)	58 (38.2)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	1.3799 (0.7228 to 1.9384)	0.7885 (0.4928 to 1.4127)
Median (95% CI)	6.5708 (3.7782 to NC)	6.2752 (3.3183 to 9.9548)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2578
Hazard ratio (95% CI) vs Pd	-	1.1878 (0.8809 to 1.6016)
P-value	-	0.2592
probability (95% CI)[b]		
2 Months	0.6779 (0.5964 to 0.7464)	0.6490 (0.5672 to 0.7192)
4 Months	0.5830 (0.4994 to 0.6574)	0.5620 (0.4790 to 0.6369)
6 Months	0.5131 (0.4296 to 0.5903)	0.5009 (0.4184 to 0.5778)
8 Months	0.4838 (0.4006 to 0.5619)	0.4735 (0.3916 to 0.5508)

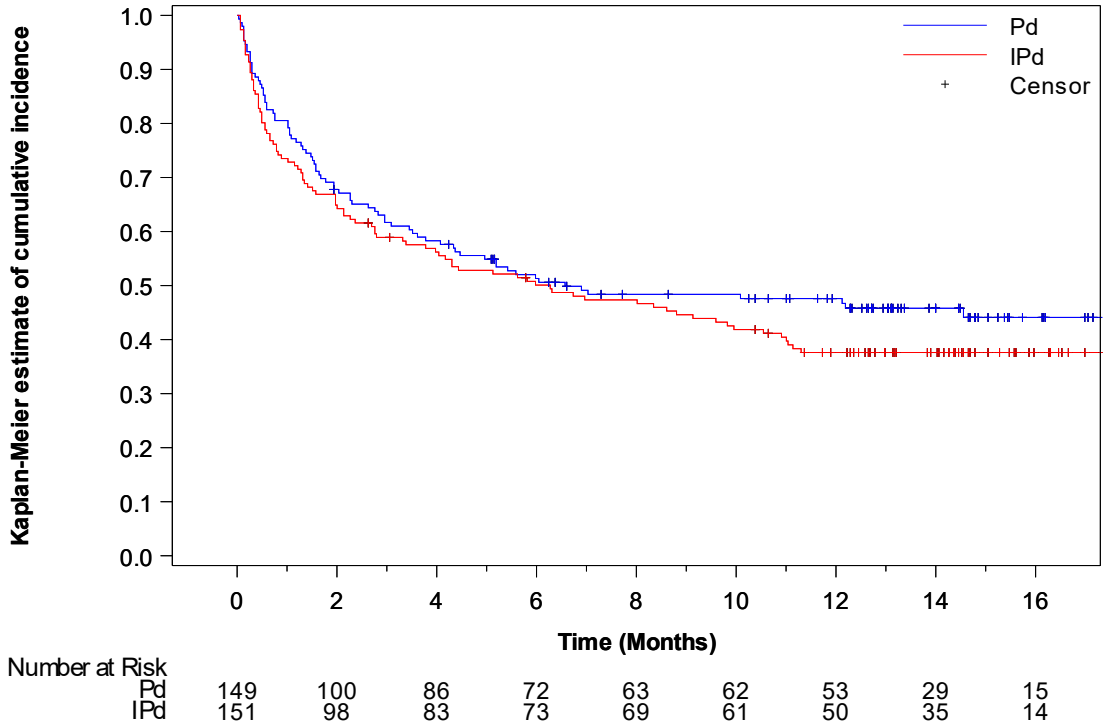
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.4 Treatment emergent serious adverse event by treatment group - Safety population

Treatment emergent serious adverse event	**Pd (N=149)**	**IPd (N=152)**
10 Months	0.4838 (0.4006 to 0.5619)	0.4186 (0.3387 to 0.4963)
12 Months	0.4760 (0.3929 to 0.5544)	0.3761 (0.2983 to 0.4536)
14 Months	0.4580 (0.3746 to 0.5374)	0.3761 (0.2983 to 0.4536)
16 Months	0.4410 (0.3545 to 0.5240)	0.3761 (0.2983 to 0.4536)
Number of patients at risk[b]		
2 Months	100	98
4 Months	86	83
6 Months	72	73
8 Months	63	69
10 Months	62	61
12 Months	53	50
14 Months	29	35
16 Months	15	14

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.5 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.6 Non-progression treatment emergent serious adverse event by treatment group - Safety population

Treatment emergent serious adverse event without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	80 (53.7)	94 (61.8)
Number (%) of patients censored	69 (46.3)	58 (38.2)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	1.3799 (0.7228 to 1.9384)	0.7885 (0.4928 to 1.4127)
Median (95% CI)	6.5708 (3.7782 to NC)	6.3080 (3.3183 to 10.5462)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2630
Hazard ratio (95% CI) vs Pd	-	1.1856 (0.8793 to 1.5987)
P-value	-	0.2643
probability (95% CI)[b]		
2 Months	0.6779 (0.5964 to 0.7464)	0.6490 (0.5672 to 0.7192)
4 Months	0.5830 (0.4994 to 0.6574)	0.5620 (0.4790 to 0.6369)
6 Months	0.5131 (0.4296 to 0.5903)	0.5078 (0.4252 to 0.5844)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.6 Non-progression treatment emergent serious adverse event by treatment group - Safety population

Treatment emergent serious adverse event without progression events	**Pd (N=149)**	**IPd (N=152)**
8 Months	0.4838 (0.4006 to 0.5619)	0.4803 (0.3983 to 0.5576)
10 Months	0.4838 (0.4006 to 0.5619)	0.4254 (0.3453 to 0.5032)
12 Months	0.4760 (0.3929 to 0.5544)	0.3759 (0.2981 to 0.4534)
14 Months	0.4580 (0.3746 to 0.5374)	0.3759 (0.2981 to 0.4534)
16 Months	0.4410 (0.3545 to 0.5240)	0.3759 (0.2981 to 0.4534)
Number of patients at risk[b]		
2 Months	100	98
4 Months	86	83
6 Months	72	74
8 Months	63	70
10 Months	62	62
12 Months	53	50
14 Months	29	35
16 Months	15	14

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesaenp_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.7 Treatment emergent adverse event leading to discontinuation of treatment by treatment group - Safety population

Any treatment emergent leading to discontinuation of treatment	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	19 (12.8)	11 (7.2)
Number (%) of patients censored	130 (87.2)	141 (92.8)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0836
Hazard ratio (95% CI) vs Pd	-	0.5250 (0.2498 to 1.1033)
P-value	-	0.0890
probability (95% CI)[b]		
2 Months	0.9120 (0.8533 to 0.9480)	0.9934 (0.9539 to 0.9991)
4 Months	0.9051 (0.8449 to 0.9427)	0.9732 (0.9302 to 0.9899)
6 Months	0.8836 (0.8193 to 0.9260)	0.9522 (0.9023 to 0.9769)
8 Months	0.8755 (0.8094 to 0.9197)	0.9444 (0.8917 to 0.9718)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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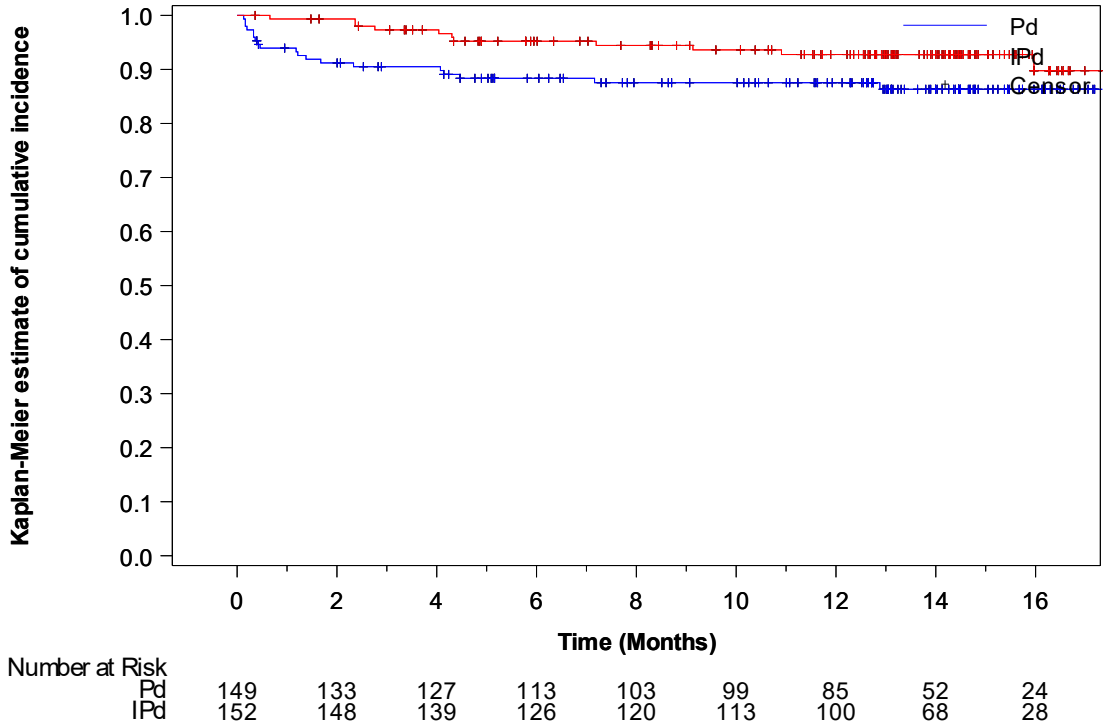
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.7 Treatment emergent adverse event leading to discontinuation of treatment by treatment group - Safety population

Any treatment emergent leading to discontinuation of treatment	**Pd (N=149)**	**IPd (N=152)**
10 Months	0.8755 (0.8094 to 0.9197)	0.9362 (0.8806 to 0.9664)
12 Months	0.8755 (0.8094 to 0.9197)	0.9276 (0.8691 to 0.9605)
14 Months	0.8633 (0.7925 to 0.9113)	0.9276 (0.8691 to 0.9605)
16 Months	0.8633 (0.7925 to 0.9113)	0.8977 (0.7981 to 0.9496)
Number of patients at risk[b]		
2 Months	133	148
4 Months	127	139
6 Months	113	126
8 Months	103	120
10 Months	99	113
12 Months	85	100
14 Months	52	68
16 Months	24	28

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.8 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.9 Non-progression treatment emergent adverse event leading to discontinuation of treatment by treatment group - Safety population

Any treatment emergent leading to discontinuation of treatment without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	19 (12.8)	10 (6.6)
Number (%) of patients censored	130 (87.2)	142 (93.4)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0527
Hazard ratio (95% CI) vs Pd	-	0.4771 (0.2218 to 1.0263)
P-value	-	0.0583
probability (95% CI)[b]		
2 Months	0.9120 (0.8533 to 0.9480)	0.9934 (0.9539 to 0.9991)
4 Months	0.9051 (0.8449 to 0.9427)	0.9732 (0.9302 to 0.9899)
6 Months	0.8836 (0.8193 to 0.9260)	0.9522 (0.9023 to 0.9769)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tediscnp_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.9 Non-progression treatment emergent adverse event leading to discontinuation of treatment by treatment group - Safety population

Any treatment emergent leading to discontinuation of treatment without progression events	**Pd (N=149)**	**IPd (N=152)**
8 Months	0.8755 (0.8094 to 0.9197)	0.9522 (0.9023 to 0.9769)
10 Months	0.8755 (0.8094 to 0.9197)	0.9440 (0.8909 to 0.9716)
12 Months	0.8755 (0.8094 to 0.9197)	0.9354 (0.8791 to 0.9660)
14 Months	0.8633 (0.7925 to 0.9113)	0.9354 (0.8791 to 0.9660)
16 Months	0.8633 (0.7925 to 0.9113)	0.9052 (0.8045 to 0.9555)
Number of patients at risk[b]		
2 Months	133	148
4 Months	127	139
6 Months	113	126
8 Months	103	121
10 Months	99	114
12 Months	85	101
14 Months	52	69
16 Months	24	28

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tediscnp_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.10 Treatment emergent mild adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1,2)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	137 (91.9)	141 (92.8)
Number (%) of patients censored	12 (8.1)	11 (7.2)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.1643 (0.1314 to 0.2628)	0.0986 (0.0657 to 0.1314)
Median (95% CI)	0.4928 (0.3285 to 0.7228)	0.2300 (0.1643 to 0.3285)
75% quantile (95% CI)	1.4456 (0.8871 to 1.8727)	0.8214 (0.6571 to 2.0698)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1456
Hazard ratio (95% CI) vs Pd	-	1.1932 (0.9403 to 1.5142)
P-value	-	0.1461
probability (95% CI)[b]		
2 Months	0.1740 (0.1167 to 0.2410)	0.1854 (0.1281 to 0.2511)
4 Months	0.0984 (0.0557 to 0.1552)	0.1215 (0.0749 to 0.1802)
6 Months	0.0820 (0.0433 to 0.1362)	0.0892 (0.0492 to 0.1439)
8 Months	0.0717 (0.0354 to 0.1251)	0.0625 (0.0293 to 0.1132)

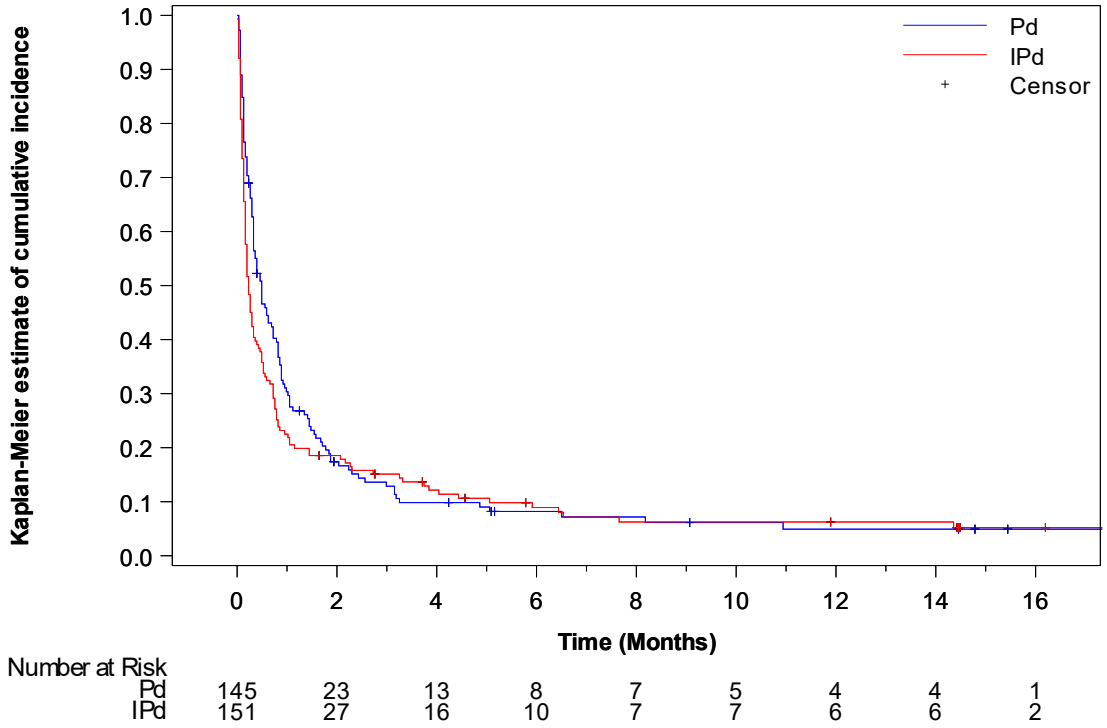
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.10 Treatment emergent mild adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1,2)	**Pd (N=149)**	**IPd (N=152)**
10 Months	0.0615 (0.0279 to 0.1137)	0.0625 (0.0293 to 0.1132)
12 Months	0.0492 (0.0191 to 0.1009)	0.0625 (0.0293 to 0.1132)
14 Months	0.0492 (0.0191 to 0.1009)	0.0625 (0.0293 to 0.1132)
16 Months	0.0492 (0.0191 to 0.1009)	0.0520 (0.0219 to 0.1017)
Number of patients at risk[b]		
2 Months	23	27
4 Months	13	16
6 Months	8	10
8 Months	7	7
10 Months	5	7
12 Months	4	6
14 Months	4	6
16 Months	1	2

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.11 Kaplan-Meier cumulative incidence curve of treatment emergent mild adverse event by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.12 Non-progression treatment emergent mild adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1,2) without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	137 (91.9)	141 (92.8)
Number (%) of patients censored	12 (8.1)	11 (7.2)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.1643 (0.1314 to 0.2628)	0.0986 (0.0657 to 0.1314)
Median (95% CI)	0.4928 (0.3285 to 0.7228)	0.2300 (0.1643 to 0.3285)
75% quantile (95% CI)	1.4456 (0.8871 to 1.8727)	0.8214 (0.6571 to 2.0698)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1456
Hazard ratio (95% CI) vs Pd	-	1.1932 (0.9403 to 1.5142)
P-value	-	0.1461
probability (95% CI)[b]		
2 Months	0.1740 (0.1167 to 0.2410)	0.1854 (0.1281 to 0.2511)
4 Months	0.0984 (0.0557 to 0.1552)	0.1215 (0.0749 to 0.1802)
6 Months	0.0820 (0.0433 to 0.1362)	0.0892 (0.0492 to 0.1439)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.12 Non-progression treatment emergent mild adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1,2) without progression events	**Pd (N=149)**	**IPd (N=152)**
8 Months	0.0717 (0.0354 to 0.1251)	0.0625 (0.0293 to 0.1132)
10 Months	0.0615 (0.0279 to 0.1137)	0.0625 (0.0293 to 0.1132)
12 Months	0.0492 (0.0191 to 0.1009)	0.0625 (0.0293 to 0.1132)
14 Months	0.0492 (0.0191 to 0.1009)	0.0625 (0.0293 to 0.1132)
16 Months	0.0492 (0.0191 to 0.1009)	0.0520 (0.0219 to 0.1017)
Number of patients at risk[b]		
2 Months	23	27
4 Months	13	16
6 Months	8	10
8 Months	7	7
10 Months	5	7
12 Months	4	6
14 Months	4	6
16 Months	1	2

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12np_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.13 Treatment emergent severe adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	103 (69.1)	129 (84.9)
Number (%) of patients censored	46 (30.9)	23 (15.1)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.5585 (0.3943 to 0.7556)	0.5257 (0.3614 to 0.5585)
Median (95% CI)	1.6756 (0.9856 to 2.9569)	0.8542 (0.7556 to 1.1499)
75% quantile (95% CI)	NC (7.0308 to NC)	3.7782 (2.1355 to 6.1766)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0021
Hazard ratio (95% CI) vs Pd	-	1.5033 (1.1575 to 1.9523)
P-value	-	0.0022
Hazard ratio inverted (95% CI) vs IPd	0.6652 (0.5122 to 0.8639)	-
probability (95% CI)[b]		
2 Months	0.4769 (0.3943 to 0.5548)	0.3405 (0.2659 to 0.4164)
4 Months	0.3815 (0.3033 to 0.4592)	0.2319 (0.1678 to 0.3024)
6 Months	0.3323 (0.2573 to 0.4089)	0.1888 (0.1302 to 0.2560)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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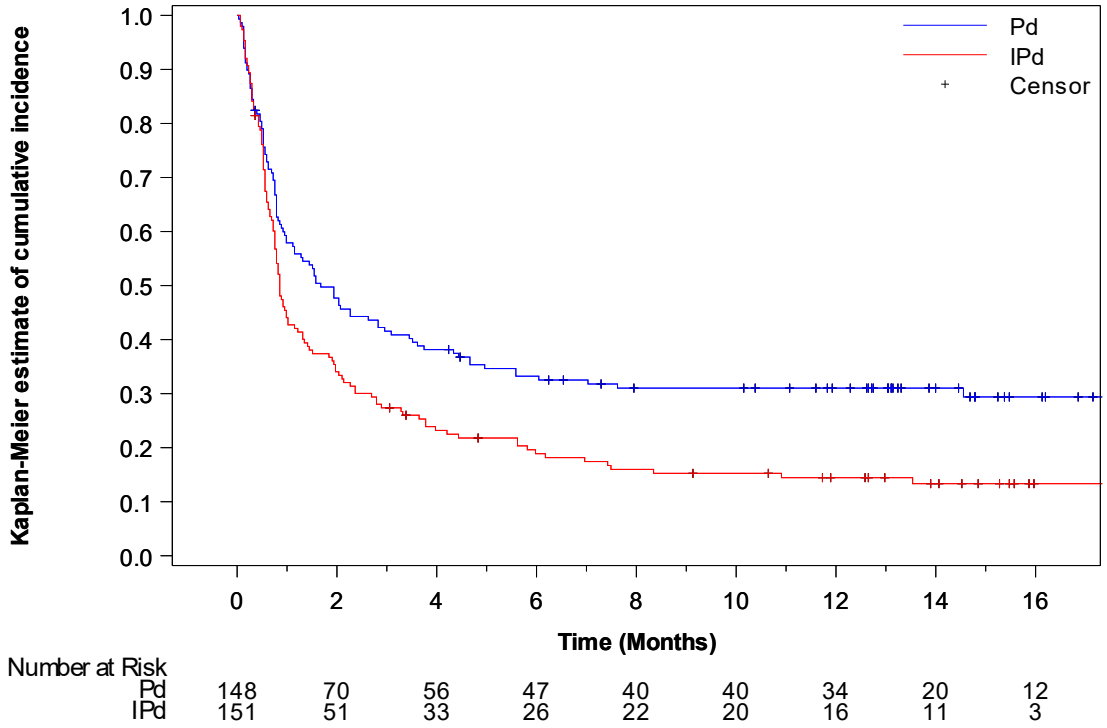
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.13 Treatment emergent severe adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4)	**Pd (N=149)**	**IPd (N=152)**
8 Months	0.3103 (0.2369 to 0.3863)	0.1598 (0.1056 to 0.2241)
10 Months	0.3103 (0.2369 to 0.3863)	0.1525 (0.0995 to 0.2160)
12 Months	0.3103 (0.2369 to 0.3863)	0.1445 (0.0928 to 0.2072)
14 Months	0.3103 (0.2369 to 0.3863)	0.1334 (0.0827 to 0.1963)
16 Months	0.2939 (0.2187 to 0.3730)	0.1334 (0.0827 to 0.1963)
Number of patients at risk[b]		
2 Months	70	51
4 Months	56	33
6 Months	47	26
8 Months	40	22
10 Months	40	20
12 Months	34	16
14 Months	20	11
16 Months	12	3

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.14 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.15 Non-progression treatment emergent severe adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4) without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	103 (69.1)	129 (84.9)
Number (%) of patients censored	46 (30.9)	23 (15.1)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.5585 (0.3943 to 0.7556)	0.5257 (0.3614 to 0.5585)
Median (95% CI)	1.6756 (0.9856 to 2.9569)	0.8542 (0.7556 to 1.1499)
75% quantile (95% CI)	NC (7.0308 to NC)	3.7782 (2.1355 to 6.9651)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0021
Hazard ratio (95% CI) vs Pd	-	1.5015 (1.1562 to 1.9499)
P-value	-	0.0023
Hazard ratio inverted (95% CI) vs IPd	0.6660 (0.5128 to 0.8649)	-
probability (95% CI)[b]		
2 Months	0.4769 (0.3943 to 0.5548)	0.3405 (0.2659 to 0.4164)
4 Months	0.3815 (0.3033 to 0.4592)	0.2319 (0.1678 to 0.3024)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34np_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.15 Non-progression treatment emergent severe adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4) without progression events	**Pd (N=149)**	**IPd (N=152)**
6 Months	0.3323 (0.2573 to 0.4089)	0.1961 (0.1364 to 0.2639)
8 Months	0.3103 (0.2369 to 0.3863)	0.1670 (0.1116 to 0.2321)
10 Months	0.3103 (0.2369 to 0.3863)	0.1598 (0.1056 to 0.2241)
12 Months	0.3103 (0.2369 to 0.3863)	0.1438 (0.0921 to 0.2066)
14 Months	0.3103 (0.2369 to 0.3863)	0.1327 (0.0821 to 0.1957)
16 Months	0.2939 (0.2187 to 0.3730)	0.1327 (0.0821 to 0.1957)
Number of patients at risk[b]		
2 Months	70	51
4 Months	56	33
6 Months	47	27
8 Months	40	23
10 Months	40	21
12 Months	34	16
14 Months	20	11
16 Months	12	3

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34np_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.16 Treatment emergent severe adverse event including death by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4,5)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	105 (70.5)	132 (86.8)
Number (%) of patients censored	44 (29.5)	20 (13.2)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.5421 (0.3285 to 0.7556)	0.5257 (0.3614 to 0.5585)
Median (95% CI)	1.6263 (0.9856 to 2.8255)	0.8542 (0.7556 to 1.1499)
75% quantile (95% CI)	NC (5.5852 to NC)	3.6468 (2.1027 to 5.9795)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0015
Hazard ratio (95% CI) vs Pd	-	1.5158 (1.1703 to 1.9633)
P-value	-	0.0016
Hazard ratio inverted (95% CI) vs IPd	0.6597 (0.5093 to 0.8545)	-
probability (95% CI)[b]		
2 Months	0.4730 (0.3908 to 0.5507)	0.3311 (0.2575 to 0.4064)
4 Months	0.3784 (0.3006 to 0.4557)	0.2241 (0.1613 to 0.2936)
6 Months	0.3233 (0.2495 to 0.3993)	0.1825 (0.1252 to 0.2484)

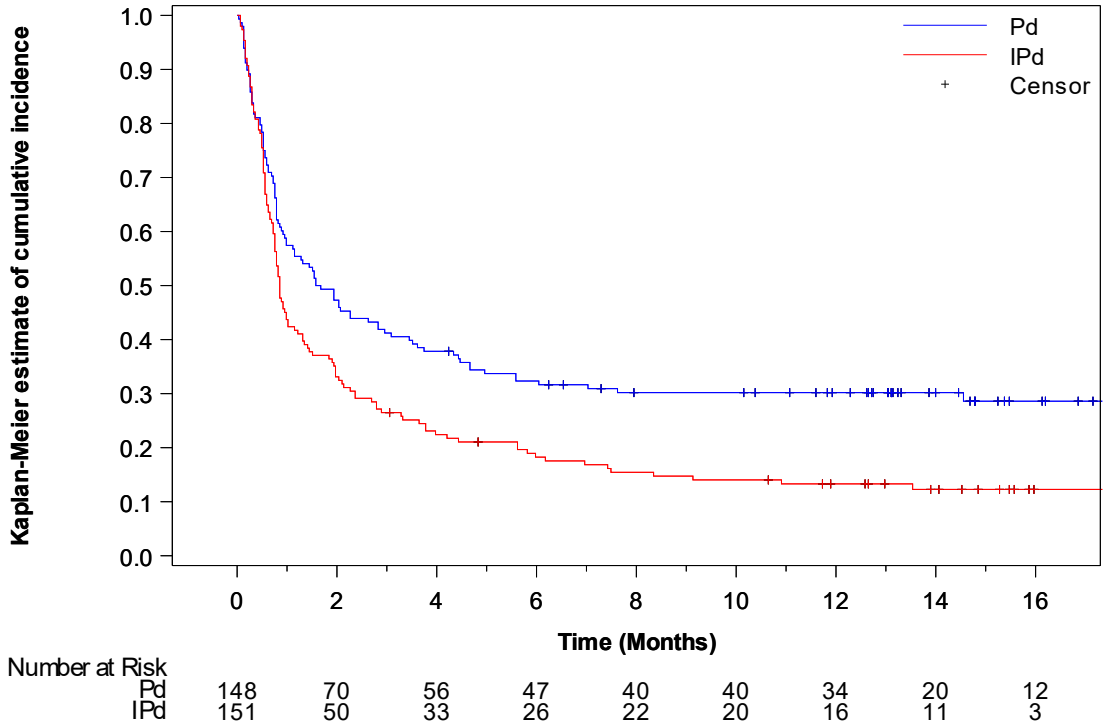
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.16 Treatment emergent severe adverse event including death by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4,5)	**Pd (N=149)**	**IPd (N=152)**
8 Months	0.3019 (0.2297 to 0.3771)	0.1544 (0.1016 to 0.2173)
10 Months	0.3019 (0.2297 to 0.3771)	0.1404 (0.0901 to 0.2016)
12 Months	0.3019 (0.2297 to 0.3771)	0.1330 (0.0840 to 0.1933)
14 Months	0.3019 (0.2297 to 0.3771)	0.1228 (0.0750 to 0.1830)
16 Months	0.2860 (0.2121 to 0.3640)	0.1228 (0.0750 to 0.1830)
Number of patients at risk[b]		
2 Months	70	50
4 Months	56	33
6 Months	47	26
8 Months	40	22
10 Months	40	20
12 Months	34	16
14 Months	20	11
16 Months	12	3

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.17 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.18 Non-progression treatment emergent severe adverse event including death by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4,5) without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	105 (70.5)	132 (86.8)
Number (%) of patients censored	44 (29.5)	20 (13.2)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.5421 (0.3285 to 0.7556)	0.5257 (0.3614 to 0.5585)
Median (95% CI)	1.6263 (0.9856 to 2.8255)	0.8542 (0.7556 to 1.1499)
75% quantile (95% CI)	NC (5.5852 to NC)	3.6468 (2.1027 to 6.1766)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0016
Hazard ratio (95% CI) vs Pd	-	1.5138 (1.1688 to 1.9606)
P-value	-	0.0017
Hazard ratio inverted (95% CI) vs IPd	0.6606 (0.5100 to 0.8556)	-
probability (95% CI)[b]		
2 Months	0.4730 (0.3908 to 0.5507)	0.3311 (0.2575 to 0.4064)
4 Months	0.3784 (0.3006 to 0.4557)	0.2241 (0.1613 to 0.2936)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345np_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.18 Non-progression treatment emergent severe adverse event including death by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4,5) without progression events	**Pd (N=149)**	**IPd (N=152)**
6 Months	0.3233 (0.2495 to 0.3993)	0.1895 (0.1312 to 0.2561)
8 Months	0.3019 (0.2297 to 0.3771)	0.1614 (0.1075 to 0.2252)
10 Months	0.3019 (0.2297 to 0.3771)	0.1474 (0.0958 to 0.2095)
12 Months	0.3019 (0.2297 to 0.3771)	0.1327 (0.0837 to 0.1930)
14 Months	0.3019 (0.2297 to 0.3771)	0.1224 (0.0747 to 0.1827)
16 Months	0.2860 (0.2121 to 0.3640)	0.1224 (0.0747 to 0.1827)
Number of patients at risk[b]		
2 Months	70	50
4 Months	56	33
6 Months	47	27
8 Months	40	23
10 Months	40	21
12 Months	34	16
14 Months	20	11
16 Months	12	3

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345np_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.19 Treatment emergent mild (grade 1) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	110 (73.8)	114 (75.0)
Number (%) of patients censored	39 (26.2)	38 (25.0)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.2957 (0.1314 to 0.3943)	0.2957 (0.2300 to 0.4600)
Median (95% CI)	0.8871 (0.7228 to 1.7741)	1.0513 (0.7228 to 2.0370)
75% quantile (95% CI)	9.0678 (3.2197 to NC)	8.3778 (3.7454 to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.8360
Hazard ratio (95% CI) vs Pd	-	0.9725 (0.7469 to 1.2662)
P-value	-	0.8359
probability (95% CI)[b]		
2 Months	0.3898 (0.3101 to 0.4686)	0.4268 (0.3473 to 0.5038)
4 Months	0.2993 (0.2255 to 0.3763)	0.3227 (0.2492 to 0.3984)
6 Months	0.2902 (0.2170 to 0.3672)	0.2685 (0.1988 to 0.3428)
8 Months	0.2702 (0.1979 to 0.3474)	0.2598 (0.1908 to 0.3340)

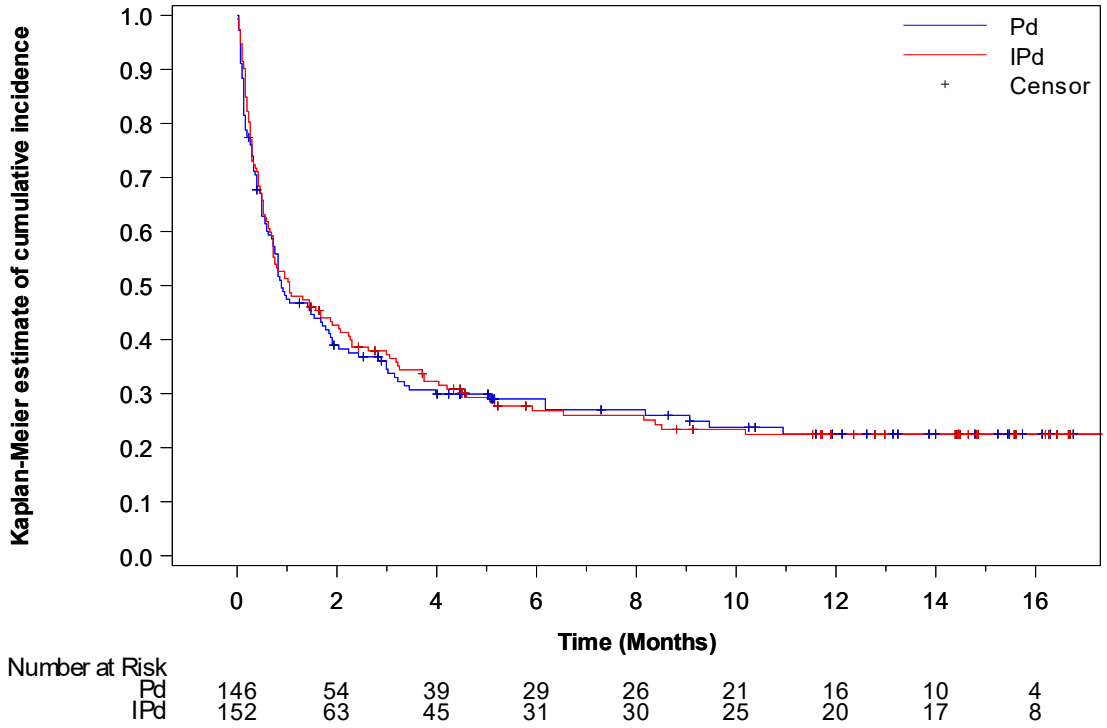
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.19 Treatment emergent mild (grade 1) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1)	**Pd (N=149)**	**IPd (N=152)**
10 Months	0.2376 (0.1671 to 0.3153)	0.2338 (0.1671 to 0.3072)
12 Months	0.2251 (0.1552 to 0.3033)	0.2245 (0.1585 to 0.2977)
14 Months	0.2251 (0.1552 to 0.3033)	0.2245 (0.1585 to 0.2977)
16 Months	0.2251 (0.1552 to 0.3033)	0.2245 (0.1585 to 0.2977)
Number of patients at risk[b]		
2 Months	54	63
4 Months	39	45
6 Months	29	31
8 Months	26	30
10 Months	21	25
12 Months	16	20
14 Months	10	17
16 Months	4	8

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.20 Kaplan-Meier cumulative incidence curve of treatment emergent mild (grade 1) adverse event by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.21 Non-progression treatment emergent mild (grade 1) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1) without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	110 (73.8)	114 (75.0)
Number (%) of patients censored	39 (26.2)	38 (25.0)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.2957 (0.1314 to 0.3943)	0.2957 (0.2300 to 0.4600)
Median (95% CI)	0.8871 (0.7228 to 1.7741)	1.0513 (0.7228 to 2.0370)
75% quantile (95% CI)	9.0678 (3.2197 to NC)	8.3778 (3.7454 to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.8360
Hazard ratio (95% CI) vs Pd	-	0.9725 (0.7469 to 1.2662)
P-value	-	0.8359
probability (95% CI)[b]		
2 Months	0.3898 (0.3101 to 0.4686)	0.4268 (0.3473 to 0.5038)
4 Months	0.2993 (0.2255 to 0.3763)	0.3227 (0.2492 to 0.3984)
6 Months	0.2902 (0.2170 to 0.3672)	0.2685 (0.1988 to 0.3428)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.21 Non-progression treatment emergent mild (grade 1) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1) without progression events	**Pd (N=149)**	**IPd (N=152)**
8 Months	0.2702 (0.1979 to 0.3474)	0.2598 (0.1908 to 0.3340)
10 Months	0.2376 (0.1671 to 0.3153)	0.2338 (0.1671 to 0.3072)
12 Months	0.2251 (0.1552 to 0.3033)	0.2245 (0.1585 to 0.2977)
14 Months	0.2251 (0.1552 to 0.3033)	0.2245 (0.1585 to 0.2977)
16 Months	0.2251 (0.1552 to 0.3033)	0.2245 (0.1585 to 0.2977)
Number of patients at risk[b]		
2 Months	54	63
4 Months	39	45
6 Months	29	31
8 Months	26	30
10 Months	21	25
12 Months	16	20
14 Months	10	17
16 Months	4	8

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev1np_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.22 Treatment emergent moderate (grade 2) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 2)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	119 (79.9)	134 (88.2)
Number (%) of patients censored	30 (20.1)	18 (11.8)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.4928 (0.3285 to 0.7228)	0.1314 (0.0986 to 0.1643)
Median (95% CI)	1.6427 (1.0513 to 2.0698)	0.5257 (0.2628 to 0.7885)
75% quantile (95% CI)	4.2710 (2.8255 to 7.8193)	2.5955 (1.4456 to 4.5339)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0015
Hazard ratio (95% CI) vs Pd	-	1.4930 (1.1633 to 1.9161)
P-value	-	0.0016
Hazard ratio inverted (95% CI) vs IPd	0.6698 (0.5219 to 0.8596)	-
probability (95% CI)[b]		
2 Months	0.4539 (0.3705 to 0.5334)	0.2979 (0.2270 to 0.3718)
4 Months	0.2556 (0.1863 to 0.3304)	0.2016 (0.1415 to 0.2695)
6 Months	0.2068 (0.1430 to 0.2788)	0.1564 (0.1026 to 0.2206)

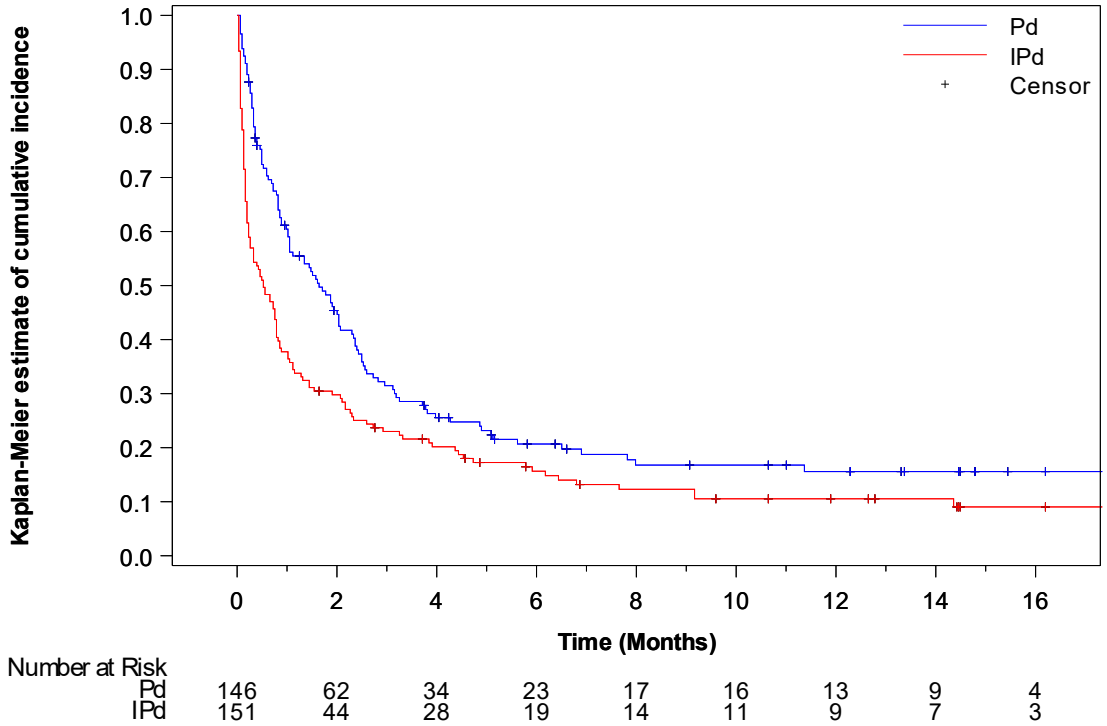
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev2_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.22 Treatment emergent moderate (grade 2) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 2)	**Pd (N=149)**	**IPd (N=152)**
8 Months	0.1678 (0.1085 to 0.2382)	0.1230 (0.0746 to 0.1840)
10 Months	0.1678 (0.1085 to 0.2382)	0.1054 (0.0605 to 0.1645)
12 Months	0.1558 (0.0977 to 0.2262)	0.1054 (0.0605 to 0.1645)
14 Months	0.1558 (0.0977 to 0.2262)	0.1054 (0.0605 to 0.1645)
16 Months	0.1558 (0.0977 to 0.2262)	0.0903 (0.0468 to 0.1514)
Number of patients at risk[b]		
2 Months	62	44
4 Months	34	28
6 Months	23	19
8 Months	17	14
10 Months	16	11
12 Months	13	9
14 Months	9	7
16 Months	4	3

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.23 Kaplan-Meier cumulative incidence curve of treatment emergent moderate (grade 2) adverse event by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.24 Non-progression treatment emergent moderate (grade 2) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 2) without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	119 (79.9)	134 (88.2)
Number (%) of patients censored	30 (20.1)	18 (11.8)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.4928 (0.3285 to 0.7228)	0.1314 (0.0986 to 0.1643)
Median (95% CI)	1.6427 (1.0513 to 2.0698)	0.5257 (0.2628 to 0.7885)
75% quantile (95% CI)	4.2710 (2.8255 to 7.8193)	2.5955 (1.4456 to 4.5339)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0015
Hazard ratio (95% CI) vs Pd	-	1.4930 (1.1633 to 1.9161)
P-value	-	0.0016
Hazard ratio inverted (95% CI) vs IPd	0.6698 (0.5219 to 0.8596)	-
probability (95% CI)[b]		
2 Months	0.4539 (0.3705 to 0.5334)	0.2979 (0.2270 to 0.3718)
4 Months	0.2556 (0.1863 to 0.3304)	0.2016 (0.1415 to 0.2695)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev2np_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.24 Non-progression treatment emergent moderate (grade 2) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 2) without progression events	**Pd (N=149)**	**IPd (N=152)**
6 Months	0.2068 (0.1430 to 0.2788)	0.1564 (0.1026 to 0.2206)
8 Months	0.1678 (0.1085 to 0.2382)	0.1230 (0.0746 to 0.1840)
10 Months	0.1678 (0.1085 to 0.2382)	0.1054 (0.0605 to 0.1645)
12 Months	0.1558 (0.0977 to 0.2262)	0.1054 (0.0605 to 0.1645)
14 Months	0.1558 (0.0977 to 0.2262)	0.1054 (0.0605 to 0.1645)
16 Months	0.1558 (0.0977 to 0.2262)	0.0903 (0.0468 to 0.1514)
Number of patients at risk[b]		
2 Months	62	44
4 Months	34	28
6 Months	23	19
8 Months	17	14
10 Months	16	11
12 Months	13	9
14 Months	9	7
16 Months	4	3

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev2np_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.25 Treatment emergent severe (grade 3) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	86 (57.7)	116 (76.3)
Number (%) of patients censored	63 (42.3)	36 (23.7)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.7885 (0.5585 to 1.1499)	0.7556 (0.4928 to 1.0842)
Median (95% CI)	3.7454 (2.0370 to 12.9774)	2.1355 (1.7084 to 3.1540)
75% quantile (95% CI)	NC (NC to NC)	9.5934 (5.8152 to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0069
Hazard ratio (95% CI) vs Pd	-	1.4670 (1.1088 to 1.9410)
P-value	-	0.0073
Hazard ratio inverted (95% CI) vs IPd	0.6817 (0.5152 to 0.9019)	-
probability (95% CI)[b]		
2 Months	0.5861 (0.5021 to 0.6607)	0.5206 (0.4378 to 0.5969)
4 Months	0.4966 (0.4133 to 0.5743)	0.3703 (0.2930 to 0.4475)
6 Months	0.4454 (0.3632 to 0.5242)	0.3118 (0.2384 to 0.3879)

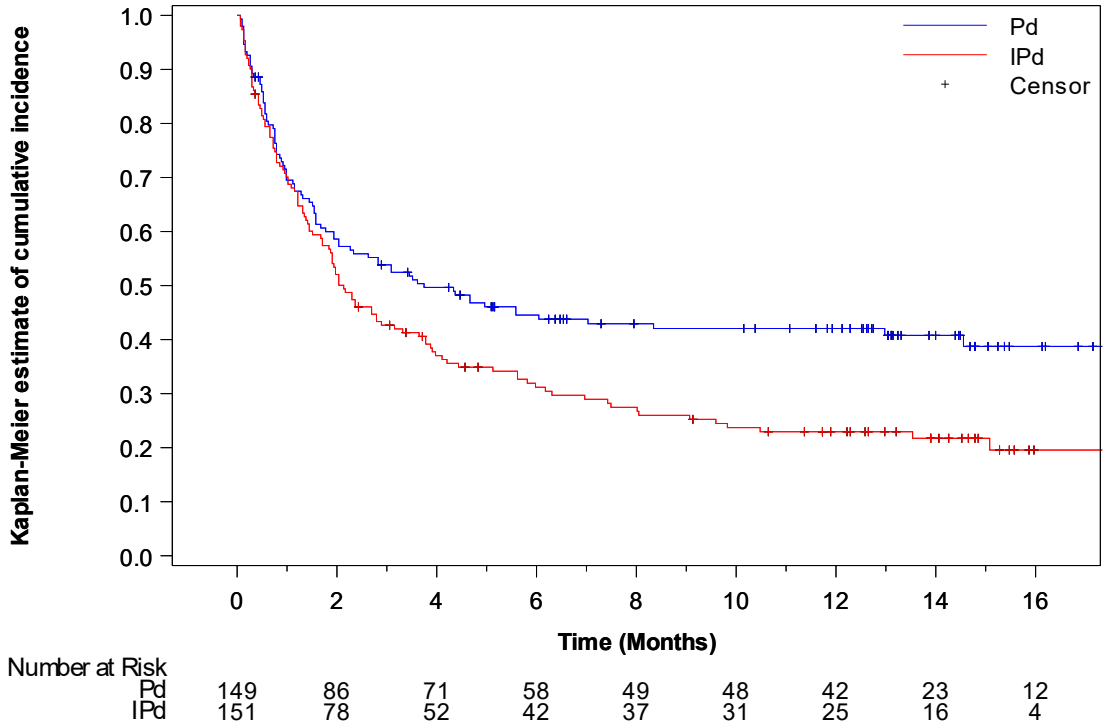
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.25 Treatment emergent severe (grade 3) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3)	**Pd (N=149)**	**IPd (N=152)**
8 Months	0.4293 (0.3474 to 0.5085)	0.2747 (0.2044 to 0.3493)
10 Months	0.4206 (0.3387 to 0.5001)	0.2371 (0.1708 to 0.3098)
12 Months	0.4206 (0.3387 to 0.5001)	0.2295 (0.1640 to 0.3017)
14 Months	0.4078 (0.3250 to 0.4888)	0.2174 (0.1522 to 0.2903)
16 Months	0.3874 (0.3002 to 0.4737)	0.1957 (0.1273 to 0.2749)
Number of patients at risk[b]		
2 Months	86	78
4 Months	71	52
6 Months	58	42
8 Months	49	37
10 Months	48	31
12 Months	42	25
14 Months	23	16
16 Months	12	4

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.26 Kaplan-Meier cumulative incidence curve of treatment emergent severe (grade 3) adverse event by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.27 Non-progression treatment emergent severe (grade 3) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3) without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	86 (57.7)	116 (76.3)
Number (%) of patients censored	63 (42.3)	36 (23.7)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.7885 (0.5585 to 1.1499)	0.7556 (0.4928 to 1.0842)
Median (95% CI)	3.7454 (2.0370 to 12.9774)	2.1355 (1.7084 to 3.1540)
75% quantile (95% CI)	NC (NC to NC)	9.8234 (5.9795 to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0072
Hazard ratio (95% CI) vs Pd	-	1.4650 (1.1073 to 1.9383)
P-value	-	0.0075
Hazard ratio inverted (95% CI) vs IPd	0.6826 (0.5159 to 0.9031)	-
probability (95% CI)[b]		
2 Months	0.5861 (0.5021 to 0.6607)	0.5206 (0.4378 to 0.5969)
4 Months	0.4966 (0.4133 to 0.5743)	0.3703 (0.2930 to 0.4475)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.27 Non-progression treatment emergent severe (grade 3) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3) without progression events	**Pd (N=149)**	**IPd (N=152)**
6 Months	0.4454 (0.3632 to 0.5242)	0.3192 (0.2452 to 0.3955)
8 Months	0.4293 (0.3474 to 0.5085)	0.2821 (0.2112 to 0.3571)
10 Months	0.4206 (0.3387 to 0.5001)	0.2446 (0.1774 to 0.3177)
12 Months	0.4206 (0.3387 to 0.5001)	0.2290 (0.1635 to 0.3013)
14 Months	0.4078 (0.3250 to 0.4888)	0.2170 (0.1517 to 0.2899)
16 Months	0.3874 (0.3002 to 0.4737)	0.1953 (0.1270 to 0.2745)
Number of patients at risk[b]		
2 Months	86	78
4 Months	71	52
6 Months	58	43
8 Months	49	38
10 Months	48	32
12 Months	42	25
14 Months	23	16
16 Months	12	4

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev3np_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.28 Treatment emergent severe (grade 4) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 4)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	47 (31.5)	66 (43.4)
Number (%) of patients censored	102 (68.5)	86 (56.6)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	2.8255 (0.8542 to 7.6222)	0.7556 (0.5914 to 0.8542)
Median (95% CI)	NC (NC to NC)	NC (7.7207 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0319
Hazard ratio (95% CI) vs Pd	-	1.5083 (1.0336 to 2.2010)
P-value	-	0.0331
Hazard ratio inverted (95% CI) vs IPd	0.6630 (0.4543 to 0.9675)	-
probability (95% CI)[b]		
2 Months	0.7672 (0.6899 to 0.8277)	0.6402 (0.5579 to 0.7112)
4 Months	0.7243 (0.6437 to 0.7897)	0.5993 (0.5162 to 0.6728)
6 Months	0.6943 (0.6117 to 0.7628)	0.5993 (0.5162 to 0.6728)

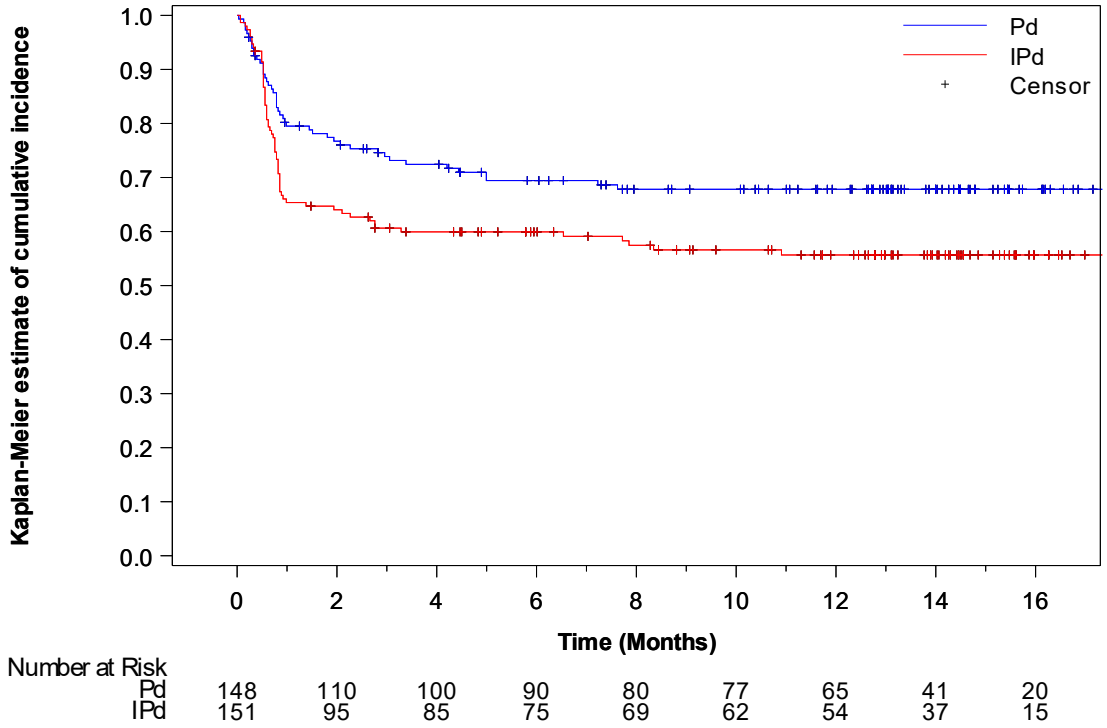
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev4_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.28 Treatment emergent severe (grade 4) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 4)	**Pd (N=149)**	**IPd (N=152)**
8 Months	0.6782 (0.5944 to 0.7484)	0.5745 (0.4902 to 0.6499)
10 Months	0.6782 (0.5944 to 0.7484)	0.5660 (0.4814 to 0.6421)
12 Months	0.6782 (0.5944 to 0.7484)	0.5566 (0.4714 to 0.6335)
14 Months	0.6782 (0.5944 to 0.7484)	0.5566 (0.4714 to 0.6335)
16 Months	0.6782 (0.5944 to 0.7484)	0.5566 (0.4714 to 0.6335)
Number of patients at risk[b]		
2 Months	110	95
4 Months	100	85
6 Months	90	75
8 Months	80	69
10 Months	77	62
12 Months	65	54
14 Months	41	37
16 Months	20	15

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.29 Kaplan-Meier cumulative incidence curve of treatment emergent severe (grade 4) adverse event by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.30 Non-progression treatment emergent severe (grade 4) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 4) without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	47 (31.5)	66 (43.4)
Number (%) of patients censored	102 (68.5)	86 (56.6)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	2.8255 (0.8542 to 7.6222)	0.7556 (0.5914 to 0.8542)
Median (95% CI)	NC (NC to NC)	NC (7.7207 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0319
Hazard ratio (95% CI) vs Pd	-	1.5083 (1.0336 to 2.2010)
P-value	-	0.0331
Hazard ratio inverted (95% CI) vs IPd	0.6630 (0.4543 to 0.9675)	-
probability (95% CI)[b]		
2 Months	0.7672 (0.6899 to 0.8277)	0.6402 (0.5579 to 0.7112)
4 Months	0.7243 (0.6437 to 0.7897)	0.5993 (0.5162 to 0.6728)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev4np_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.30 Non-progression treatment emergent severe (grade 4) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 4) without progression events	**Pd (N=149)**	**IPd (N=152)**
6 Months	0.6943 (0.6117 to 0.7628)	0.5993 (0.5162 to 0.6728)
8 Months	0.6782 (0.5944 to 0.7484)	0.5745 (0.4902 to 0.6499)
10 Months	0.6782 (0.5944 to 0.7484)	0.5660 (0.4814 to 0.6421)
12 Months	0.6782 (0.5944 to 0.7484)	0.5566 (0.4714 to 0.6335)
14 Months	0.6782 (0.5944 to 0.7484)	0.5566 (0.4714 to 0.6335)
16 Months	0.6782 (0.5944 to 0.7484)	0.5566 (0.4714 to 0.6335)
Number of patients at risk[b]		
2 Months	110	95
4 Months	100	85
6 Months	90	75
8 Months	80	69
10 Months	77	62
12 Months	65	54
14 Months	41	37
16 Months	20	15

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev4np_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.31 Treatment emergent severe (grade 5) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 5)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	14 (9.4)	12 (7.9)
Number (%) of patients censored	135 (90.6)	140 (92.1)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.5706
Hazard ratio (95% CI) vs Pd	-	0.8004 (0.3701 to 1.7308)
P-value	-	0.5715
probability (95% CI)[b]		
2 Months	0.9530 (0.9040 to 0.9773)	0.9671 (0.9228 to 0.9862)
4 Months	0.9322 (0.8776 to 0.9629)	0.9605 (0.9142 to 0.9820)
6 Months	0.9106 (0.8510 to 0.9471)	0.9331 (0.8793 to 0.9635)
8 Months	0.9106 (0.8510 to 0.9471)	0.9257 (0.8698 to 0.9582)

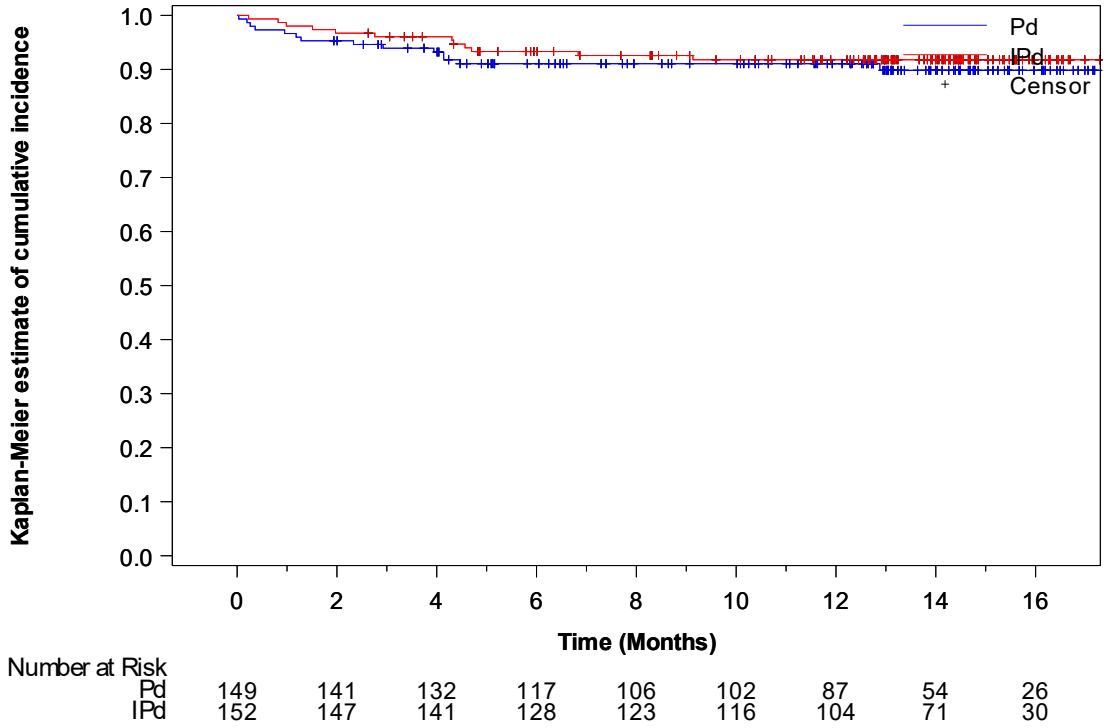
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev5_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.31 Treatment emergent severe (grade 5) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 5)	**Pd (N=149)**	**IPd (N=152)**
10 Months	0.9106 (0.8510 to 0.9471)	0.9179 (0.8597 to 0.9526)
12 Months	0.9106 (0.8510 to 0.9471)	0.9179 (0.8597 to 0.9526)
14 Months	0.8983 (0.8325 to 0.9392)	0.9179 (0.8597 to 0.9526)
16 Months	0.8983 (0.8325 to 0.9392)	0.9179 (0.8597 to 0.9526)
Number of patients at risk[b]		
2 Months	141	147
4 Months	132	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	30

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.32 Kaplan-Meier cumulative incidence curve of treatment emergent severe (grade 5) adverse event by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.33 Non-progression treatment emergent severe (grade 5) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 5) without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	14 (9.4)	12 (7.9)
Number (%) of patients censored	135 (90.6)	140 (92.1)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.5706
Hazard ratio (95% CI) vs Pd	-	0.8004 (0.3701 to 1.7308)
P-value	-	0.5715
probability (95% CI)[b]		
2 Months	0.9530 (0.9040 to 0.9773)	0.9671 (0.9228 to 0.9862)
4 Months	0.9322 (0.8776 to 0.9629)	0.9605 (0.9142 to 0.9820)
6 Months	0.9106 (0.8510 to 0.9471)	0.9331 (0.8793 to 0.9635)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev5np_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.33 Non-progression treatment emergent severe (grade 5) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 5) without progression events	**Pd (N=149)**	**IPd (N=152)**
8 Months	0.9106 (0.8510 to 0.9471)	0.9257 (0.8698 to 0.9582)
10 Months	0.9106 (0.8510 to 0.9471)	0.9179 (0.8597 to 0.9526)
12 Months	0.9106 (0.8510 to 0.9471)	0.9179 (0.8597 to 0.9526)
14 Months	0.8983 (0.8325 to 0.9392)	0.9179 (0.8597 to 0.9526)
16 Months	0.8983 (0.8325 to 0.9392)	0.9179 (0.8597 to 0.9526)
Number of patients at risk[b]		
2 Months	141	147
4 Months	132	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	30

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev5np_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.34 Treatment emergent adverse event of interest by treatment group - Safety population

Any treatment emergent AESI	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	1 (0.7)	10 (6.6)
Number (%) of patients censored	148 (99.3)	142 (93.4)
Kaplan-Meier estimates of AESI in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0086
Hazard ratio (95% CI) vs Pd	-	9.4935 (1.2151 to 74.1716)
P-value	-	0.0319
Hazard ratio inverted (95% CI) vs IPd	0.1053 (0.0135 to 0.8230)	-
probability (95% CI)[b]		
2 Months	1.0000 (1.0000 to 1.0000)	0.9671 (0.9227 to 0.9862)
4 Months	1.0000 (1.0000 to 1.0000)	0.9602 (0.9135 to 0.9819)

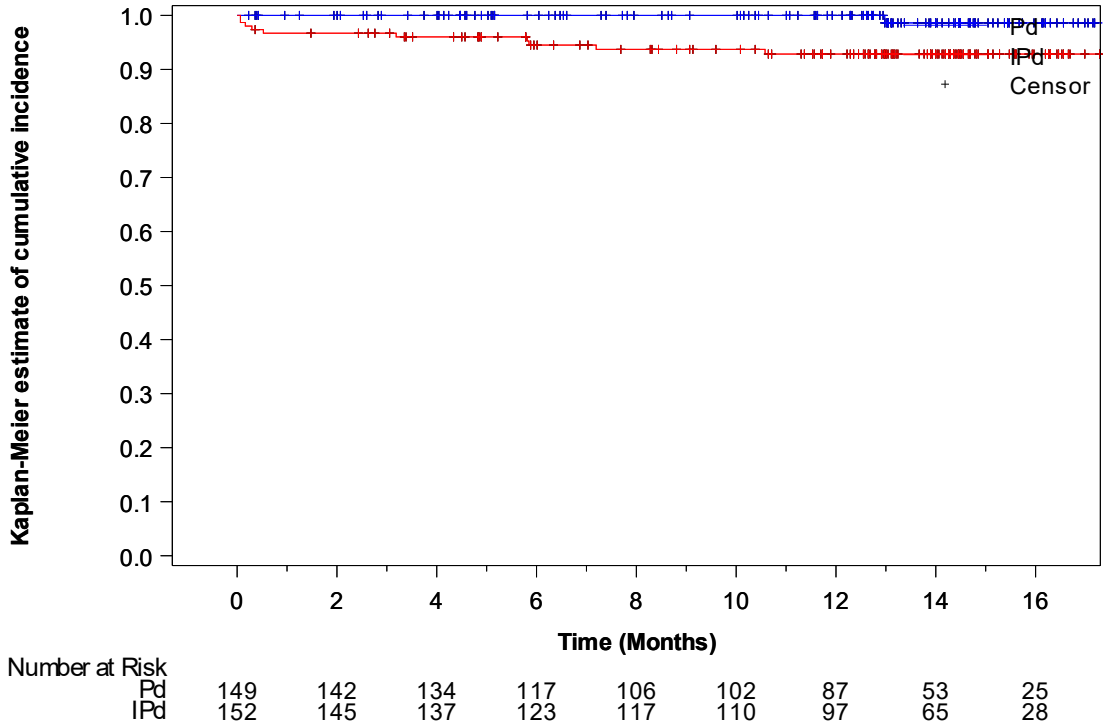
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tsiae_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.34 Treatment emergent adverse event of interest by treatment group - Safety population

Any treatment emergent AESI	**Pd (N=149)**	**IPd (N=152)**
6 Months	1.0000 (1.0000 to 1.0000)	0.9451 (0.8930 to 0.9722)
8 Months	1.0000 (1.0000 to 1.0000)	0.9371 (0.8824 to 0.9669)
10 Months	1.0000 (1.0000 to 1.0000)	0.9371 (0.8824 to 0.9669)
12 Months	1.0000 (1.0000 to 1.0000)	0.9285 (0.8706 to 0.9610)
14 Months	0.9861 (0.9055 to 0.9980)	0.9285 (0.8706 to 0.9610)
16 Months	0.9861 (0.9055 to 0.9980)	0.9285 (0.8706 to 0.9610)
Number of patients at risk[b]		
2 Months	142	145
4 Months	134	137
6 Months	117	123
8 Months	106	117
10 Months	102	110
12 Months	87	97
14 Months	53	65
16 Months	25	28

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tsiae_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.35 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event of interest by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.36 Treatment emergent serious adverse event of interest by treatment group - Safety population

Any serious treatment emergent AESI	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	0 (0.0)	8 (5.3)
Number (%) of patients censored	149 (100.0)	144 (94.7)
Kaplan-Meier estimates of AESI in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0054
Hazard ratio (95% CI) vs Pd	-	. (. to .)
P-value	-	0.9929
probability (95% CI)[b]		
2 Months	1.0000 (1.0000 to 1.0000)	0.9671 (0.9227 to 0.9862)
4 Months	1.0000 (1.0000 to 1.0000)	0.9602 (0.9135 to 0.9819)
6 Months	1.0000 (1.0000 to 1.0000)	0.9526 (0.9031 to 0.9772)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
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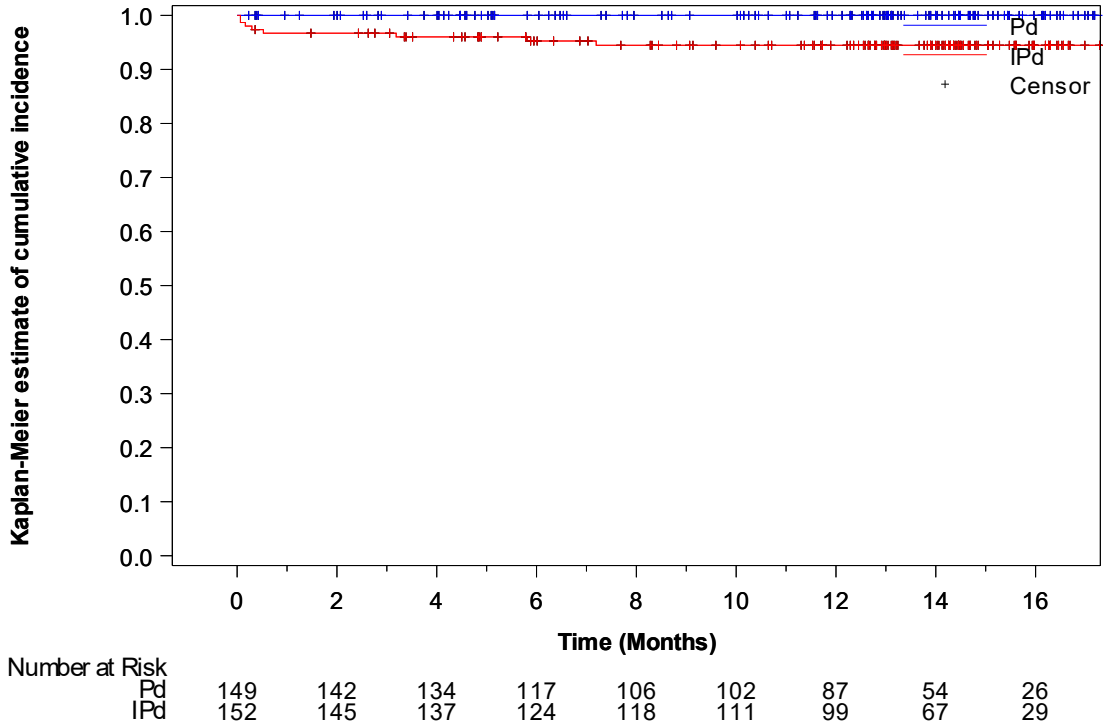
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.36 Treatment emergent serious adverse event of interest by treatment group - Safety population

Any serious treatment emergent AESI	**Pd (N=149)**	**IPd (N=152)**
8 Months	1.0000 (1.0000 to 1.0000)	0.9447 (0.8922 to 0.9720)
10 Months	1.0000 (1.0000 to 1.0000)	0.9447 (0.8922 to 0.9720)
12 Months	1.0000 (1.0000 to 1.0000)	0.9447 (0.8922 to 0.9720)
14 Months	1.0000 (1.0000 to 1.0000)	0.9447 (0.8922 to 0.9720)
16 Months	1.0000 (1.0000 to 1.0000)	0.9447 (0.8922 to 0.9720)
Number of patients at risk[b]		
2 Months	142	145
4 Months	134	137
6 Months	117	124
8 Months	106	118
10 Months	102	111
12 Months	87	99
14 Months	54	67
16 Months	26	29

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tsiser_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.37 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event of interest by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.38 Treatment emergent severe (grade 3,4) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 3,4)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	0 (0.0)	8 (5.3)
Number (%) of patients censored	149 (100.0)	144 (94.7)
Kaplan-Meier estimates of AESI in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0056
Hazard ratio (95% CI) vs Pd	-	. (. to .)
P-value	-	0.9929
probability (95% CI)[b]		
2 Months	1.0000 (1.0000 to 1.0000)	0.9671 (0.9227 to 0.9862)
4 Months	1.0000 (1.0000 to 1.0000)	0.9671 (0.9227 to 0.9862)
6 Months	1.0000 (1.0000 to 1.0000)	0.9594 (0.9118 to 0.9816)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
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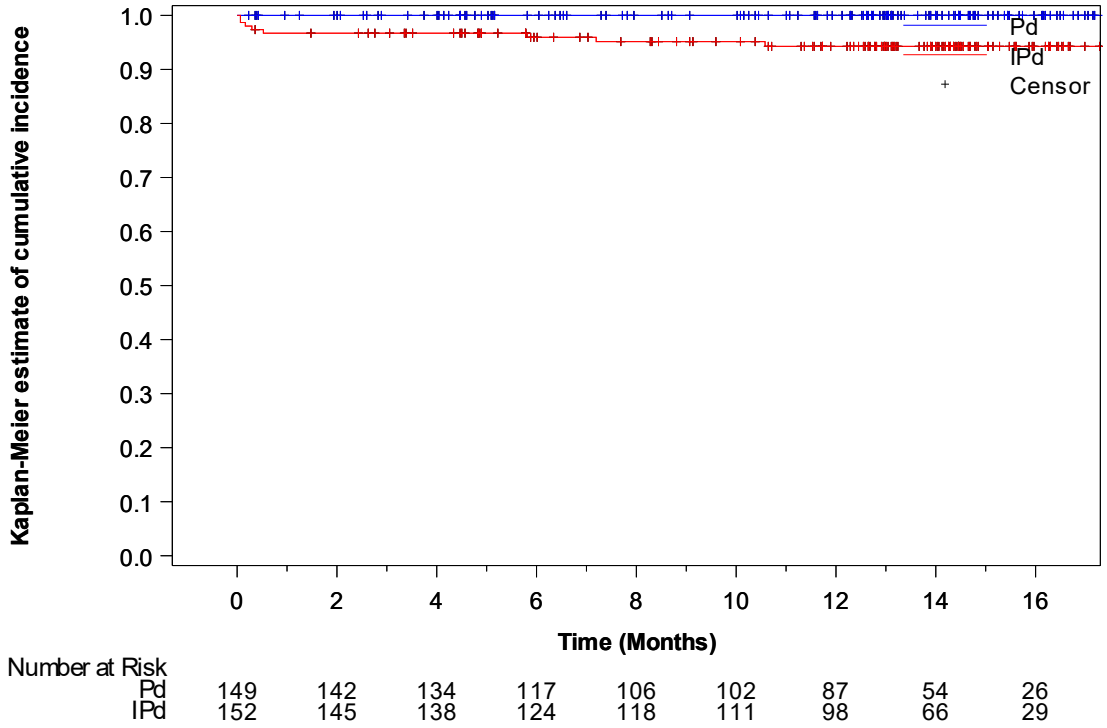
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.38 Treatment emergent severe (grade 3,4) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 3,4)	**Pd (N=149)**	**IPd (N=152)**
8 Months	1.0000 (1.0000 to 1.0000)	0.9515 (0.9006 to 0.9766)
10 Months	1.0000 (1.0000 to 1.0000)	0.9515 (0.9006 to 0.9766)
12 Months	1.0000 (1.0000 to 1.0000)	0.9427 (0.8882 to 0.9711)
14 Months	1.0000 (1.0000 to 1.0000)	0.9427 (0.8882 to 0.9711)
16 Months	1.0000 (1.0000 to 1.0000)	0.9427 (0.8882 to 0.9711)
Number of patients at risk[b]		
2 Months	142	145
4 Months	134	138
6 Months	117	124
8 Months	106	118
10 Months	102	111
12 Months	87	98
14 Months	54	66
16 Months	26	29

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tsisv34_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.39 Kaplan-Meier cumulative incidence curve of treatment emergent severe (grade 3,4) adverse event of interest by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.40 Treatment emergent not severe (grade 1) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 1)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	0 (0.0)	0 (0.0)
Number (%) of patients censored	149 (100.0)	152 (100.0)
Kaplan-Meier estimates of AESI in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Hazard ratio (95% CI) vs Pd	-	. (. to .)
probability (95% CI)[b]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)

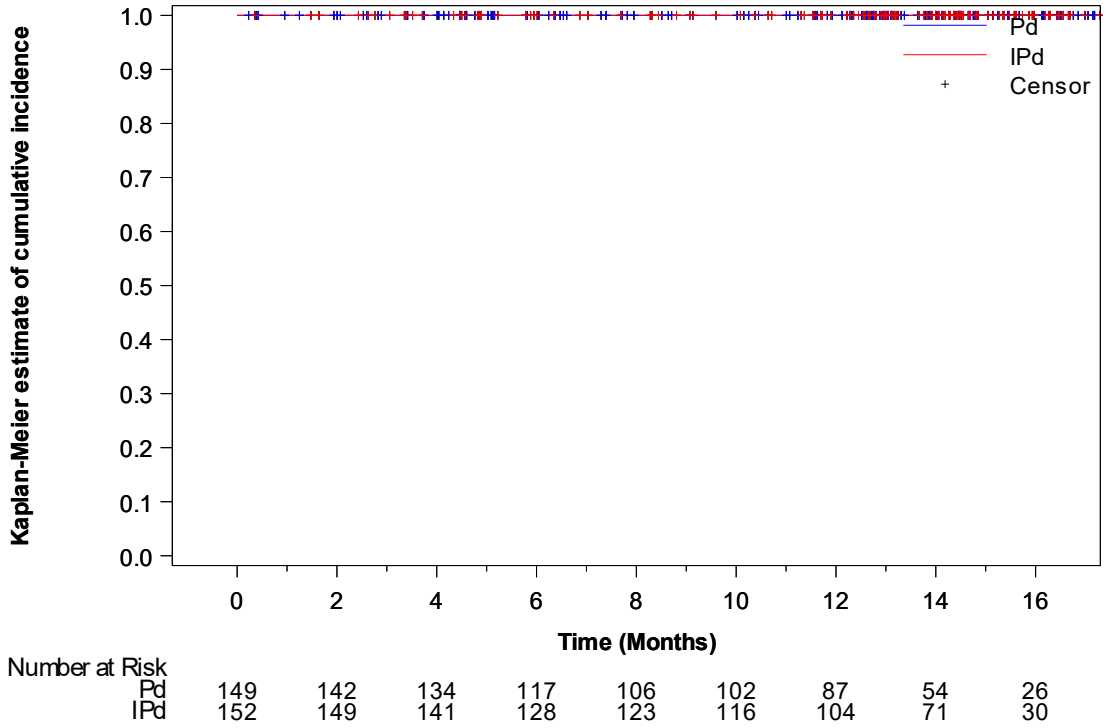
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tsisv1_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.40 Treatment emergent not severe (grade 1) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 1)	**Pd (N=149)**	**IPd (N=152)**
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	30

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tsisv1_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.41 Kaplan-Meier cumulative incidence curve of treatment emergent not severe (grade 1) adverse event of interest by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.42 Treatment emergent not severe (grade 2) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 2)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	1 (0.7)	3 (2.0)
Number (%) of patients censored	148 (99.3)	149 (98.0)
Kaplan-Meier estimates of AESI in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3735
Hazard ratio (95% CI) vs Pd	-	2.6837 (0.2790 to 25.8117)
P-value	-	0.3927
probability (95% CI)[b]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	0.9931 (0.9521 to 0.9990)
6 Months	1.0000 (1.0000 to 1.0000)	0.9778 (0.9327 to 0.9928)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
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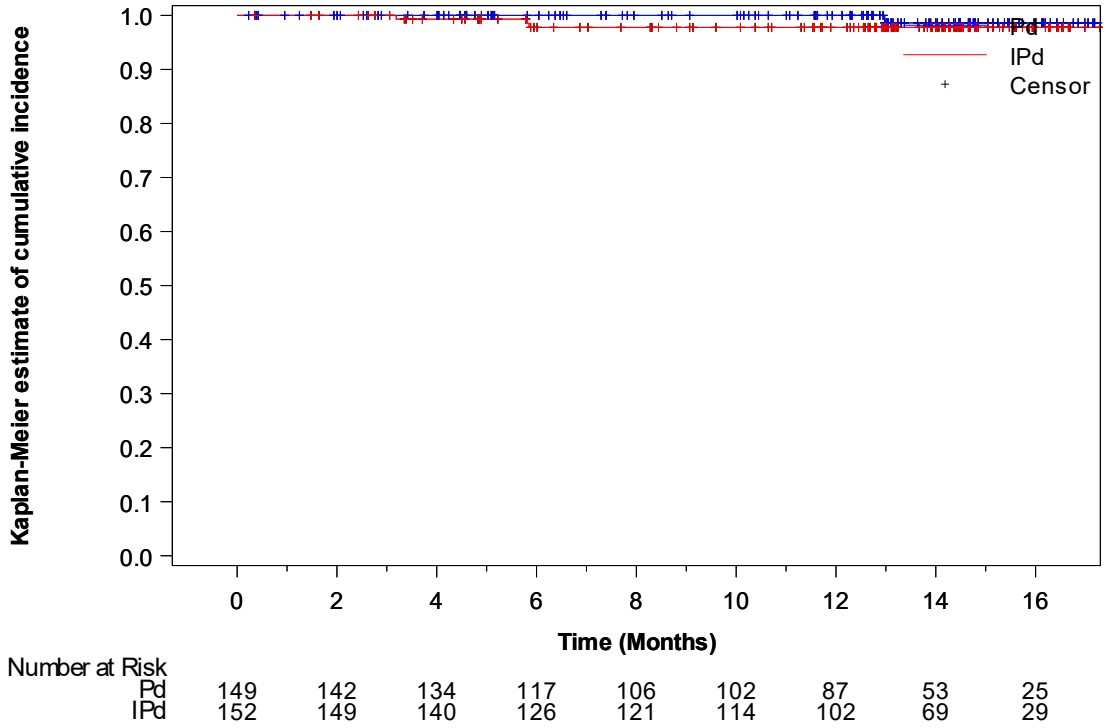
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.42 Treatment emergent not severe (grade 2) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 2)	**Pd (N=149)**	**IPd (N=152)**
8 Months	1.0000 (1.0000 to 1.0000)	0.9778 (0.9327 to 0.9928)
10 Months	1.0000 (1.0000 to 1.0000)	0.9778 (0.9327 to 0.9928)
12 Months	1.0000 (1.0000 to 1.0000)	0.9778 (0.9327 to 0.9928)
14 Months	0.9861 (0.9055 to 0.9980)	0.9778 (0.9327 to 0.9928)
16 Months	0.9861 (0.9055 to 0.9980)	0.9778 (0.9327 to 0.9928)
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	140
6 Months	117	126
8 Months	106	121
10 Months	102	114
12 Months	87	102
14 Months	53	69
16 Months	25	29

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tsisv2_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.43 Kaplan-Meier cumulative incidence curve of treatment emergent not severe (grade 2) adverse event of interest by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.44 Treatment emergent severe (grade 3) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 3)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	0 (0.0)	5 (3.3)
Number (%) of patients censored	149 (100.0)	147 (96.7)
Kaplan-Meier estimates of AESI in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0299
Hazard ratio (95% CI) vs Pd	-	. (. to .)
P-value	-	0.9944
probability (95% CI)[b]		
2 Months	1.0000 (1.0000 to 1.0000)	0.9802 (0.9399 to 0.9936)
4 Months	1.0000 (1.0000 to 1.0000)	0.9802 (0.9399 to 0.9936)
6 Months	1.0000 (1.0000 to 1.0000)	0.9726 (0.9284 to 0.9896)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.44 Treatment emergent severe (grade 3) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 3)	**Pd (N=149)**	**IPd (N=152)**
8 Months	1.0000 (1.0000 to 1.0000)	0.9726 (0.9284 to 0.9896)
10 Months	1.0000 (1.0000 to 1.0000)	0.9726 (0.9284 to 0.9896)
12 Months	1.0000 (1.0000 to 1.0000)	0.9638 (0.9146 to 0.9849)
14 Months	1.0000 (1.0000 to 1.0000)	0.9638 (0.9146 to 0.9849)
16 Months	1.0000 (1.0000 to 1.0000)	0.9638 (0.9146 to 0.9849)
Number of patients at risk[b]		
2 Months	142	147
4 Months	134	139
6 Months	117	125
8 Months	106	120
10 Months	102	113
12 Months	87	100
14 Months	54	68
16 Months	26	30

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
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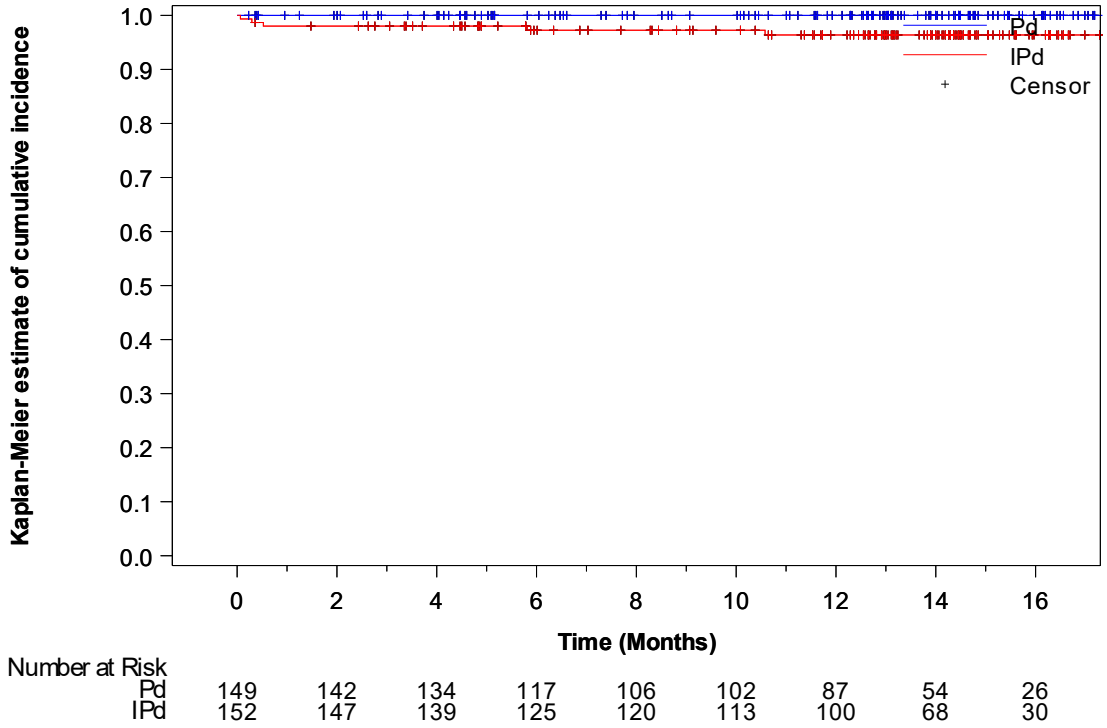
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.45 Kaplan-Meier cumulative incidence curve of treatment emergent severe (grade 3) adverse event of interest by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.46 Treatment emergent severe (grade 4) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 4)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	0 (0.0)	3 (2.0)
Number (%) of patients censored	149 (100.0)	149 (98.0)
Kaplan-Meier estimates of AESI in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0903
Hazard ratio (95% CI) vs Pd	-	. (. to .)
P-value	-	0.9956
probability (95% CI)[b]		
2 Months	1.0000 (1.0000 to 1.0000)	0.9868 (0.9484 to 0.9967)
4 Months	1.0000 (1.0000 to 1.0000)	0.9868 (0.9484 to 0.9967)
6 Months	1.0000 (1.0000 to 1.0000)	0.9868 (0.9484 to 0.9967)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.46 Treatment emergent severe (grade 4) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 4)	**Pd (N=149)**	**IPd (N=152)**
8 Months	1.0000 (1.0000 to 1.0000)	0.9788 (0.9354 to 0.9932)
10 Months	1.0000 (1.0000 to 1.0000)	0.9788 (0.9354 to 0.9932)
12 Months	1.0000 (1.0000 to 1.0000)	0.9788 (0.9354 to 0.9932)
14 Months	1.0000 (1.0000 to 1.0000)	0.9788 (0.9354 to 0.9932)
16 Months	1.0000 (1.0000 to 1.0000)	0.9788 (0.9354 to 0.9932)
Number of patients at risk[b]		
2 Months	142	147
4 Months	134	140
6 Months	117	127
8 Months	106	121
10 Months	102	114
12 Months	87	102
14 Months	54	69
16 Months	26	29

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
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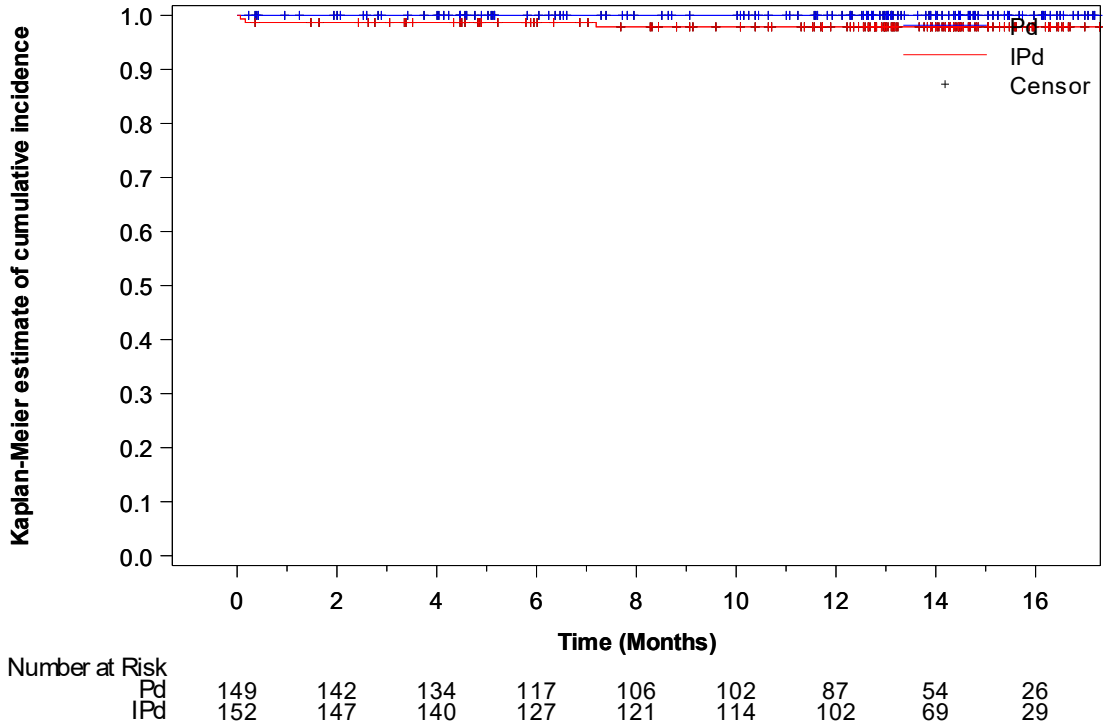
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.1 Safety population
16.2.7.1.1.1.47 Kaplan-Meier cumulative incidence curve of treatment emergent severe (grade 4) adverse event of interest by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.2 Subgroup analyses by age (IRT)
16.2.7.1.1.2.1 Treatment emergent adverse event by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	66 (97.1)	53 (98.1)	52 (98.1)	66 (100.0)	28 (100.0)	32 (100.0)	0.2194
Number (%) of patients censored	2 (2.9)	1 (1.9)	1 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	0.1643 (0.1314 to 0.2628)	0.0986 (0.0657 to 0.1314)	0.1314 (0.0657 to 0.1314)	0.0986 (0.0657 to 0.1314)	0.1314 (0.0657 to 0.1971)	0.0986 (0.0329 to 0.1643)	
Median (95% CI)	0.3943 (0.2957 to 0.7228)	0.1643 (0.1314 to 0.2300)	0.2957 (0.1314 to 0.4928)	0.2300 (0.1643 to 0.2957)	0.3285 (0.1643 to 0.6899)	0.1807 (0.1314 to 0.3943)	
75% quantile (95% CI)	1.0513 (0.7885 to 1.8727)	0.4928 (0.2300 to 0.7556)	0.8542 (0.4928 to 1.5113)	0.7228 (0.3285 to 1.3470)	0.7228 (0.4600 to 1.7084)	0.5092 (0.2300 to 0.8542)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd		0.0020		0.4533		0.1007	
Hazard ratio (95% CI) vs Pd		1.7842 (1.2313 to 2.5855)		1.1535 (0.7940 to 1.6756)		1.5743 (0.9118 to 2.7183)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.2 Subgroup analyses by age (IRT)
16.2.7.1.1.2.1 Treatment emergent adverse event by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
P-value		0.0022		0.4536		0.1034	
Hazard ratio inverted (95% CI) vs IPd	0.5605 (0.3868 to 0.8121)						
probability (95% CI)[b]							
2 Months	0.1343 (0.0660 to 0.2270)	0.0370 (0.0069 to 0.1129)	0.0962 (0.0353 to 0.1939)	0.0938 (0.0382 to 0.1798)	0.0800 (0.0139 to 0.2249)	0.0313 (0.0024 to 0.1372)	
4 Months	0.0597 (0.0193 to 0.1338)	0.0370 (0.0069 to 0.1129)	0.0577 (0.0151 to 0.1436)	0.0156 (0.0013 to 0.0739)	0.0400 (0.0029 to 0.1699)	0.0313 (0.0024 to 0.1372)	
6 Months	0.0398 (0.0087 to 0.1116)	0.0370 (0.0069 to 0.1129)	0.0577 (0.0151 to 0.1436)	0.0156 (0.0013 to 0.0739)	0.0400 (0.0029 to 0.1699)	0.0313 (0.0024 to 0.1372)	
8 Months	0.0398 (0.0087 to 0.1116)	0.0185 (0.0015 to 0.0862)	0.0385 (0.0071 to 0.1168)	0.0156 (0.0013 to 0.0739)	0.0400 (0.0029 to 0.1699)	0.0313 (0.0024 to 0.1372)	
10 Months	0.0398 (0.0087 to 0.1116)	0.0185 (0.0015 to 0.0862)	0.0192 (0.0016 to 0.0891)	0.0156 (0.0013 to 0.0739)	0.0400 (0.0029 to 0.1699)	0.0313 (0.0024 to 0.1372)	
12 Months	0.0199 (0.0018 to 0.0875)	0.0185 (0.0015 to 0.0862)	0.0192 (0.0016 to 0.0891)	0.0156 (0.0013 to 0.0739)	0.0400 (0.0029 to 0.1699)	0.0313 (0.0024 to 0.1372)	
14 Months	0.0199 (0.0018 to 0.0875)	0.0185 (0.0015 to 0.0862)	0.0192 (0.0016 to 0.0891)	0.0156 (0.0013 to 0.0739)	0.0400 (0.0029 to 0.1699)	0.0313 (0.0024 to 0.1372)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.2 Subgroup analyses by age (IRT)
16.2.7.1.1.2.1 Treatment emergent adverse event by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0199 (0.0018 to 0.0875)	0.0185 (0.0015 to 0.0862)	0.0192 (0.0016 to 0.0891)	0.0156 (0.0013 to 0.0739)	0.0400 (0.0029 to 0.1699)	0.0313 (0.0024 to 0.1372)	
Number of patients at risk[b]							
2 Months	9	2	5	6	2	1	
4 Months	4	2	3	1	0	0	
6 Months	2	2	3	0	0	0	
8 Months	2	1	2	0	0	0	
10 Months	2	1	1	0	0	0	
12 Months	1	0	1	0	0	0	
14 Months	1	0	1	0	0	0	
16 Months	0	0	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_age_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.2 Subgroup analyses by age (IRT)
16.2.7.1.1.2.2 Treatment emergent serious adverse event by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (47.1)	31 (57.4)	32 (60.4)	41 (62.1)	16 (57.1)	22 (68.8)	0.7480
Number (%) of patients censored	36 (52.9)	23 (42.6)	21 (39.6)	25 (37.9)	12 (42.9)	10 (31.3)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	1.9384 (1.2813 to 2.9569)	0.6571 (0.2957 to 2.2669)	1.0842 (0.2957 to 2.6283)	1.3470 (0.4271 to 2.1355)	0.6407 (0.1314 to 1.1828)	0.7556 (0.1643 to 1.5770)	
Median (95% CI)	NC (3.5154 to NC)	8.8049 (2.2669 to NC)	5.9795 (2.2669 to 14.5544)	4.4353 (2.3655 to 9.5934)	5.0760 (0.7556 to NC)	5.8152 (1.1499 to 11.0062)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.5544 to NC)	NC (NC to NC)	NC (6.5708 to NC)	NC (10.5462 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd		0.2561		0.9272		0.7942	
Hazard ratio (95% CI) vs Pd		1.3304 (0.8115 to 2.1811)		1.0219 (0.6418 to 1.6272)		1.0897 (0.5715 to 2.0778)	
P-value		0.2577		0.9273		0.7943	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_age_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.2 Subgroup analyses by age (IRT)
16.2.7.1.1.2.2 Treatment emergent serious adverse event by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]							
2 Months	0.7353 (0.6133 to 0.8242)	0.6481 (0.5055 to 0.7591)	0.6604 (0.5164 to 0.7706)	0.6769 (0.5488 to 0.7759)	0.5714 (0.3706 to 0.7295)	0.5938 (0.4052 to 0.7402)	
4 Months	0.6002 (0.4734 to 0.7058)	0.6105 (0.4676 to 0.7260)	0.5849 (0.4410 to 0.7037)	0.5231 (0.3957 to 0.6358)	0.5357 (0.3381 to 0.6982)	0.5608 (0.3736 to 0.7119)	
6 Months	0.5541 (0.4275 to 0.6634)	0.5533 (0.4112 to 0.6743)	0.4885 (0.3486 to 0.6145)	0.4610 (0.3370 to 0.5762)	0.4583 (0.2683 to 0.6297)	0.4948 (0.3127 to 0.6532)	
8 Months	0.5387 (0.4125 to 0.6491)	0.5342 (0.3928 to 0.6567)	0.4461 (0.3084 to 0.5746)	0.4133 (0.2929 to 0.5295)	0.4167 (0.2319 to 0.5919)	0.4948 (0.3127 to 0.6532)	
10 Months	0.5387 (0.4125 to 0.6491)	0.4579 (0.3212 to 0.5844)	0.4461 (0.3084 to 0.5746)	0.3815 (0.2643 to 0.4978)	0.4167 (0.2319 to 0.5919)	0.4288 (0.2550 to 0.5918)	
12 Months	0.5224 (0.3964 to 0.6340)	0.4181 (0.2847 to 0.5459)	0.4461 (0.3084 to 0.5746)	0.3815 (0.2643 to 0.4978)	0.4167 (0.2319 to 0.5919)	0.2859 (0.1390 to 0.4517)	
14 Months	0.5224 (0.3964 to 0.6340)	0.4181 (0.2847 to 0.5459)	0.3965 (0.2610 to 0.5288)	0.3815 (0.2643 to 0.4978)	0.4167 (0.2319 to 0.5919)	0.2859 (0.1390 to 0.4517)	
16 Months	0.5224 (0.3964 to 0.6340)	0.4181 (0.2847 to 0.5459)	0.3304 (0.1764 to 0.4932)	0.3815 (0.2643 to 0.4978)	0.4167 (0.2319 to 0.5919)	0.2859 (0.1390 to 0.4517)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_age_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.2 Subgroup analyses by age (IRT)
16.2.7.1.1.2.2 Treatment emergent serious adverse event by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	49	35	35	44	16	19	
4 Months	40	32	31	34	15	17	
6 Months	36	29	25	29	11	15	
8 Months	33	28	21	26	9	15	
10 Months	33	24	21	24	8	13	
12 Months	30	19	18	23	5	8	
14 Months	19	11	7	17	3	7	
16 Months	12	5	1	8	2	1	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.2 Subgroup analyses by age (IRT)
16.2.7.1.1.2.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (10.3)	4 (7.4)	8 (15.1)	2 (3.0)	4 (14.3)	5 (15.6)	0.2256
Number (%) of patients censored	61 (89.7)	50 (92.6)	45 (84.9)	64 (97.0)	24 (85.7)	27 (84.4)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.1622 to NC)	NC (NC to NC)	NC (1.1828 to NC)	15.9671 (4.3368 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.9671 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.9671 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd		0.5515		0.0147		0.9838	
Hazard ratio (95% CI) vs Pd		0.6899 (0.2019 to 2.3570)		0.1803 (0.0383 to 0.8496)		0.9864 (0.2638 to 3.6880)	
P-value		0.5538		0.0303		0.9838	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.2 Subgroup analyses by age (IRT)
16.2.7.1.1.2.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]							
2 Months	0.9118 (0.8141 to 0.9594)	1.0000 (1.0000 to 1.0000)	0.9241 (0.8104 to 0.9708)	1.0000 (1.0000 to 1.0000)	0.8901 (0.6967 to 0.9632)	0.9688 (0.7982 to 0.9955)	
4 Months	0.9118 (0.8141 to 0.9594)	0.9623 (0.8574 to 0.9904)	0.9241 (0.8104 to 0.9708)	1.0000 (1.0000 to 1.0000)	0.8514 (0.6507 to 0.9416)	0.9375 (0.7725 to 0.9840)	
6 Months	0.8960 (0.7942 to 0.9491)	0.9230 (0.8076 to 0.9704)	0.8831 (0.7578 to 0.9458)	1.0000 (1.0000 to 1.0000)	0.8514 (0.6507 to 0.9416)	0.9014 (0.7237 to 0.9673)	
8 Months	0.8960 (0.7942 to 0.9491)	0.9230 (0.8076 to 0.9704)	0.8610 (0.7297 to 0.9314)	0.9825 (0.8819 to 0.9975)	0.8514 (0.6507 to 0.9416)	0.9014 (0.7237 to 0.9673)	
10 Months	0.8960 (0.7942 to 0.9491)	0.9230 (0.8076 to 0.9704)	0.8610 (0.7297 to 0.9314)	0.9643 (0.8645 to 0.9909)	0.8514 (0.6507 to 0.9416)	0.9014 (0.7237 to 0.9673)	
12 Months	0.8960 (0.7942 to 0.9491)	0.9230 (0.8076 to 0.9704)	0.8610 (0.7297 to 0.9314)	0.9643 (0.8645 to 0.9909)	0.8514 (0.6507 to 0.9416)	0.8605 (0.6668 to 0.9458)	
14 Months	0.8960 (0.7942 to 0.9491)	0.9230 (0.8076 to 0.9704)	0.8291 (0.6821 to 0.9123)	0.9643 (0.8645 to 0.9909)	0.8514 (0.6507 to 0.9416)	0.8605 (0.6668 to 0.9458)	
16 Months	0.8960 (0.7942 to 0.9491)	0.9230 (0.8076 to 0.9704)	0.8291 (0.6821 to 0.9123)	0.9643 (0.8645 to 0.9909)	0.8514 (0.6507 to 0.9416)	0.6454 (0.1890 to 0.8912)	
Number of patients at risk[b]							

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_age_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.2 Subgroup analyses by age (IRT)
16.2.7.1.1.2.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	62	53	47	64	24	31	
4 Months	60	49	45	64	22	26	
6 Months	53	44	42	58	18	24	
8 Months	49	40	38	56	16	24	
10 Months	47	38	37	52	15	23	
12 Months	41	34	33	47	11	19	
14 Months	25	21	19	33	8	14	
16 Months	14	11	6	15	4	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_age_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.2 Subgroup analyses by age (IRT)
16.2.7.1.1.2.4 Treatment emergent mild adverse event by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	63 (92.6)	50 (92.6)	48 (90.6)	61 (92.4)	26 (92.9)	30 (93.8)	0.8220
Number (%) of patients censored	5 (7.4)	4 (7.4)	5 (9.4)	5 (7.6)	2 (7.1)	2 (6.3)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	0.1971 (0.1314 to 0.3285)	0.0986 (0.0657 to 0.1314)	0.1314 (0.0657 to 0.2957)	0.1314 (0.0657 to 0.1643)	0.1971 (0.0657 to 0.2957)	0.1150 (0.0329 to 0.1643)	
Median (95% CI)	0.4600 (0.3285 to 0.7885)	0.1971 (0.1314 to 0.2957)	0.4928 (0.2957 to 0.8871)	0.2628 (0.1643 to 0.4928)	0.5421 (0.1971 to 0.8542)	0.2793 (0.1643 to 0.7228)	
75% quantile (95% CI)	1.3470 (0.8214 to 1.8727)	0.7556 (0.2957 to 2.1684)	1.5770 (0.8542 to 2.9897)	0.8214 (0.4928 to 3.3183)	1.7084 (0.6242 to 2.5626)	0.9035 (0.4271 to 4.4353)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd		0.1384		0.4184		0.8248	
Hazard ratio (95% CI) vs Pd		1.3260 (0.9118 to 1.9283)		1.1712 (0.7984 to 1.7182)		1.0635 (0.6157 to 1.8369)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.2 Subgroup analyses by age (IRT)
16.2.7.1.1.2.4 Treatment emergent mild adverse event by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
P-value		0.1397		0.4189		0.8252	
probability (95% CI)[b]							
2 Months	0.1524 (0.0783 to 0.2493)	0.1481 (0.0693 to 0.2551)	0.1795 (0.0888 to 0.2957)	0.2154 (0.1253 to 0.3215)	0.2244 (0.0879 to 0.3991)	0.1875 (0.0761 to 0.3369)	
4 Months	0.1016 (0.0428 to 0.1904)	0.1111 (0.0452 to 0.2104)	0.1197 (0.0487 to 0.2250)	0.1325 (0.0631 to 0.2281)	0.0449 (0.0033 to 0.1856)	0.1172 (0.0336 to 0.2580)	
6 Months	0.0610 (0.0177 to 0.1438)	0.0833 (0.0265 to 0.1826)	0.1197 (0.0487 to 0.2250)	0.0994 (0.0411 to 0.1884)	0.0449 (0.0033 to 0.1856)	0.0781 (0.0151 to 0.2122)	
8 Months	0.0610 (0.0177 to 0.1438)	0.0556 (0.0119 to 0.1519)	0.0957 (0.0335 to 0.1978)	0.0596 (0.0171 to 0.1419)	0.0449 (0.0033 to 0.1856)	0.0781 (0.0151 to 0.2122)	
10 Months	0.0610 (0.0177 to 0.1438)	0.0556 (0.0119 to 0.1519)	0.0718 (0.0202 to 0.1691)	0.0596 (0.0171 to 0.1419)	0.0449 (0.0033 to 0.1856)	0.0781 (0.0151 to 0.2122)	
12 Months	0.0305 (0.0033 to 0.1188)	0.0556 (0.0119 to 0.1519)	0.0718 (0.0202 to 0.1691)	0.0596 (0.0171 to 0.1419)	0.0449 (0.0033 to 0.1856)	0.0781 (0.0151 to 0.2122)	
14 Months	0.0305 (0.0033 to 0.1188)	0.0556 (0.0119 to 0.1519)	0.0718 (0.0202 to 0.1691)	0.0596 (0.0171 to 0.1419)	0.0449 (0.0033 to 0.1856)	0.0781 (0.0151 to 0.2122)	
16 Months	0.0305 (0.0033 to 0.1188)	0.0556 (0.0119 to 0.1519)	0.0718 (0.0202 to 0.1691)	0.0596 (0.0171 to 0.1419)	0.0449 (0.0033 to 0.1856)	0.0391 (0.0031 to 0.1626)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.2 Subgroup analyses by age (IRT)
16.2.7.1.1.2.4 Treatment emergent mild adverse event by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	9	8	9	13	5	6	
4 Months	6	5	6	8	1	3	
6 Months	3	3	5	5	0	2	
8 Months	3	2	4	3	0	2	
10 Months	2	2	3	3	0	2	
12 Months	1	1	3	3	0	2	
14 Months	1	1	3	3	0	2	
16 Months	0	1	1	0	0	1	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.2 Subgroup analyses by age (IRT)
16.2.7.1.1.2.5 Treatment emergent severe adverse event by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (63.2)	45 (83.3)	39 (73.6)	54 (81.8)	21 (75.0)	30 (93.8)	0.1598
Number (%) of patients censored	25 (36.8)	9 (16.7)	14 (26.4)	12 (18.2)	7 (25.0)	2 (6.3)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	0.8049 (0.5257 to 1.5770)	0.5257 (0.2628 to 0.5914)	0.5257 (0.1971 to 0.7556)	0.5585 (0.3285 to 0.7885)	0.3943 (0.1314 to 0.5585)	0.3614 (0.1643 to 0.5257)	
Median (95% CI)	3.0226 (1.9384 to 6.0452)	0.7721 (0.5914 to 1.0185)	1.3142 (0.7556 to 2.6283)	1.3470 (0.7885 to 1.9713)	0.7228 (0.4600 to 1.1170)	0.7885 (0.4928 to 1.1499)	
75% quantile (95% CI)	NC (7.6222 to NC)	2.8912 (1.0185 to NC)	14.5544 (2.6283 to NC)	5.6181 (2.1355 to NC)	NC (0.7885 to NC)	2.8255 (0.8542 to 8.3450)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd		0.0011		0.5573		0.3705	
Hazard ratio (95% CI) vs Pd		1.9960 (1.3081 to 3.0457)		1.1319 (0.7481 to 1.7127)		1.2952 (0.7342 to 2.2848)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_age_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.2 Subgroup analyses by age (IRT)
16.2.7.1.1.2.5 Treatment emergent severe adverse event by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
P-value		0.0013		0.5575		0.3718	
Hazard ratio inverted (95% CI) vs IPd	0.5010 (0.3283 to 0.7645)						
probability (95% CI)[b]							
2 Months	0.5882 (0.4621 to 0.6943)	0.3333 (0.2125 to 0.4587)	0.4252 (0.2901 to 0.5538)	0.3761 (0.2591 to 0.4925)	0.2963 (0.1406 to 0.4703)	0.2813 (0.1404 to 0.4406)	
4 Months	0.4559 (0.3351 to 0.5687)	0.1970 (0.1024 to 0.3140)	0.3286 (0.2063 to 0.4562)	0.2821 (0.1783 to 0.3949)	0.2963 (0.1406 to 0.4703)	0.1875 (0.0761 to 0.3369)	
6 Months	0.3935 (0.2773 to 0.5075)	0.1751 (0.0860 to 0.2901)	0.2899 (0.1744 to 0.4157)	0.2173 (0.1256 to 0.3252)	0.2593 (0.1148 to 0.4309)	0.1563 (0.0570 to 0.3003)	
8 Months	0.3613 (0.2481 to 0.4754)	0.1751 (0.0860 to 0.2901)	0.2692 (0.1574 to 0.3940)	0.1671 (0.0872 to 0.2693)	0.2593 (0.1148 to 0.4309)	0.1250 (0.0395 to 0.2623)	
10 Months	0.3613 (0.2481 to 0.4754)	0.1751 (0.0860 to 0.2901)	0.2692 (0.1574 to 0.3940)	0.1671 (0.0872 to 0.2693)	0.2593 (0.1148 to 0.4309)	0.0938 (0.0240 to 0.2228)	
12 Months	0.3613 (0.2481 to 0.4754)	0.1751 (0.0860 to 0.2901)	0.2692 (0.1574 to 0.3940)	0.1671 (0.0872 to 0.2693)	0.2593 (0.1148 to 0.4309)	0.0625 (0.0111 to 0.1811)	
14 Months	0.3613 (0.2481 to 0.4754)	0.1401 (0.0570 to 0.2595)	0.2692 (0.1574 to 0.3940)	0.1671 (0.0872 to 0.2693)	0.2593 (0.1148 to 0.4309)	0.0625 (0.0111 to 0.1811)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_age_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.2 Subgroup analyses by age (IRT)
16.2.7.1.1.2.5 Treatment emergent severe adverse event by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3613 (0.2481 to 0.4754)	0.1401 (0.0570 to 0.2595)	0.2154 (0.0991 to 0.3606)	0.1671 (0.0872 to 0.2693)	0.2593 (0.1148 to 0.4309)	0.0625 (0.0111 to 0.1811)	
Number of patients at risk[b]							
2 Months	40	18	22	24	8	9	
4 Months	31	9	17	18	8	6	
6 Months	25	8	15	13	7	5	
8 Months	22	8	13	10	5	4	
10 Months	22	8	13	9	5	3	
12 Months	20	6	11	8	3	2	
14 Months	13	4	6	5	1	2	
16 Months	10	0	1	3	1	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_age_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.2 Subgroup analyses by age (IRT)
16.2.7.1.1.2.6 Treatment emergent severe adverse event including death by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (64.7)	46 (85.2)	40 (75.5)	56 (84.8)	21 (75.0)	30 (93.8)	0.1595
Number (%) of patients censored	24 (35.3)	8 (14.8)	13 (24.5)	10 (15.2)	7 (25.0)	2 (6.3)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	0.8049 (0.5257 to 1.5770)	0.5257 (0.2628 to 0.5914)	0.4928 (0.1971 to 0.7556)	0.5585 (0.2957 to 0.7556)	0.3285 (0.1314 to 0.5585)	0.3614 (0.1643 to 0.5257)	
Median (95% CI)	3.0226 (1.9384 to 5.5852)	0.7721 (0.5914 to 1.0185)	1.1499 (0.7228 to 2.6283)	1.3142 (0.7885 to 1.9713)	0.7228 (0.4600 to 1.1170)	0.7885 (0.4928 to 1.1499)	
75% quantile (95% CI)	NC (7.6222 to NC)	2.7926 (1.0185 to 13.5359)	14.5544 (2.2669 to NC)	4.4353 (2.1355 to 9.1335)	NC (0.7885 to NC)	2.8255 (0.8542 to 8.3450)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd		0.0007		0.5011		0.3881	
Hazard ratio (95% CI) vs Pd		2.0277 (1.3347 to 3.0805)		1.1502 (0.7649 to 1.7297)		1.2832 (0.7274 to 2.2638)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_age_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.2 Subgroup analyses by age (IRT)
16.2.7.1.1.2.6 Treatment emergent severe adverse event including death by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
P-value		0.0009		0.5014		0.3893	
Hazard ratio inverted (95% CI) vs IPd	0.4932 (0.3246 to 0.7492)						
probability (95% CI)[b]							
2 Months	0.5882 (0.4621 to 0.6943)	0.3148 (0.1970 to 0.4394)	0.4151 (0.2823 to 0.5426)	0.3692 (0.2540 to 0.4847)	0.2963 (0.1406 to 0.4703)	0.2813 (0.1404 to 0.4406)	
4 Months	0.4559 (0.3351 to 0.5687)	0.1818 (0.0922 to 0.2955)	0.3208 (0.2009 to 0.4468)	0.2769 (0.1749 to 0.3885)	0.2963 (0.1406 to 0.4703)	0.1875 (0.0761 to 0.3369)	
6 Months	0.3799 (0.2654 to 0.4935)	0.1616 (0.0776 to 0.2727)	0.2830 (0.1699 to 0.4070)	0.2133 (0.1233 to 0.3198)	0.2593 (0.1148 to 0.4309)	0.1563 (0.0570 to 0.3003)	
8 Months	0.3488 (0.2377 to 0.4621)	0.1616 (0.0776 to 0.2727)	0.2628 (0.1534 to 0.3858)	0.1641 (0.0856 to 0.2648)	0.2593 (0.1148 to 0.4309)	0.1250 (0.0395 to 0.2623)	
10 Months	0.3488 (0.2377 to 0.4621)	0.1616 (0.0776 to 0.2727)	0.2628 (0.1534 to 0.3858)	0.1477 (0.0737 to 0.2459)	0.2593 (0.1148 to 0.4309)	0.0938 (0.0240 to 0.2228)	
12 Months	0.3488 (0.2377 to 0.4621)	0.1616 (0.0776 to 0.2727)	0.2628 (0.1534 to 0.3858)	0.1477 (0.0737 to 0.2459)	0.2593 (0.1148 to 0.4309)	0.0625 (0.0111 to 0.1811)	
14 Months	0.3488 (0.2377 to 0.4621)	0.1293 (0.0518 to 0.2433)	0.2628 (0.1534 to 0.3858)	0.1477 (0.0737 to 0.2459)	0.2593 (0.1148 to 0.4309)	0.0625 (0.0111 to 0.1811)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_age_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.2 Subgroup analyses by age (IRT)
16.2.7.1.1.2.6 Treatment emergent severe adverse event including death by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3488 (0.2377 to 0.4621)	0.1293 (0.0518 to 0.2433)	0.2102 (0.0967 to 0.3530)	0.1477 (0.0737 to 0.2459)	0.2593 (0.1148 to 0.4309)	0.0625 (0.0111 to 0.1811)	
Number of patients at risk[b]							
2 Months	40	17	22	24	8	9	
4 Months	31	9	17	18	8	6	
6 Months	25	8	15	13	7	5	
8 Months	22	8	13	10	5	4	
10 Months	22	8	13	9	5	3	
12 Months	20	6	11	8	3	2	
14 Months	13	4	6	5	1	2	
16 Months	10	0	1	3	1	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_age_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.1.3.1 Treatment emergent adverse event by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	IPd (N=101)	Pd (N=49)	IPd (N=51)	p-value of treatment-by-sub group interaction[c]
Number (%) of events	98 (98.0)	101 (100.0)	48 (98.0)	50 (98.0)	0.5502
Number (%) of patients censored	2 (2.0)	0 (0.0)	1 (2.0)	1 (2.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0986 to 0.1643)	0.0657 (0.0657 to 0.0986)	0.1643 (0.0986 to 0.2628)	0.1314 (0.1314 to 0.1643)	
Median (95% CI)	0.3285 (0.1971 to 0.4928)	0.1971 (0.1314 to 0.2628)	0.3285 (0.2300 to 0.5257)	0.1971 (0.1314 to 0.3614)	
75% quantile (95% CI)	0.9856 (0.7228 to 1.4784)	0.5585 (0.3285 to 0.7885)	0.8214 (0.5257 to 1.5113)	0.5914 (0.2957 to 0.7885)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0069		0.2296	
Hazard ratio (95% CI) vs Pd		1.4751 (1.1105 to 1.9594)		1.2808 (0.8544 to 1.9200)	
P-value		0.0073		0.2308	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_plne_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.1.3.1 Treatment emergent adverse event by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6779 (0.5104 to 0.9005)				
probability (95% CI)[b]					
2 Months	0.1122 (0.0595 to 0.1835)	0.0505 (0.0188 to 0.1062)	0.1087 (0.0399 to 0.2169)	0.0784 (0.0251 to 0.1722)	
4 Months	0.0408 (0.0133 to 0.0935)	0.0101 (0.0009 to 0.0495)	0.0652 (0.0170 to 0.1606)	0.0392 (0.0073 to 0.1189)	
6 Months	0.0408 (0.0133 to 0.0935)	0.0101 (0.0009 to 0.0495)	0.0435 (0.0080 to 0.1307)	0.0196 (0.0016 to 0.0907)	
8 Months	0.0272 (0.0061 to 0.0782)	0.0101 (0.0009 to 0.0495)	0.0435 (0.0080 to 0.1307)	0.0196 (0.0016 to 0.0907)	
10 Months	0.0272 (0.0061 to 0.0782)	0.0101 (0.0009 to 0.0495)	0.0217 (0.0017 to 0.0995)	0.0196 (0.0016 to 0.0907)	
12 Months	0.0136 (0.0013 to 0.0618)	0.0101 (0.0009 to 0.0495)	0.0217 (0.0017 to 0.0995)	0.0196 (0.0016 to 0.0907)	
14 Months	0.0136 (0.0013 to 0.0618)	0.0101 (0.0009 to 0.0495)	0.0217 (0.0017 to 0.0995)	0.0196 (0.0016 to 0.0907)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_plne_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.1.3.1 Treatment emergent adverse event by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0136 (0.0013 to 0.0618)	0.0101 (0.0009 to 0.0495)	0.0217 (0.0017 to 0.0995)	0.0196 (0.0016 to 0.0907)	
Number of patients at risk[b]					
2 Months	11	5	5	4	
4 Months	4	1	3	2	
6 Months	3	1	2	1	
8 Months	2	0	2	1	
10 Months	2	0	1	1	
12 Months	1	0	1	0	
14 Months	1	0	1	0	
16 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_plne_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.1.3.2 Treatment emergent serious adverse event by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (49.0)	65 (64.4)	31 (63.3)	29 (56.9)	0.0771
Number (%) of patients censored	51 (51.0)	36 (35.6)	18 (36.7)	22 (43.1)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.4620 (0.5914 to 2.9569)	0.7556 (0.4271 to 1.4127)	1.2813 (0.4928 to 1.9384)	0.8214 (0.2628 to 4.0411)	
Median (95% CI)	12.1232 (4.4682 to NC)	4.4353 (2.1355 to 9.5934)	3.7782 (1.7741 to 14.5544)	8.8049 (3.9754 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.1889 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0529		0.4346	
Hazard ratio (95% CI) vs Pd		1.4414 (0.9933 to 2.0917)		0.8170 (0.4917 to 1.3576)	
P-value		0.0543		0.4353	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_plne_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.1.3.2 Treatment emergent serious adverse event by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.7200 (0.6209 to 0.7974)	0.6200 (0.5174 to 0.7070)	0.5918 (0.4417 to 0.7141)	0.7059 (0.5603 to 0.8110)	
4 Months	0.6287 (0.5260 to 0.7152)	0.5189 (0.4168 to 0.6116)	0.4898 (0.3447 to 0.6199)	0.6471 (0.4998 to 0.7609)	
6 Months	0.5448 (0.4413 to 0.6370)	0.4772 (0.3762 to 0.5713)	0.4481 (0.3063 to 0.5800)	0.5490 (0.4034 to 0.6730)	
8 Months	0.5118 (0.4086 to 0.6058)	0.4454 (0.3456 to 0.5402)	0.4256 (0.2857 to 0.5586)	0.5294 (0.3847 to 0.6548)	
10 Months	0.5118 (0.4086 to 0.6058)	0.3923 (0.2958 to 0.4874)	0.4256 (0.2857 to 0.5586)	0.4706 (0.3299 to 0.5991)	
12 Months	0.5118 (0.4086 to 0.6058)	0.3499 (0.2568 to 0.4444)	0.4020 (0.2640 to 0.5361)	0.4278 (0.2902 to 0.5584)	
14 Months	0.4984 (0.3948 to 0.5934)	0.3499 (0.2568 to 0.4444)	0.3752 (0.2389 to 0.5111)	0.4278 (0.2902 to 0.5584)	
16 Months	0.4984 (0.3948 to 0.5934)	0.3499 (0.2568 to 0.4444)	0.3127 (0.1634 to 0.4742)	0.4278 (0.2902 to 0.5584)	
Number of patients at risk[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_plne_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.1.3.2 Treatment emergent serious adverse event by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	71	62	29	36	
4 Months	62	50	24	33	
6 Months	51	45	21	28	
8 Months	45	42	18	27	
10 Months	44	37	18	24	
12 Months	38	31	15	19	
14 Months	22	22	7	13	
16 Months	11	9	4	5	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.1.3.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (13.0)	6 (5.9)	6 (12.2)	5 (9.8)	0.4670
Number (%) of patients censored	87 (87.0)	95 (94.1)	43 (87.8)	46 (90.2)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.8789 to NC)	NC (15.9671 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0757		0.6415	
Hazard ratio (95% CI) vs Pd		0.4272 (0.1624 to 1.1240)		0.7548 (0.2302 to 2.4749)	
P-value		0.0848		0.6425	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_plne_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.1.3.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.8984 (0.8193 to 0.9440)	0.9900 (0.9311 to 0.9986)	0.9388 (0.8221 to 0.9798)	1.0000 (1.0000 to 1.0000)	
4 Months	0.8984 (0.8193 to 0.9440)	0.9697 (0.9090 to 0.9901)	0.9179 (0.7959 to 0.9684)	0.9800 (0.8664 to 0.9972)	
6 Months	0.8765 (0.7925 to 0.9279)	0.9697 (0.9090 to 0.9901)	0.8971 (0.7701 to 0.9558)	0.9200 (0.8007 to 0.9692)	
8 Months	0.8648 (0.7782 to 0.9193)	0.9576 (0.8905 to 0.9839)	0.8971 (0.7701 to 0.9558)	0.9200 (0.8007 to 0.9692)	
10 Months	0.8648 (0.7782 to 0.9193)	0.9448 (0.8717 to 0.9768)	0.8971 (0.7701 to 0.9558)	0.9200 (0.8007 to 0.9692)	
12 Months	0.8648 (0.7782 to 0.9193)	0.9319 (0.8537 to 0.9690)	0.8971 (0.7701 to 0.9558)	0.9200 (0.8007 to 0.9692)	
14 Months	0.8648 (0.7782 to 0.9193)	0.9319 (0.8537 to 0.9690)	0.8563 (0.6955 to 0.9358)	0.9200 (0.8007 to 0.9692)	
16 Months	0.8648 (0.7782 to 0.9193)	0.9319 (0.8537 to 0.9690)	0.8563 (0.6955 to 0.9358)	0.8178 (0.5066 to 0.9422)	
Number of patients at risk[b]					
2 Months	87	98	46	50	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_plne_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.1.3.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	83	90	44	49	
6 Months	76	82	37	44	
8 Months	71	79	32	41	
10 Months	70	74	29	39	
12 Months	59	67	26	33	
14 Months	36	46	16	22	
16 Months	15	20	9	8	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_plne_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.1.3.4 Treatment emergent mild adverse event by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	91 (91.0)	94 (93.1)	46 (93.9)	47 (92.2)	0.7311
Number (%) of patients censored	9 (9.0)	7 (6.9)	3 (6.1)	4 (7.8)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1643 (0.0986 to 0.2628)	0.0986 (0.0657 to 0.0986)	0.1643 (0.0986 to 0.2957)	0.1314 (0.1314 to 0.1643)	
Median (95% CI)	0.5914 (0.3285 to 0.8542)	0.2300 (0.1643 to 0.3614)	0.3778 (0.2957 to 0.5914)	0.2300 (0.1643 to 0.4600)	
75% quantile (95% CI)	1.5441 (0.9856 to 2.2998)	0.9199 (0.6571 to 2.2998)	0.8871 (0.5585 to 1.8727)	0.7556 (0.3943 to 1.4456)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.2226		0.4428	
Hazard ratio (95% CI) vs Pd		1.1983 (0.8957 to 1.6031)		1.1764 (0.7768 to 1.7815)	
P-value		0.2232		0.4429	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_plne_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.1.3.4 Treatment emergent mild adverse event by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.1950 (0.1225 to 0.2800)	0.2100 (0.1365 to 0.2943)	0.1304 (0.0530 to 0.2436)	0.1373 (0.0603 to 0.2455)	
4 Months	0.0918 (0.0435 to 0.1620)	0.1227 (0.0665 to 0.1972)	0.1087 (0.0399 to 0.2169)	0.1176 (0.0478 to 0.2217)	
6 Months	0.0787 (0.0344 to 0.1468)	0.0947 (0.0448 to 0.1672)	0.0870 (0.0278 to 0.1893)	0.0784 (0.0251 to 0.1722)	
8 Months	0.0629 (0.0236 to 0.1298)	0.0473 (0.0139 to 0.1136)	0.0870 (0.0278 to 0.1893)	0.0784 (0.0251 to 0.1722)	
10 Months	0.0629 (0.0236 to 0.1298)	0.0473 (0.0139 to 0.1136)	0.0580 (0.0124 to 0.1576)	0.0784 (0.0251 to 0.1722)	
12 Months	0.0472 (0.0142 to 0.1117)	0.0473 (0.0139 to 0.1136)	0.0580 (0.0124 to 0.1576)	0.0784 (0.0251 to 0.1722)	
14 Months	0.0472 (0.0142 to 0.1117)	0.0473 (0.0139 to 0.1136)	0.0580 (0.0124 to 0.1576)	0.0784 (0.0251 to 0.1722)	
16 Months	0.0472 (0.0142 to 0.1117)	0.0316 (0.0065 to 0.0936)	0.0580 (0.0124 to 0.1576)	0.0784 (0.0251 to 0.1722)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.1.3.4 Treatment emergent mild adverse event by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	17	20	6	7	
4 Months	8	10	5	6	
6 Months	5	6	3	4	
8 Months	4	3	3	4	
10 Months	4	3	1	4	
12 Months	3	3	1	3	
14 Months	3	3	1	3	
16 Months	1	1	0	1	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_plne_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.1.3.5 Treatment emergent severe adverse event by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	67 (67.0)	83 (82.2)	36 (73.5)	46 (90.2)	0.6821
Number (%) of patients censored	33 (33.0)	18 (17.8)	13 (26.5)	5 (9.8)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.5257 (0.2957 to 0.7885)	0.4928 (0.3285 to 0.5585)	0.5914 (0.2628 to 0.7885)	0.5257 (0.2628 to 0.6899)	
Median (95% CI)	2.2669 (0.9199 to 4.4353)	0.8542 (0.7556 to 1.3142)	1.5770 (0.7556 to 2.0370)	0.8214 (0.6242 to 2.0370)	
75% quantile (95% CI)	NC (7.0308 to NC)	2.7926 (1.9713 to 13.5359)	14.5544 (2.0370 to NC)	3.7782 (1.9384 to 6.1766)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0096		0.1208	
Hazard ratio (95% CI) vs Pd		1.5341 (1.1069 to 2.1262)		1.4151 (0.9107 to 2.1990)	
P-value		0.0102		0.1226	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_plne_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.1.3.5 Treatment emergent severe adverse event by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6518 (0.4703 to 0.9034)				
probability (95% CI)[b]					
2 Months	0.5152 (0.4128 to 0.6082)	0.3240 (0.2343 to 0.4166)	0.3972 (0.2600 to 0.5310)	0.3725 (0.2426 to 0.5024)	
4 Months	0.4242 (0.3261 to 0.5189)	0.2430 (0.1638 to 0.3308)	0.2927 (0.1724 to 0.4237)	0.2157 (0.1156 to 0.3360)	
6 Months	0.3611 (0.2673 to 0.4554)	0.2087 (0.1344 to 0.2944)	0.2718 (0.1558 to 0.4014)	0.1569 (0.0734 to 0.2688)	
8 Months	0.3289 (0.2380 to 0.4225)	0.1855 (0.1150 to 0.2693)	0.2718 (0.1558 to 0.4014)	0.1176 (0.0478 to 0.2217)	
10 Months	0.3289 (0.2380 to 0.4225)	0.1855 (0.1150 to 0.2693)	0.2718 (0.1558 to 0.4014)	0.0980 (0.0360 to 0.1973)	
12 Months	0.3289 (0.2380 to 0.4225)	0.1732 (0.1047 to 0.2560)	0.2718 (0.1558 to 0.4014)	0.0980 (0.0360 to 0.1973)	
14 Months	0.3289 (0.2380 to 0.4225)	0.1574 (0.0910 to 0.2403)	0.2718 (0.1558 to 0.4014)	0.0980 (0.0360 to 0.1973)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_plne_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.1.3.5 Treatment emergent severe adverse event by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3289 (0.2380 to 0.4225)	0.1574 (0.0910 to 0.2403)	0.2265 (0.1105 to 0.3675)	0.0980 (0.0360 to 0.1973)	
Number of patients at risk[b]					
2 Months	51	32	19	19	
4 Months	42	22	14	11	
6 Months	34	18	13	8	
8 Months	29	16	11	6	
10 Months	29	15	11	5	
12 Months	23	13	11	3	
14 Months	13	9	7	2	
16 Months	8	3	4	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_plne_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.1.3.6 Treatment emergent severe adverse event including death by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	68 (68.0)	86 (85.1)	37 (75.5)	46 (90.2)	0.5449
Number (%) of patients censored	32 (32.0)	15 (14.9)	12 (24.5)	5 (9.8)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.5257 (0.2957 to 0.7885)	0.4928 (0.3285 to 0.5585)	0.5585 (0.2628 to 0.7885)	0.5257 (0.2628 to 0.6899)	
Median (95% CI)	2.2669 (0.9199 to 4.4353)	0.8542 (0.7228 to 1.3142)	1.5113 (0.7556 to 2.0370)	0.8214 (0.6242 to 2.0370)	
75% quantile (95% CI)	NC (6.0452 to NC)	2.7433 (1.9055 to 9.1335)	14.5544 (2.0370 to NC)	3.7782 (1.9384 to 6.1766)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0050		0.1524	
Hazard ratio (95% CI) vs Pd		1.5807 (1.1449 to 2.1826)		1.3744 (0.8875 to 2.1282)	
P-value		0.0054		0.1541	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_plne_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.1.3.6 Treatment emergent severe adverse event including death by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6326 (0.4582 to 0.8735)				
probability (95% CI)[b]					
2 Months	0.5152 (0.4128 to 0.6082)	0.3100 (0.2224 to 0.4016)	0.3878 (0.2532 to 0.5202)	0.3725 (0.2426 to 0.5024)	
4 Months	0.4242 (0.3261 to 0.5189)	0.2300 (0.1532 to 0.3162)	0.2857 (0.1680 to 0.4149)	0.2157 (0.1156 to 0.3360)	
6 Months	0.3518 (0.2591 to 0.4457)	0.1976 (0.1259 to 0.2812)	0.2653 (0.1518 to 0.3930)	0.1569 (0.0734 to 0.2688)	
8 Months	0.3204 (0.2308 to 0.4134)	0.1756 (0.1078 to 0.2571)	0.2653 (0.1518 to 0.3930)	0.1176 (0.0478 to 0.2217)	
10 Months	0.3204 (0.2308 to 0.4134)	0.1647 (0.0990 to 0.2449)	0.2653 (0.1518 to 0.3930)	0.0980 (0.0360 to 0.1973)	
12 Months	0.3204 (0.2308 to 0.4134)	0.1537 (0.0903 to 0.2326)	0.2653 (0.1518 to 0.3930)	0.0980 (0.0360 to 0.1973)	
14 Months	0.3204 (0.2308 to 0.4134)	0.1397 (0.0786 to 0.2180)	0.2653 (0.1518 to 0.3930)	0.0980 (0.0360 to 0.1973)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_plne_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.1.3.6 Treatment emergent severe adverse event including death by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3204 (0.2308 to 0.4134)	0.1397 (0.0786 to 0.2180)	0.2211 (0.1078 to 0.3597)	0.0980 (0.0360 to 0.1973)	
Number of patients at risk[b]					
2 Months	51	31	19	19	
4 Months	42	22	14	11	
6 Months	34	18	13	8	
8 Months	29	16	11	6	
10 Months	29	15	11	5	
12 Months	23	13	11	3	
14 Months	13	9	7	2	
16 Months	8	3	4	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.4 Subgroup analyses by gender
16.2.7.1.1.4.1 Treatment emergent adverse event by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	66 (97.1)	87 (98.9)	80 (98.8)	64 (100.0)	0.5631
Number (%) of patients censored	2 (2.9)	1 (1.1)	1 (1.2)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0986 to 0.1971)	0.0986 (0.0657 to 0.1314)	0.1314 (0.0986 to 0.1643)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.3285 (0.2300 to 0.7228)	0.1807 (0.1314 to 0.2628)	0.3285 (0.1971 to 0.4928)	0.1971 (0.1314 to 0.2957)	
75% quantile (95% CI)	1.0185 (0.7885 to 1.8727)	0.5914 (0.3285 to 0.7885)	0.7885 (0.5257 to 1.3470)	0.5257 (0.3614 to 0.7885)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0117		0.0910	
Hazard ratio (95% CI) vs Pd		1.5147 (1.0943 to 2.0967)		1.3369 (0.9536 to 1.8741)	
P-value		0.0123		0.0921	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_sex_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.4 Subgroup analyses by gender
16.2.7.1.1.4.1 Treatment emergent adverse event by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6602 (0.4769 to 0.9138)				
probability (95% CI)[b]					
2 Months	0.1493 (0.0766 to 0.2445)	0.0568 (0.0211 to 0.1187)	0.0779 (0.0318 to 0.1513)	0.0645 (0.0208 to 0.1438)	
4 Months	0.0597 (0.0193 to 0.1338)	0.0114 (0.0010 to 0.0552)	0.0390 (0.0104 to 0.0997)	0.0323 (0.0061 to 0.0994)	
6 Months	0.0398 (0.0087 to 0.1116)	0.0114 (0.0010 to 0.0552)	0.0390 (0.0104 to 0.0997)	0.0161 (0.0013 to 0.0760)	
8 Months	0.0398 (0.0087 to 0.1116)	0.0114 (0.0010 to 0.0552)	0.0260 (0.0049 to 0.0813)	0.0161 (0.0013 to 0.0760)	
10 Months	0.0199 (0.0018 to 0.0875)	0.0114 (0.0010 to 0.0552)	0.0260 (0.0049 to 0.0813)	0.0161 (0.0013 to 0.0760)	
12 Months	0.0199 (0.0018 to 0.0875)	0.0114 (0.0010 to 0.0552)	0.0130 (0.0011 to 0.0624)	0.0161 (0.0013 to 0.0760)	
14 Months	0.0199 (0.0018 to 0.0875)	0.0114 (0.0010 to 0.0552)	0.0130 (0.0011 to 0.0624)	0.0161 (0.0013 to 0.0760)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_sex_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.4 Subgroup analyses by gender
16.2.7.1.1.4.1 Treatment emergent adverse event by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0199 (0.0018 to 0.0875)	0.0114 (0.0010 to 0.0552)	0.0130 (0.0011 to 0.0624)	0.0161 (0.0013 to 0.0760)	
Number of patients at risk[b]					
2 Months	10	5	6	4	
4 Months	4	1	3	2	
6 Months	2	1	3	1	
8 Months	2	1	2	0	
10 Months	1	1	2	0	
12 Months	1	0	1	0	
14 Months	1	0	1	0	
16 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.4 Subgroup analyses by gender
16.2.7.1.1.4.2 Treatment emergent serious adverse event by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (55.9)	59 (67.0)	42 (51.9)	35 (54.7)	0.4511
Number (%) of patients censored	30 (44.1)	29 (33.0)	39 (48.1)	29 (45.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.5606 (0.2957 to 2.8255)	0.7228 (0.3285 to 1.3470)	1.3142 (0.5914 to 2.2669)	1.1499 (0.4600 to 2.7598)	
Median (95% CI)	6.0452 (2.9569 to NC)	5.1253 (2.1355 to 9.8234)	6.8994 (3.4497 to NC)	8.6078 (2.7926 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (11.0390 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.2158		0.8960	
Hazard ratio (95% CI) vs Pd		1.2928 (0.8598 to 1.9438)		1.0307 (0.6556 to 1.6202)	
P-value		0.2171		0.8958	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_sex_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.4 Subgroup analyses by gender
16.2.7.1.1.4.2 Treatment emergent serious adverse event by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.6912 (0.5667 to 0.7864)	0.6250 (0.5152 to 0.7167)	0.6667 (0.5528 to 0.7578)	0.6825 (0.5523 to 0.7821)	
4 Months	0.5735 (0.4476 to 0.6808)	0.5564 (0.4465 to 0.6528)	0.5912 (0.4759 to 0.6893)	0.5702 (0.4388 to 0.6817)	
6 Months	0.5132 (0.3887 to 0.6243)	0.4636 (0.3567 to 0.5637)	0.5130 (0.3984 to 0.6162)	0.5539 (0.4229 to 0.6666)	
8 Months	0.4669 (0.3446 to 0.5802)	0.4405 (0.3348 to 0.5409)	0.4987 (0.3843 to 0.6028)	0.5203 (0.3901 to 0.6354)	
10 Months	0.4669 (0.3446 to 0.5802)	0.3825 (0.2812 to 0.4829)	0.4987 (0.3843 to 0.6028)	0.4700 (0.3422 to 0.5876)	
12 Months	0.4669 (0.3446 to 0.5802)	0.3245 (0.2291 to 0.4234)	0.4836 (0.3693 to 0.5887)	0.4526 (0.3257 to 0.5710)	
14 Months	0.4483 (0.3262 to 0.5629)	0.3245 (0.2291 to 0.4234)	0.4663 (0.3516 to 0.5730)	0.4526 (0.3257 to 0.5710)	
16 Months	0.4184 (0.2924 to 0.5393)	0.3245 (0.2291 to 0.4234)	0.4663 (0.3516 to 0.5730)	0.4526 (0.3257 to 0.5710)	
Number of patients at risk[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_sex_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.4 Subgroup analyses by gender
16.2.7.1.1.4.2 Treatment emergent serious adverse event by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	47	55	53	43	
4 Months	39	48	47	35	
6 Months	34	40	38	33	
8 Months	30	38	33	31	
10 Months	29	33	33	28	
12 Months	25	26	28	24	
14 Months	16	18	13	17	
16 Months	8	9	7	5	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_sex_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.4 Subgroup analyses by gender
16.2.7.1.1.4.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (11.8)	8 (9.1)	11 (13.6)	3 (4.7)	0.2695
Number (%) of patients censored	60 (88.2)	80 (90.9)	70 (86.4)	61 (95.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (12.8789 to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.9671 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.5616		0.0529	
Hazard ratio (95% CI) vs Pd		0.7488 (0.2810 to 1.9953)		0.3036 (0.0845 to 1.0908)	
P-value		0.5630		0.0677	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_sex_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.4 Subgroup analyses by gender
16.2.7.1.1.4.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9409 (0.8503 to 0.9774)	0.9885 (0.9212 to 0.9984)	0.8876 (0.7950 to 0.9399)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9409 (0.8503 to 0.9774)	0.9651 (0.8957 to 0.9886)	0.8745 (0.7792 to 0.9305)	0.9841 (0.8926 to 0.9977)	
6 Months	0.9098 (0.8101 to 0.9585)	0.9410 (0.8639 to 0.9750)	0.8613 (0.7634 to 0.9207)	0.9674 (0.8760 to 0.9918)	
8 Months	0.8927 (0.7876 to 0.9474)	0.9275 (0.8455 to 0.9668)	0.8613 (0.7634 to 0.9207)	0.9674 (0.8760 to 0.9918)	
10 Months	0.8927 (0.7876 to 0.9474)	0.9133 (0.8261 to 0.9578)	0.8613 (0.7634 to 0.9207)	0.9674 (0.8760 to 0.9918)	
12 Months	0.8927 (0.7876 to 0.9474)	0.8985 (0.8065 to 0.9482)	0.8613 (0.7634 to 0.9207)	0.9674 (0.8760 to 0.9918)	
14 Months	0.8672 (0.7475 to 0.9326)	0.8985 (0.8065 to 0.9482)	0.8613 (0.7634 to 0.9207)	0.9674 (0.8760 to 0.9918)	
16 Months	0.8672 (0.7475 to 0.9326)	0.8985 (0.8065 to 0.9482)	0.8613 (0.7634 to 0.9207)	0.8983 (0.6414 to 0.9745)	
Number of patients at risk[b]					
2 Months	63	85	70	63	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_sex_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.4 Subgroup analyses by gender
16.2.7.1.1.4.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	61	80	66	59	
6 Months	55	72	58	54	
8 Months	52	68	51	52	
10 Months	49	63	50	50	
12 Months	41	55	44	45	
14 Months	27	35	25	33	
16 Months	15	17	9	11	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_sex_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.4 Subgroup analyses by gender
16.2.7.1.1.4.4 Treatment emergent mild adverse event by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	62 (91.2)	84 (95.5)	75 (92.6)	57 (89.1)	0.1094
Number (%) of patients censored	6 (8.8)	4 (4.5)	6 (7.4)	7 (10.9)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1643 (0.1314 to 0.3285)	0.1150 (0.0657 to 0.1314)	0.1643 (0.0986 to 0.2628)	0.0986 (0.0657 to 0.1643)	
Median (95% CI)	0.4928 (0.3285 to 0.8871)	0.2300 (0.1643 to 0.3285)	0.4271 (0.2957 to 0.7228)	0.2300 (0.1643 to 0.5257)	
75% quantile (95% CI)	1.6756 (0.8871 to 2.5626)	0.7392 (0.4600 to 1.0513)	1.1992 (0.8214 to 1.8398)	2.2669 (0.5585 to 5.0595)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0337		0.9053	
Hazard ratio (95% CI) vs Pd		1.4296 (1.0261 to 1.9917)		0.9789 (0.6881 to 1.3925)	
P-value		0.0347		0.9054	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_sex_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.4 Subgroup analyses by gender
16.2.7.1.1.4.4 Treatment emergent mild adverse event by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6995 (0.5021 to 0.9745)				
probability (95% CI)[b]					
2 Months	0.2093 (0.1202 to 0.3151)	0.1364 (0.0747 to 0.2165)	0.1447 (0.0771 to 0.2328)	0.2540 (0.1547 to 0.3655)	
4 Months	0.0966 (0.0396 to 0.1841)	0.0758 (0.0320 to 0.1446)	0.1013 (0.0459 to 0.1824)	0.1847 (0.0995 to 0.2905)	
6 Months	0.0773 (0.0273 to 0.1619)	0.0631 (0.0241 to 0.1289)	0.0868 (0.0364 to 0.1649)	0.1267 (0.0564 to 0.2265)	
8 Months	0.0773 (0.0273 to 0.1619)	0.0473 (0.0145 to 0.1112)	0.0651 (0.0214 to 0.1437)	0.0844 (0.0291 to 0.1778)	
10 Months	0.0579 (0.0165 to 0.1385)	0.0473 (0.0145 to 0.1112)	0.0651 (0.0214 to 0.1437)	0.0844 (0.0291 to 0.1778)	
12 Months	0.0579 (0.0165 to 0.1385)	0.0473 (0.0145 to 0.1112)	0.0434 (0.0096 to 0.1201)	0.0844 (0.0291 to 0.1778)	
14 Months	0.0579 (0.0165 to 0.1385)	0.0473 (0.0145 to 0.1112)	0.0434 (0.0096 to 0.1201)	0.0844 (0.0291 to 0.1778)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_sex_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.4 Subgroup analyses by gender
16.2.7.1.1.4.4 Treatment emergent mild adverse event by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0579 (0.0165 to 0.1385)	0.0237 (0.0027 to 0.0934)	0.0434 (0.0096 to 0.1201)	0.0844 (0.0291 to 0.1778)	
Number of patients at risk[b]					
2 Months	13	12	10	15	
4 Months	6	6	7	10	
6 Months	4	4	4	6	
8 Months	4	3	3	4	
10 Months	2	3	3	4	
12 Months	2	2	2	4	
14 Months	2	2	2	4	
16 Months	0	1	1	1	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_sex_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.4 Subgroup analyses by gender
16.2.7.1.1.4.5 Treatment emergent severe adverse event by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (63.2)	73 (83.0)	60 (74.1)	56 (87.5)	0.5346
Number (%) of patients censored	25 (36.8)	15 (17.0)	21 (25.9)	8 (12.5)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.7885 (0.2957 to 0.9856)	0.5257 (0.2957 to 0.6242)	0.5257 (0.3285 to 0.6899)	0.4928 (0.2957 to 0.5585)	
Median (95% CI)	2.8912 (1.5441 to 7.0308)	1.0185 (0.7556 to 1.9713)	1.1499 (0.7556 to 2.2669)	0.7885 (0.6242 to 0.9199)	
75% quantile (95% CI)	NC (14.5544 to NC)	4.2053 (2.1355 to 13.5359)	NC (3.4497 to NC)	2.8912 (0.9528 to 6.9651)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0057		0.0735	
Hazard ratio (95% CI) vs Pd		1.6961 (1.1614 to 2.4770)		1.3992 (0.9669 to 2.0249)	
P-value		0.0062		0.0749	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_sex_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.4 Subgroup analyses by gender
16.2.7.1.1.4.5 Treatment emergent severe adverse event by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.5896 (0.4037 to 0.8610)				
probability (95% CI)[b]					
2 Months	0.5294 (0.4047 to 0.6395)	0.3804 (0.2792 to 0.4808)	0.4315 (0.3212 to 0.5370)	0.2857 (0.1807 to 0.3996)	
4 Months	0.4412 (0.3215 to 0.5543)	0.2536 (0.1678 to 0.3482)	0.3300 (0.2294 to 0.4339)	0.2027 (0.1134 to 0.3103)	
6 Months	0.4102 (0.2928 to 0.5239)	0.2057 (0.1280 to 0.2964)	0.2665 (0.1748 to 0.3670)	0.1658 (0.0850 to 0.2699)	
8 Months	0.3773 (0.2624 to 0.4915)	0.1815 (0.1085 to 0.2696)	0.2532 (0.1635 to 0.3528)	0.1290 (0.0586 to 0.2279)	
10 Months	0.3773 (0.2624 to 0.4915)	0.1815 (0.1085 to 0.2696)	0.2532 (0.1635 to 0.3528)	0.1105 (0.0464 to 0.2061)	
12 Months	0.3773 (0.2624 to 0.4915)	0.1686 (0.0981 to 0.2554)	0.2532 (0.1635 to 0.3528)	0.1105 (0.0464 to 0.2061)	
14 Months	0.3773 (0.2624 to 0.4915)	0.1517 (0.0838 to 0.2383)	0.2532 (0.1635 to 0.3528)	0.1105 (0.0464 to 0.2061)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_sex_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.4 Subgroup analyses by gender
16.2.7.1.1.4.5 Treatment emergent severe adverse event by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3458 (0.2276 to 0.4668)	0.1517 (0.0838 to 0.2383)	0.2532 (0.1635 to 0.3528)	0.1105 (0.0464 to 0.2061)	
Number of patients at risk[b]					
2 Months	36	33	34	18	
4 Months	30	22	26	11	
6 Months	26	17	21	9	
8 Months	22	15	18	7	
10 Months	22	14	18	6	
12 Months	17	11	17	5	
14 Months	12	8	8	3	
16 Months	8	2	4	1	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_sex_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.4 Subgroup analyses by gender
16.2.7.1.1.4.6 Treatment emergent severe adverse event including death by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (64.7)	75 (85.2)	61 (75.3)	57 (89.1)	0.5391
Number (%) of patients censored	24 (35.3)	13 (14.8)	20 (24.7)	7 (10.9)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.7885 (0.2628 to 0.9856)	0.5257 (0.2628 to 0.5914)	0.5257 (0.3285 to 0.6242)	0.4928 (0.2957 to 0.5585)	
Median (95% CI)	2.8912 (1.5441 to 6.0452)	1.0021 (0.7556 to 1.9384)	1.1499 (0.7228 to 2.2669)	0.7885 (0.6242 to 0.9199)	
75% quantile (95% CI)	NC (14.5544 to NC)	4.0903 (2.1355 to 10.9076)	7.6222 (2.8255 to NC)	2.6940 (0.9528 to 6.9651)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0045		0.0657	
Hazard ratio (95% CI) vs Pd		1.7099 (1.1762 to 2.4858)		1.4086 (0.9763 to 2.0321)	
P-value		0.0050		0.0670	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.4 Subgroup analyses by gender
16.2.7.1.1.4.6 Treatment emergent severe adverse event including death by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.5848 (0.4023 to 0.8502)				
probability (95% CI)[b]					
2 Months	0.5294 (0.4047 to 0.6395)	0.3750 (0.2749 to 0.4747)	0.4250 (0.3158 to 0.5298)	0.2698 (0.1676 to 0.3826)	
4 Months	0.4412 (0.3215 to 0.5543)	0.2500 (0.1653 to 0.3438)	0.3250 (0.2257 to 0.4280)	0.1880 (0.1026 to 0.2933)	
6 Months	0.3955 (0.2796 to 0.5091)	0.2028 (0.1261 to 0.2926)	0.2625 (0.1720 to 0.3619)	0.1538 (0.0772 to 0.2547)	
8 Months	0.3638 (0.2508 to 0.4775)	0.1790 (0.1069 to 0.2661)	0.2494 (0.1609 to 0.3479)	0.1197 (0.0535 to 0.2146)	
10 Months	0.3638 (0.2508 to 0.4775)	0.1670 (0.0975 to 0.2527)	0.2494 (0.1609 to 0.3479)	0.1026 (0.0424 to 0.1939)	
12 Months	0.3638 (0.2508 to 0.4775)	0.1551 (0.0883 to 0.2391)	0.2494 (0.1609 to 0.3479)	0.1026 (0.0424 to 0.1939)	
14 Months	0.3638 (0.2508 to 0.4775)	0.1396 (0.0756 to 0.2229)	0.2494 (0.1609 to 0.3479)	0.1026 (0.0424 to 0.1939)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_sex_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.4 Subgroup analyses by gender
16.2.7.1.1.4.6 Treatment emergent severe adverse event including death by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3335 (0.2179 to 0.4532)	0.1396 (0.0756 to 0.2229)	0.2494 (0.1609 to 0.3479)	0.1026 (0.0424 to 0.1939)	
Number of patients at risk[b]					
2 Months	36	33	34	17	
4 Months	30	22	26	11	
6 Months	26	17	21	9	
8 Months	22	15	18	7	
10 Months	22	14	18	6	
12 Months	17	11	17	5	
14 Months	12	8	8	3	
16 Months	8	2	4	1	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_sex_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.5 Subgroup analyses by race
16.2.7.1.1.5.1 Treatment emergent adverse event by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	119 (97.5)	115 (99.1)	19 (100.0)	24 (100.0)	0.8677
Number (%) of patients censored	3 (2.5)	1 (0.9)	0 (0.0)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0986 to 0.1643)	0.0986 (0.0657 to 0.1314)	0.1643 (0.0329 to 0.2957)	0.0821 (0.0657 to 0.1314)	
Median (95% CI)	0.3285 (0.2628 to 0.4928)	0.1971 (0.1643 to 0.2628)	0.3285 (0.1643 to 0.8871)	0.1643 (0.0986 to 0.2957)	
75% quantile (95% CI)	0.9856 (0.7228 to 1.5113)	0.5585 (0.3943 to 0.7228)	0.8871 (0.3285 to 1.0513)	0.4271 (0.1643 to 0.8542)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0101		0.0984	
Hazard ratio (95% CI) vs Pd		1.4052 (1.0831 to 1.8229)		1.6958 (0.9004 to 3.1937)	
P-value		0.0104		0.1020	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_race_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.5 Subgroup analyses by race
16.2.7.1.1.5.1 Treatment emergent adverse event by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.7117 (0.5486 to 0.9233)				
probability (95% CI)[b]					
2 Months	0.1261 (0.0741 to 0.1924)	0.0696 (0.0325 to 0.1256)	0.0556 (0.0037 to 0.2242)	0.0417 (0.0030 to 0.1759)	
4 Months	0.0504 (0.0207 to 0.1001)	0.0261 (0.0071 to 0.0683)	0.0556 (0.0037 to 0.2242)	0.0417 (0.0030 to 0.1759)	
6 Months	0.0403 (0.0144 to 0.0881)	0.0174 (0.0034 to 0.0558)	0.0556 (0.0037 to 0.2242)	0.0417 (0.0030 to 0.1759)	
8 Months	0.0403 (0.0144 to 0.0881)	0.0087 (0.0008 to 0.0431)	0.0556 (0.0037 to 0.2242)	0.0417 (0.0030 to 0.1759)	
10 Months	0.0303 (0.0088 to 0.0754)	0.0087 (0.0008 to 0.0431)	0.0556 (0.0037 to 0.2242)	0.0417 (0.0030 to 0.1759)	
12 Months	0.0202 (0.0042 to 0.0621)	0.0087 (0.0008 to 0.0431)	0.0556 (0.0037 to 0.2242)	0.0417 (0.0030 to 0.1759)	
14 Months	0.0202 (0.0042 to 0.0621)	0.0087 (0.0008 to 0.0431)	0.0556 (0.0037 to 0.2242)	0.0417 (0.0030 to 0.1759)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_race_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.5 Subgroup analyses by race
16.2.7.1.1.5.1 Treatment emergent adverse event by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0202 (0.0042 to 0.0621)	0.0087 (0.0008 to 0.0431)	0.0556 (0.0037 to 0.2242)	0.0417 (0.0030 to 0.1759)	
Number of patients at risk[b]					
2 Months	15	8	1	1	
4 Months	6	3	1	0	
6 Months	4	2	1	0	
8 Months	4	1	0	0	
10 Months	3	1	0	0	
12 Months	2	0	0	0	
14 Months	2	0	0	0	
16 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_race_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.5 Subgroup analyses by race
16.2.7.1.1.5.2 Treatment emergent serious adverse event by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	69 (56.6)	75 (64.7)	7 (36.8)	11 (45.8)	0.7728
Number (%) of patients censored	53 (43.4)	41 (35.3)	12 (63.2)	13 (54.2)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.2813 (0.5585 to 1.9384)	0.7228 (0.4600 to 1.5113)	2.8255 (0.2957 to 14.5544)	3.3347 (0.1314 to 8.3450)	
Median (95% CI)	5.4209 (3.4497 to NC)	5.9795 (2.7598 to 9.8234)	14.5544 (2.8255 to 14.5544)	NC (4.3039 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	14.5544 (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.3527		0.6395	
Hazard ratio (95% CI) vs Pd		1.1684 (0.8416 to 1.6221)		1.2566 (0.4822 to 3.2749)	
P-value		0.3526		0.6402	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_race_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.5 Subgroup analyses by race
16.2.7.1.1.5.2 Treatment emergent serious adverse event by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.6721 (0.5812 to 0.7476)	0.6435 (0.5487 to 0.7234)	0.7895 (0.5319 to 0.9153)	0.7917 (0.5698 to 0.9075)	
4 Months	0.5643 (0.4714 to 0.6470)	0.5463 (0.4507 to 0.6321)	0.7368 (0.4789 to 0.8810)	0.7500 (0.5262 to 0.8791)	
6 Months	0.4874 (0.3956 to 0.5730)	0.4922 (0.3976 to 0.5800)	0.6842 (0.4279 to 0.8439)	0.6250 (0.4030 to 0.7842)	
8 Months	0.4513 (0.3603 to 0.5379)	0.4558 (0.3623 to 0.5444)	0.6842 (0.4279 to 0.8439)	0.6250 (0.4030 to 0.7842)	
10 Months	0.4513 (0.3603 to 0.5379)	0.4011 (0.3104 to 0.4899)	0.6842 (0.4279 to 0.8439)	0.5417 (0.3271 to 0.7143)	
12 Months	0.4415 (0.3507 to 0.5284)	0.3440 (0.2572 to 0.4323)	0.6842 (0.4279 to 0.8439)	0.5417 (0.3271 to 0.7143)	
14 Months	0.4205 (0.3299 to 0.5082)	0.3440 (0.2572 to 0.4323)	0.6842 (0.4279 to 0.8439)	0.5417 (0.3271 to 0.7143)	
16 Months	0.4205 (0.3299 to 0.5082)	0.3440 (0.2572 to 0.4323)	0.6842 (0.4279 to 0.8439)	0.5417 (0.3271 to 0.7143)	
Number of patients at risk[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_race_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.5 Subgroup analyses by race
16.2.7.1.1.5.2 Treatment emergent serious adverse event by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	81	74	15	19	
4 Months	68	61	14	18	
6 Months	56	54	13	15	
8 Months	47	50	13	15	
10 Months	46	44	13	13	
12 Months	42	34	10	12	
14 Months	27	24	1	8	
16 Months	14	10	0	4	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_race_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.5 Subgroup analyses by race
16.2.7.1.1.5.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (14.8)	9 (7.8)	0 (0.0)	2 (8.3)	0.9857
Number (%) of patients censored	104 (85.2)	107 (92.2)	19 (100.0)	22 (91.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.1951 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.9671 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.9671 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0639		0.3041	
Hazard ratio (95% CI) vs Pd		0.4773 (0.2144 to 1.0627)		NC (NC to NC)	
P-value		0.0701		0.9980	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_race_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.5 Subgroup analyses by race
16.2.7.1.1.5.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9010 (0.8322 to 0.9425)	0.9914 (0.9404 to 0.9988)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
4 Months	0.8925 (0.8220 to 0.9361)	0.9655 (0.9107 to 0.9869)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
6 Months	0.8663 (0.7910 to 0.9159)	0.9389 (0.8762 to 0.9704)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
8 Months	0.8564 (0.7789 to 0.9083)	0.9389 (0.8762 to 0.9704)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	
10 Months	0.8564 (0.7789 to 0.9083)	0.9287 (0.8623 to 0.9638)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	
12 Months	0.8564 (0.7789 to 0.9083)	0.9179 (0.8478 to 0.9566)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	
14 Months	0.8425 (0.7602 to 0.8985)	0.9179 (0.8478 to 0.9566)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	
16 Months	0.8425 (0.7602 to 0.8985)	0.9179 (0.8478 to 0.9566)	1.0000 (1.0000 to 1.0000)	0.7600 (0.2435 to 0.9481)	
Number of patients at risk[b]					
2 Months	108	115	19	23	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_race_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.5 Subgroup analyses by race
16.2.7.1.1.5.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	103	109	19	22	
6 Months	90	99	19	22	
8 Months	81	96	18	19	
10 Months	78	90	17	18	
12 Months	70	79	13	16	
14 Months	47	52	3	12	
16 Months	21	23	1	4	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_race_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.5 Subgroup analyses by race
16.2.7.1.1.5.4 Treatment emergent mild adverse event by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	112 (91.8)	106 (91.4)	19 (100.0)	24 (100.0)	0.6325
Number (%) of patients censored	10 (8.2)	10 (8.6)	0 (0.0)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1643 (0.1314 to 0.2628)	0.0986 (0.0657 to 0.1314)	0.1971 (0.0329 to 0.2957)	0.0821 (0.0657 to 0.1314)	
Median (95% CI)	0.4928 (0.3285 to 0.7228)	0.2464 (0.1643 to 0.3943)	0.3285 (0.1971 to 0.8871)	0.1643 (0.0986 to 0.2957)	
75% quantile (95% CI)	1.5770 (0.8871 to 2.2341)	1.0021 (0.6571 to 2.7269)	0.8871 (0.3285 to 1.0513)	0.6242 (0.1643 to 1.0185)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.3854		0.2208	
Hazard ratio (95% CI) vs Pd		1.1267 (0.8612 to 1.4740)		1.4771 (0.7881 to 2.7687)	
P-value		0.3842		0.2236	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_race_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.5 Subgroup analyses by race
16.2.7.1.1.5.4 Treatment emergent mild adverse event by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.1925 (0.1267 to 0.2686)	0.2155 (0.1460 to 0.2941)	0.0556 (0.0037 to 0.2242)	0.0833 (0.0144 to 0.2330)	
4 Months	0.1008 (0.0540 to 0.1647)	0.1446 (0.0876 to 0.2154)	0.0556 (0.0037 to 0.2242)	0.0417 (0.0030 to 0.1759)	
6 Months	0.0807 (0.0393 to 0.1412)	0.1133 (0.0625 to 0.1807)	0.0556 (0.0037 to 0.2242)	0.0417 (0.0030 to 0.1759)	
8 Months	0.0807 (0.0393 to 0.1412)	0.0793 (0.0371 to 0.1422)	0.0556 (0.0037 to 0.2242)	0.0417 (0.0030 to 0.1759)	
10 Months	0.0691 (0.0310 to 0.1282)	0.0793 (0.0371 to 0.1422)	0.0556 (0.0037 to 0.2242)	0.0417 (0.0030 to 0.1759)	
12 Months	0.0553 (0.0212 to 0.1136)	0.0793 (0.0371 to 0.1422)	0.0556 (0.0037 to 0.2242)	0.0417 (0.0030 to 0.1759)	
14 Months	0.0553 (0.0212 to 0.1136)	0.0793 (0.0371 to 0.1422)	0.0556 (0.0037 to 0.2242)	0.0417 (0.0030 to 0.1759)	
16 Months	0.0553 (0.0212 to 0.1136)	0.0661 (0.0277 to 0.1277)	0.0556 (0.0037 to 0.2242)	0.0417 (0.0030 to 0.1759)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.5 Subgroup analyses by race
16.2.7.1.1.5.4 Treatment emergent mild adverse event by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	21	25	1	2	
4 Months	11	15	1	1	
6 Months	7	10	1	0	
8 Months	7	7	0	0	
10 Months	5	7	0	0	
12 Months	4	6	0	0	
14 Months	4	6	0	0	
16 Months	1	2	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_race_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.5 Subgroup analyses by race
16.2.7.1.1.5.5 Treatment emergent severe adverse event by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	84 (68.9)	100 (86.2)	14 (73.7)	22 (91.7)	0.4402
Number (%) of patients censored	38 (31.1)	16 (13.8)	5 (26.3)	2 (8.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.5585 (0.3285 to 0.7556)	0.4928 (0.2957 to 0.5585)	1.1499 (0.1643 to 1.9384)	0.5421 (0.1314 to 0.7228)	
Median (95% CI)	1.5441 (0.8542 to 2.8255)	0.8542 (0.7228 to 1.3142)	2.8255 (1.1499 to 14.5544)	0.8049 (0.5585 to 1.9055)	
75% quantile (95% CI)	NC (4.9610 to NC)	3.9754 (2.0370 to 6.9651)	14.5544 (2.8255 to 14.5544)	2.5791 (0.8871 to 8.3450)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0078		0.0242	
Hazard ratio (95% CI) vs Pd		1.4817 (1.1070 to 1.9833)		2.1556 (1.0892 to 4.2662)	
P-value		0.0082		0.0274	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_race_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.5 Subgroup analyses by race
16.2.7.1.1.5.5 Treatment emergent severe adverse event by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6749 (0.5042 to 0.9034)		0.4639 (0.2344 to 0.9181)		
probability (95% CI)[b]					
2 Months	0.4719 (0.3809 to 0.5575)	0.3391 (0.2543 to 0.4257)	0.5263 (0.2872 to 0.7188)	0.2917 (0.1295 to 0.4758)	
4 Months	0.3643 (0.2794 to 0.4494)	0.2421 (0.1682 to 0.3236)	0.4737 (0.2444 to 0.6728)	0.1250 (0.0314 to 0.2865)	
6 Months	0.3213 (0.2399 to 0.4053)	0.1883 (0.1226 to 0.2649)	0.3684 (0.1652 to 0.5748)	0.1250 (0.0314 to 0.2865)	
8 Months	0.3034 (0.2236 to 0.3869)	0.1524 (0.0935 to 0.2247)	0.3158 (0.1291 to 0.5225)	0.1250 (0.0314 to 0.2865)	
10 Months	0.3034 (0.2236 to 0.3869)	0.1524 (0.0935 to 0.2247)	0.3158 (0.1291 to 0.5225)	0.0833 (0.0144 to 0.2330)	
12 Months	0.3034 (0.2236 to 0.3869)	0.1423 (0.0852 to 0.2135)	0.3158 (0.1291 to 0.5225)	0.0833 (0.0144 to 0.2330)	
14 Months	0.3034 (0.2236 to 0.3869)	0.1281 (0.0727 to 0.1996)	0.3158 (0.1291 to 0.5225)	0.0833 (0.0144 to 0.2330)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_race_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.5 Subgroup analyses by race
16.2.7.1.1.5.5 Treatment emergent severe adverse event by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3034 (0.2236 to 0.3869)	0.1281 (0.0727 to 0.1996)	0.3158 (0.1291 to 0.5225)	0.0833 (0.0144 to 0.2330)	
Number of patients at risk[b]					
2 Months	57	39	10	7	
4 Months	44	27	9	3	
6 Months	37	21	7	3	
8 Months	31	17	6	3	
10 Months	31	16	6	2	
12 Months	28	13	5	1	
14 Months	18	8	1	1	
16 Months	11	3	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.5 Subgroup analyses by race
16.2.7.1.1.5.6 Treatment emergent severe adverse event including death by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	86 (70.5)	101 (87.1)	14 (73.7)	22 (91.7)	0.4131
Number (%) of patients censored	36 (29.5)	15 (12.9)	5 (26.3)	2 (8.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.5257 (0.3285 to 0.7556)	0.4928 (0.2957 to 0.5585)	1.1499 (0.1643 to 1.9384)	0.5421 (0.1314 to 0.7228)	
Median (95% CI)	1.5277 (0.8214 to 2.8255)	0.8542 (0.7228 to 1.3142)	2.8255 (1.1499 to 14.5544)	0.8049 (0.5585 to 1.9055)	
75% quantile (95% CI)	NC (4.6653 to NC)	3.9754 (2.0370 to 6.9651)	14.5544 (2.8255 to 14.5544)	2.5791 (0.8871 to 8.3450)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0093		0.0242	
Hazard ratio (95% CI) vs Pd		1.4645 (1.0968 to 1.9554)		2.1556 (1.0892 to 4.2662)	
P-value		0.0097		0.0274	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.5 Subgroup analyses by race
16.2.7.1.1.5.6 Treatment emergent severe adverse event including death by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6828 (0.5114 to 0.9117)		0.4639 (0.2344 to 0.9181)		
probability (95% CI)[b]					
2 Months	0.4672 (0.3768 to 0.5525)	0.3391 (0.2543 to 0.4257)	0.5263 (0.2872 to 0.7188)	0.2917 (0.1295 to 0.4758)	
4 Months	0.3607 (0.2765 to 0.4453)	0.2421 (0.1682 to 0.3236)	0.4737 (0.2444 to 0.6728)	0.1250 (0.0314 to 0.2865)	
6 Months	0.3103 (0.2305 to 0.3934)	0.1883 (0.1226 to 0.2649)	0.3684 (0.1652 to 0.5748)	0.1250 (0.0314 to 0.2865)	
8 Months	0.2931 (0.2148 to 0.3755)	0.1524 (0.0935 to 0.2247)	0.3158 (0.1291 to 0.5225)	0.1250 (0.0314 to 0.2865)	
10 Months	0.2931 (0.2148 to 0.3755)	0.1435 (0.0864 to 0.2145)	0.3158 (0.1291 to 0.5225)	0.0833 (0.0144 to 0.2330)	
12 Months	0.2931 (0.2148 to 0.3755)	0.1339 (0.0788 to 0.2037)	0.3158 (0.1291 to 0.5225)	0.0833 (0.0144 to 0.2330)	
14 Months	0.2931 (0.2148 to 0.3755)	0.1205 (0.0674 to 0.1902)	0.3158 (0.1291 to 0.5225)	0.0833 (0.0144 to 0.2330)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_race_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.5 Subgroup analyses by race
16.2.7.1.1.5.6 Treatment emergent severe adverse event including death by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.2931 (0.2148 to 0.3755)	0.1205 (0.0674 to 0.1902)	0.3158 (0.1291 to 0.5225)	0.0833 (0.0144 to 0.2330)	
Number of patients at risk[b]					
2 Months	57	39	10	7	
4 Months	44	27	9	3	
6 Months	37	21	7	3	
8 Months	31	17	6	3	
10 Months	31	16	6	2	
12 Months	28	13	5	1	
14 Months	18	8	1	1	
16 Months	11	3	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.6 Subgroup analyses by ethnic origin
16.2.7.1.1.6.1 Treatment emergent adverse event by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (100.0)	4 (100.0)	127 (97.7)	127 (99.2)	0.6190
Number (%) of patients censored	0 (0.0)	0 (0.0)	3 (2.3)	1 (0.8)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.1314 to 0.4600)	0.0821 (0.0657 to 0.2628)	0.1643 (0.1314 to 0.1971)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.1971 (0.1314 to 0.4600)	0.1807 (0.0657 to 0.7885)	0.3614 (0.2957 to 0.5257)	0.1807 (0.1643 to 0.2300)	
75% quantile (95% CI)	0.4600 (0.1314 to 0.4600)	0.5257 (0.0657 to 0.7885)	0.9199 (0.7885 to 1.4456)	0.5421 (0.3614 to 0.7556)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.9089		0.0033	
Hazard ratio (95% CI) vs Pd		0.9096 (0.1796 to 4.6060)		1.4503 (1.1303 to 1.8607)	
P-value		0.9088		0.0035	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_ethn_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.6 Subgroup analyses by ethnic origin
16.2.7.1.1.6.1 Treatment emergent adverse event by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.6895 (0.5374 to 0.8847)		
probability (95% CI)[b]					
2 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.1102 (0.0634 to 0.1716)	0.0703 (0.0345 to 0.1232)	
4 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.0551 (0.0243 to 0.1043)	0.0234 (0.0064 to 0.0616)	
6 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.0459 (0.0183 to 0.0932)	0.0156 (0.0031 to 0.0504)	
8 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.0367 (0.0128 to 0.0818)	0.0078 (0.0007 to 0.0390)	
10 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.0276 (0.0079 to 0.0699)	0.0078 (0.0007 to 0.0390)	
12 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.0184 (0.0037 to 0.0574)	0.0078 (0.0007 to 0.0390)	
14 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.0184 (0.0037 to 0.0574)	0.0078 (0.0007 to 0.0390)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.6 Subgroup analyses by ethnic origin
16.2.7.1.1.6.1 Treatment emergent adverse event by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.0184 (0.0037 to 0.0574)	0.0078 (0.0007 to 0.0390)	
Number of patients at risk[b]					
2 Months	0	0	14	9	
4 Months	0	0	7	3	
6 Months	0	0	5	2	
8 Months	0	0	4	1	
10 Months	0	0	3	1	
12 Months	0	0	2	0	
14 Months	0	0	2	0	
16 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.6 Subgroup analyses by ethnic origin
16.2.7.1.1.6.2 Treatment emergent serious adverse event by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (66.7)	3 (75.0)	69 (53.1)	77 (60.2)	0.9450
Number (%) of patients censored	1 (33.3)	1 (25.0)	61 (46.9)	51 (39.8)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.3614 (0.3614 to NC)	0.2464 (0.0657 to 1.3142)	1.5441 (1.0185 to 2.2669)	0.8542 (0.4928 to 1.9713)	
Median (95% CI)	0.4271 (0.3614 to NC)	0.8706 (0.0657 to NC)	6.8994 (4.0739 to NC)	6.9651 (4.0411 to 10.9076)	
75% quantile (95% CI)	NC (0.3614 to NC)	NC (0.0657 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.9549		0.3664	
Hazard ratio (95% CI) vs Pd		1.0531 (0.1741 to 6.3698)		1.1613 (0.8391 to 1.6073)	
P-value		0.9551		0.3670	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.6 Subgroup analyses by ethnic origin
16.2.7.1.1.6.2 Treatment emergent serious adverse event by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.6923 (0.6052 to 0.7639)	0.6719 (0.5832 to 0.7458)	
4 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.5912 (0.5014 to 0.6702)	0.5927 (0.5022 to 0.6721)	
6 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.5194 (0.4298 to 0.6016)	0.5284 (0.4380 to 0.6108)	
8 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.4859 (0.3966 to 0.5692)	0.4959 (0.4060 to 0.5793)	
10 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.4859 (0.3966 to 0.5692)	0.4308 (0.3433 to 0.5152)	
12 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.4769 (0.3877 to 0.5606)	0.3887 (0.3033 to 0.4732)	
14 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.4667 (0.3774 to 0.5510)	0.3887 (0.3033 to 0.4732)	
16 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.4473 (0.3541 to 0.5360)	0.3887 (0.3033 to 0.4732)	
Number of patients at risk[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.6 Subgroup analyses by ethnic origin
16.2.7.1.1.6.2 Treatment emergent serious adverse event by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1	1	89	86	
4 Months	1	1	76	74	
6 Months	1	1	64	65	
8 Months	1	1	55	61	
10 Months	1	1	54	53	
12 Months	0	1	47	43	
14 Months	0	1	26	30	
16 Months	0	1	13	13	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.6 Subgroup analyses by ethnic origin
16.2.7.1.1.6.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (66.7)	0 (0.0)	15 (11.5)	11 (8.6)	0.9874
Number (%) of patients censored	1 (33.3)	4 (100.0)	115 (88.5)	117 (91.4)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.3614 (0.3614 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	0.4271 (0.3614 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (0.3614 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0701		0.3503	
Hazard ratio (95% CI) vs Pd		NC (NC to NC)		0.6916 (0.3176 to 1.5060)	
P-value		0.9986		0.3530	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.6 Subgroup analyses by ethnic origin
16.2.7.1.1.6.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.3333 (0.0090 to 0.7741)	1.0000 (1.0000 to 1.0000)	0.9225 (0.8608 to 0.9575)	0.9922 (0.9458 to 0.9989)	
4 Months	0.3333 (0.0090 to 0.7741)	1.0000 (1.0000 to 1.0000)	0.9225 (0.8608 to 0.9575)	0.9686 (0.9184 to 0.9881)	
6 Months	0.3333 (0.0090 to 0.7741)	1.0000 (1.0000 to 1.0000)	0.8981 (0.8309 to 0.9395)	0.9441 (0.8864 to 0.9730)	
8 Months	0.3333 (0.0090 to 0.7741)	1.0000 (1.0000 to 1.0000)	0.8888 (0.8193 to 0.9327)	0.9352 (0.8744 to 0.9671)	
10 Months	0.3333 (0.0090 to 0.7741)	1.0000 (1.0000 to 1.0000)	0.8888 (0.8193 to 0.9327)	0.9256 (0.8616 to 0.9607)	
12 Months	0.3333 (0.0090 to 0.7741)	1.0000 (1.0000 to 1.0000)	0.8888 (0.8193 to 0.9327)	0.9156 (0.8482 to 0.9538)	
14 Months	0.3333 (0.0090 to 0.7741)	1.0000 (1.0000 to 1.0000)	0.8752 (0.7996 to 0.9236)	0.9156 (0.8482 to 0.9538)	
16 Months	0.3333 (0.0090 to 0.7741)	1.0000 (1.0000 to 1.0000)	0.8752 (0.7996 to 0.9236)	0.8816 (0.7696 to 0.9412)	
Number of patients at risk[b]					
2 Months	1	4	118	126	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_ethn_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.6 Subgroup analyses by ethnic origin
16.2.7.1.1.6.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	1	4	114	119	
6 Months	1	4	101	109	
8 Months	1	4	91	103	
10 Months	1	4	87	96	
12 Months	0	4	75	83	
14 Months	0	4	46	56	
16 Months	0	1	21	24	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_ethn_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.6 Subgroup analyses by ethnic origin
16.2.7.1.1.6.4 Treatment emergent mild adverse event by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (100.0)	4 (100.0)	120 (92.3)	118 (92.2)	0.4294
Number (%) of patients censored	0 (0.0)	0 (0.0)	10 (7.7)	10 (7.8)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.1314 to 0.4600)	0.0821 (0.0657 to 0.2628)	0.1971 (0.1314 to 0.2957)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.1971 (0.1314 to 0.4600)	0.1807 (0.0657 to 5.9138)	0.4928 (0.3285 to 0.7228)	0.1971 (0.1643 to 0.2957)	
75% quantile (95% CI)	0.4600 (0.1314 to 0.4600)	3.0883 (0.0657 to 5.9138)	1.4456 (0.8871 to 1.8727)	0.8378 (0.5585 to 2.2998)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.9089		0.2036	
Hazard ratio (95% CI) vs Pd		0.9096 (0.1796 to 4.6060)		1.1814 (0.9134 to 1.5280)	
P-value		0.9088		0.2041	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_ethn_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.6 Subgroup analyses by ethnic origin
16.2.7.1.1.6.4 Treatment emergent mild adverse event by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	IPd (N=4)	Pd (N=130)	IPd (N=128)	p-value of treatment-by-sub group interaction[c]
probability (95% CI)[b]					
2 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.1721 (0.1118 to 0.2434)	0.2031 (0.1385 to 0.2766)	
4 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.0947 (0.0507 to 0.1550)	0.1303 (0.0785 to 0.1954)	
6 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.0852 (0.0437 to 0.1440)	0.1035 (0.0575 to 0.1650)	
8 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.0745 (0.0358 to 0.1321)	0.0725 (0.0341 to 0.1300)	
10 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.0639 (0.0283 to 0.1198)	0.0725 (0.0341 to 0.1300)	
12 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.0511 (0.0194 to 0.1060)	0.0725 (0.0341 to 0.1300)	
14 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.0511 (0.0194 to 0.1060)	0.0725 (0.0341 to 0.1300)	
16 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.0511 (0.0194 to 0.1060)	0.0604 (0.0255 to 0.1168)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_ethn_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.6 Subgroup analyses by ethnic origin
16.2.7.1.1.6.4 Treatment emergent mild adverse event by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	0	1	20	26	
4 Months	0	1	11	15	
6 Months	0	0	8	10	
8 Months	0	0	7	7	
10 Months	0	0	5	7	
12 Months	0	0	4	6	
14 Months	0	0	4	6	
16 Months	0	0	1	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_ethn_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.6 Subgroup analyses by ethnic origin
16.2.7.1.1.6.5 Treatment emergent severe adverse event by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (33.3)	3 (75.0)	89 (68.5)	111 (86.7)	0.9225
Number (%) of patients censored	2 (66.7)	1 (25.0)	41 (31.5)	17 (13.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.3285 (0.3285 to NC)	0.6078 (0.4271 to 1.3142)	0.6242 (0.4600 to 0.7885)	0.4928 (0.3285 to 0.5585)	
Median (95% CI)	NC (0.3285 to NC)	1.0513 (0.4271 to NC)	1.9384 (1.1499 to 2.9569)	0.8049 (0.6899 to 0.9528)	
75% quantile (95% CI)	NC (0.3285 to NC)	NC (0.4271 to NC)	NC (7.0308 to NC)	3.6468 (1.9713 to 6.1766)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.8144		0.0006	
Hazard ratio (95% CI) vs Pd		1.3161 (0.1319 to 13.1277)		1.6256 (1.2283 to 2.1515)	
P-value		0.8149		0.0007	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.6 Subgroup analyses by ethnic origin
16.2.7.1.1.6.5 Treatment emergent severe adverse event by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.6152 (0.4648 to 0.8141)		
probability (95% CI)[b]					
2 Months	0.6667 (0.0541 to 0.9452)	0.2500 (0.0089 to 0.6653)	0.4846 (0.3964 to 0.5671)	0.3281 (0.2486 to 0.4098)	
4 Months	0.6667 (0.0541 to 0.9452)	0.2500 (0.0089 to 0.6653)	0.3846 (0.3013 to 0.4672)	0.2252 (0.1571 to 0.3009)	
6 Months	0.6667 (0.0541 to 0.9452)	0.2500 (0.0089 to 0.6653)	0.3447 (0.2641 to 0.4266)	0.1850 (0.1230 to 0.2570)	
8 Months	0.6667 (0.0541 to 0.9452)	0.2500 (0.0089 to 0.6653)	0.3196 (0.2409 to 0.4009)	0.1528 (0.0965 to 0.2210)	
10 Months	0.6667 (0.0541 to 0.9452)	0.2500 (0.0089 to 0.6653)	0.3196 (0.2409 to 0.4009)	0.1448 (0.0901 to 0.2119)	
12 Months	0.6667 (0.0541 to 0.9452)	0.2500 (0.0089 to 0.6653)	0.3196 (0.2409 to 0.4009)	0.1357 (0.0827 to 0.2019)	
14 Months	0.6667 (0.0541 to 0.9452)	0.2500 (0.0089 to 0.6653)	0.3196 (0.2409 to 0.4009)	0.1221 (0.0705 to 0.1889)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.6 Subgroup analyses by ethnic origin
16.2.7.1.1.6.5 Treatment emergent severe adverse event by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.6667 (0.0541 to 0.9452)	0.2500 (0.0089 to 0.6653)	0.3008 (0.2197 to 0.3859)	0.1221 (0.0705 to 0.1889)	
Number of patients at risk[b]					
2 Months	1	1	63	42	
4 Months	1	1	50	28	
6 Months	1	1	43	23	
8 Months	1	1	36	19	
10 Months	1	1	36	17	
12 Months	0	1	32	13	
14 Months	0	1	18	8	
16 Months	0	0	10	3	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_ethn_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.6 Subgroup analyses by ethnic origin
16.2.7.1.1.6.6 Treatment emergent severe adverse event including death by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (66.7)	3 (75.0)	90 (69.2)	112 (87.5)	0.5360
Number (%) of patients censored	1 (33.3)	1 (25.0)	40 (30.8)	16 (12.5)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.3285 (0.3285 to NC)	0.6078 (0.4271 to 1.3142)	0.6242 (0.4600 to 0.7885)	0.4928 (0.3285 to 0.5585)	
Median (95% CI)	0.3614 (0.3285 to NC)	1.0513 (0.4271 to NC)	1.9384 (1.1499 to 2.9569)	0.8049 (0.6899 to 0.9528)	
75% quantile (95% CI)	NC (0.3285 to NC)	NC (0.4271 to NC)	NC (7.0308 to NC)	3.6468 (1.9713 to 6.1766)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.6552		0.0006	
Hazard ratio (95% CI) vs Pd		0.6624 (0.1074 to 4.0844)		1.6271 (1.2311 to 2.1505)	
P-value		0.6572		0.0006	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_ethn_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.6 Subgroup analyses by ethnic origin
16.2.7.1.1.6.6 Treatment emergent severe adverse event including death by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.6146 (0.4650 to 0.8123)		
probability (95% CI)[b]					
2 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.4846 (0.3964 to 0.5671)	0.3281 (0.2486 to 0.4098)	
4 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.3846 (0.3013 to 0.4672)	0.2252 (0.1571 to 0.3009)	
6 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.3375 (0.2576 to 0.4190)	0.1850 (0.1230 to 0.2570)	
8 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.3130 (0.2350 to 0.3938)	0.1528 (0.0965 to 0.2210)	
10 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.3130 (0.2350 to 0.3938)	0.1367 (0.0837 to 0.2027)	
12 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.3130 (0.2350 to 0.3938)	0.1282 (0.0768 to 0.1931)	
14 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.3130 (0.2350 to 0.3938)	0.1154 (0.0656 to 0.1805)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_ethn_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.6 Subgroup analyses by ethnic origin
16.2.7.1.1.6.6 Treatment emergent severe adverse event including death by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3333 (0.0090 to 0.7741)	0.2500 (0.0089 to 0.6653)	0.2946 (0.2144 to 0.3790)	0.1154 (0.0656 to 0.1805)	
Number of patients at risk[b]					
2 Months	1	1	63	42	
4 Months	1	1	50	28	
6 Months	1	1	43	23	
8 Months	1	1	36	19	
10 Months	1	1	36	17	
12 Months	0	1	32	13	
14 Months	0	1	18	8	
16 Months	0	0	10	3	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_ethn_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.1 Treatment emergent adverse event by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Number (%) of events	71 (95.9)	54 (98.2)	20 (100.0)	28 (100.0)	5 (100.0)	7 (100.0)	15 (100.0)	21 (100.0)	35 (100.0)	41 (100.0)	0.4508
Number (%) of patients censored	3 (4.1)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months											
25% quantile (95% CI)	0.1314 (0.0657 to 0.1314)	0.0657 (0.0329 to 0.0986)	0.1314 (0.0329 to 0.2628)	0.1314 (0.0329 to 0.1971)	0.1971 (0.0657 to 0.4600)	0.0986 (0.0329 to 0.1971)	0.1643 (0.0657 to 0.2957)	0.0657 (0.0657 to 0.1314)	0.2628 (0.0986 to 0.3285)	0.1314 (0.0657 to 0.1643)	
Median (95% CI)	0.3285 (0.1314 to 0.5257)	0.1807 (0.0986 to 0.2628)	0.2957 (0.1314 to 0.8871)	0.2628 (0.1643 to 0.5914)	0.2957 (0.0657 to 0.8871)	0.1971 (0.0329 to 0.4271)	0.3285 (0.1643 to 0.8871)	0.1314 (0.0657 to 0.1971)	0.4600 (0.2957 to 0.7885)	0.1971 (0.1314 to 0.4928)	
75% quantile (95% CI)	1.0185 (0.6242 to 2.2341)	0.4928 (0.2628 to 0.7885)	0.9363 (0.2957 to 1.7741)	1.0513 (0.2628 to 3.3183)	0.4600 (0.0657 to 0.8871)	0.4271 (0.0986 to 0.7228)	0.9199 (0.3285 to 6.5051)	0.2300 (0.1643 to 0.8542)	0.8542 (0.5914 to 1.8727)	0.5749 (0.3285 to 0.8214)	
Comparison vs. Pd											

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_greg_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.1 Treatment emergent adverse event by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Log-Rank test p-value[a] vs Pd		0.0199		0.4686		0.4498		0.0413		0.0521	
Hazard ratio (95% CI) vs Pd		1.5393 (1.0679 to 2.2189)		0.8006 (0.4382 to 1.4627)		1.6078 (0.4641 to 5.5693)		2.0348 (1.0156 to 4.0767)		1.5884 (0.9919 to 2.5435)	
P-value		0.0208		0.4694		0.4538		0.0451		0.0541	
Hazard ratio inverted (95% CI) vs IPd	0.6496 (0.4507 to 0.9364)						0.4915 (0.2453 to 0.9846)				
probability (95% CI)[b]											
2 Months	0.1690 (0.0929 to 0.2645)	0.0370 (0.0069 to 0.1129)	0.0500 (0.0035 to 0.2053)	0.1429 (0.0450 to 0.2950)	0.2000 (0.0084 to 0.5819)	0.1429 (0.0071 to 0.4649)	0.0667 (0.0043 to 0.2603)	0.0476 (0.0033 to 0.1970)	0.0909 (0.0233 to 0.2167)	0.0500 (0.0091 to 0.1483)	
4 Months	0.0704 (0.0260 to 0.1452)	0.0185 (0.0015 to 0.0862)	0.0500 (0.0035 to 0.2053)	0.0714 (0.0126 to 0.2037)	0.2000 (0.0084 to 0.5819)	0.1429 (0.0071 to 0.4649)	0.0667 (0.0043 to 0.2603)	0.0476 (0.0033 to 0.1970)	0.0303 (0.0023 to 0.1335)	0.0250 (0.0020 to 0.1127)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_greg_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.1 Treatment emergent adverse event by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
6 Months	0.0528 (0.0157 to 0.1248)	0.0185 (0.0015 to 0.0862)	0.0500 (0.0035 to 0.2053)	0.0357 (0.0026 to 0.1541)	0.2000 (0.0084 to 0.5819)	0.1429 (0.0071 to 0.4649)	0.0667 (0.0043 to 0.2603)	0.0476 (0.0033 to 0.1970)	0.0303 (0.0023 to 0.1335)	0.0250 (0.0020 to 0.1127)	
8 Months	0.0528 (0.0157 to 0.1248)	0.0185 (0.0015 to 0.0862)	0.0500 (0.0035 to 0.2053)	0.0357 (0.0026 to 0.1541)	0.2000 (0.0084 to 0.5819)	0.1429 (0.0071 to 0.4649)	0.0667 (0.0043 to 0.2603)	0.0476 (0.0033 to 0.1970)	0.0303 (0.0023 to 0.1335)	0.0250 (0.0020 to 0.1127)	
10 Months	0.0528 (0.0157 to 0.1248)	0.0185 (0.0015 to 0.0862)	0.0500 (0.0035 to 0.2053)	0.0357 (0.0026 to 0.1541)	0.2000 (0.0084 to 0.5819)	0.1429 (0.0071 to 0.4649)	0.0667 (0.0043 to 0.2603)	0.0476 (0.0033 to 0.1970)	0.0303 (0.0023 to 0.1335)	0.0250 (0.0020 to 0.1127)	
12 Months	0.0352 (0.0073 to 0.1030)	0.0185 (0.0015 to 0.0862)	0.0500 (0.0035 to 0.2053)	0.0357 (0.0026 to 0.1541)	0.2000 (0.0084 to 0.5819)	0.1429 (0.0071 to 0.4649)	0.0667 (0.0043 to 0.2603)	0.0476 (0.0033 to 0.1970)	0.0303 (0.0023 to 0.1335)	0.0250 (0.0020 to 0.1127)	
14 Months	0.0352 (0.0073 to 0.1030)	0.0185 (0.0015 to 0.0862)	0.0500 (0.0035 to 0.2053)	0.0357 (0.0026 to 0.1541)	0.2000 (0.0084 to 0.5819)	0.1429 (0.0071 to 0.4649)	0.0667 (0.0043 to 0.2603)	0.0476 (0.0033 to 0.1970)	0.0303 (0.0023 to 0.1335)	0.0250 (0.0020 to 0.1127)	
16 Months	0.0352 (0.0073 to 0.1030)	0.0185 (0.0015 to 0.0862)	0.0500 (0.0035 to 0.2053)	0.0357 (0.0026 to 0.1541)	0.2000 (0.0084 to 0.5819)	0.1429 (0.0071 to 0.4649)	0.0667 (0.0043 to 0.2603)	0.0476 (0.0033 to 0.1970)	0.0303 (0.0023 to 0.1335)	0.0250 (0.0020 to 0.1127)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_greg_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.1 Treatment emergent adverse event by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Number of patients at risk[b]											
2 Months	12	2	0	4	0	0	1	1	3	2	
4 Months	5	1	0	2	0	0	1	0	1	0	
6 Months	3	1	0	1	0	0	1	0	1	0	
8 Months	3	1	0	0	0	0	0	0	1	0	
10 Months	3	1	0	0	0	0	0	0	0	0	
12 Months	2	0	0	0	0	0	0	0	0	0	
14 Months	2	0	0	0	0	0	0	0	0	0	
16 Months	0	0	0	0	0	0	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.2 Treatment emergent serious adverse event by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Number (%) of events	41 (55.4)	35 (63.6)	13 (65.0)	17 (60.7)	2 (40.0)	5 (71.4)	4 (26.7)	9 (42.9)	20 (57.1)	28 (68.3)	0.7361
Number (%) of patients censored	33 (44.6)	20 (36.4)	7 (35.0)	11 (39.3)	3 (60.0)	2 (28.6)	11 (73.3)	12 (57.1)	15 (42.9)	13 (31.7)	
Kaplan-Meier estimates of TEAE in months											
25% quantile (95% CI)	1.1828 (0.5585 to 2.9569)	0.6571 (0.3285 to 1.2813)	0.7392 (0.1314 to 1.9384)	1.4127 (0.1643 to 4.3039)	0.2957 (0.1971 to NC)	0.4271 (0.3614 to 2.0041)	14.5544 (1.5770 to 14.5544)	4.3039 (0.1314 to 9.5934)	1.2813 (0.2957 to 2.0370)	0.7392 (0.4271 to 3.3183)	
Median (95% CI)	6.0452 (3.4497 to NC)	4.1725 (1.2813 to 11.0062)	3.1869 (0.7228 to NC)	7.9343 (1.5770 to NC)	NC (0.1971 to NC)	2.0041 (0.3614 to NC)	14.5544 (2.8255 to 14.5544)	NC (4.3039 to NC)	4.3696 (1.6756 to NC)	4.0411 (2.6940 to 10.9076)	
75% quantile (95% CI)	NC (NC to NC)	NC (11.0062 to NC)	NC (3.6140 to NC)	NC (10.5462 to NC)	NC (0.1971 to NC)	NC (1.0185 to NC)	14.5544 (NC to NC)	NC (NC to NC)	NC (7.0308 to NC)	NC (6.9651 to NC)	
Comparison vs. Pd											

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.2 Treatment emergent serious adverse event by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Log-Rank test p-value[a] vs Pd		0.2751		0.6216		0.5750		0.3929		0.6849	
Hazard ratio (95% CI) vs Pd		1.2850 (0.8181 to 2.0181)		0.8336 (0.4044 to 1.7186)		1.5970 (0.3063 to 8.3268)		1.6701 (0.5084 to 5.4863)		1.1272 (0.6319 to 2.0107)	
P-value		0.2764		0.6220		0.5784		0.3980		0.6851	
probability (95% CI)[b]											
2 Months	0.7027 (0.5845 to 0.7931)	0.5636 (0.4231 to 0.6824)	0.5500 (0.3134 to 0.7349)	0.6429 (0.4381 to 0.7894)	0.6000 (0.1257 to 0.8818)	0.5714 (0.1719 to 0.8371)	0.8667 (0.5639 to 0.9649)	0.8095 (0.5689 to 0.9239)	0.6286 (0.4477 to 0.7647)	0.7000 (0.5326 to 0.8171)	
4 Months	0.6081 (0.4875 to 0.7087)	0.5091 (0.3710 to 0.6315)	0.4500 (0.2311 to 0.6471)	0.6071 (0.4039 to 0.7598)	0.6000 (0.1257 to 0.8818)	0.4286 (0.0978 to 0.7344)	0.8000 (0.4998 to 0.9307)	0.7619 (0.5194 to 0.8933)	0.5088 (0.3333 to 0.6600)	0.5192 (0.3544 to 0.6609)	
6 Months	0.5099 (0.3905 to 0.6173)	0.4517 (0.3171 to 0.5771)	0.4000 (0.1928 to 0.6005)	0.5714 (0.3706 to 0.7295)	0.6000 (0.1257 to 0.8818)	0.4286 (0.0978 to 0.7344)	0.8000 (0.4998 to 0.9307)	0.6667 (0.4254 to 0.8250)	0.4490 (0.2798 to 0.6044)	0.4413 (0.2839 to 0.5878)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.2 Treatment emergent serious adverse event by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
8 Months	0.4662 (0.3484 to 0.5756)	0.4517 (0.3171 to 0.5771)	0.4000 (0.1928 to 0.6005)	0.5000 (0.3064 to 0.6662)	0.6000 (0.1257 to 0.8818)	0.4286 (0.0978 to 0.7344)	0.8000 (0.4998 to 0.9307)	0.6667 (0.4254 to 0.8250)	0.4116 (0.2449 to 0.5711)	0.3894 (0.2391 to 0.5371)	
10 Months	0.4662 (0.3484 to 0.5756)	0.3928 (0.2634 to 0.5197)	0.4000 (0.1928 to 0.6005)	0.4643 (0.2756 to 0.6333)	0.6000 (0.1257 to 0.8818)	0.2857 (0.0411 to 0.6115)	0.8000 (0.4998 to 0.9307)	0.5714 (0.3380 to 0.7492)	0.4116 (0.2449 to 0.5711)	0.3635 (0.2173 to 0.5111)	
12 Months	0.4501 (0.3328 to 0.5603)	0.3492 (0.2239 to 0.4772)	0.4000 (0.1928 to 0.6005)	0.3929 (0.2167 to 0.5651)	0.6000 (0.1257 to 0.8818)	0.2857 (0.0411 to 0.6115)	0.8000 (0.4998 to 0.9307)	0.5714 (0.3380 to 0.7492)	0.4116 (0.2449 to 0.5711)	0.3115 (0.1753 to 0.4579)	
14 Months	0.4321 (0.3149 to 0.5436)	0.3492 (0.2239 to 0.4772)	0.3333 (0.1386 to 0.5430)	0.3929 (0.2167 to 0.5651)	0.6000 (0.1257 to 0.8818)	0.2857 (0.0411 to 0.6115)	0.8000 (0.4998 to 0.9307)	0.5714 (0.3380 to 0.7492)	0.4116 (0.2449 to 0.5711)	0.3115 (0.1753 to 0.4579)	
16 Months	0.4321 (0.3149 to 0.5436)	0.3492 (0.2239 to 0.4772)	0.3333 (0.1386 to 0.5430)	0.3929 (0.2167 to 0.5651)	0.6000 (0.1257 to 0.8818)	0.2857 (0.0411 to 0.6115)	0.8000 (0.4998 to 0.9307)	0.5714 (0.3380 to 0.7492)	0.4116 (0.2449 to 0.5711)	0.3115 (0.1753 to 0.4579)	
Number of patients at risk[b]											
2 Months	52	31	11	18	3	4	13	17	21	28	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.2 Treatment emergent serious adverse event by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
4 Months	45	27	9	17	3	3	12	16	17	20	
6 Months	36	23	8	16	3	3	12	14	13	17	
8 Months	29	23	8	14	3	3	12	14	11	15	
10 Months	29	20	7	13	3	2	12	12	11	14	
12 Months	25	15	6	10	1	2	10	11	11	12	
14 Months	17	11	4	6	0	1	1	7	7	10	
16 Months	8	3	2	2	0	1	0	4	5	4	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_greg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Number (%) of events	9 (12.2)	0 (0.0)	4 (20.0)	5 (17.9)	0 (0.0)	0 (0.0)	0 (0.0)	2 (9.5)	6 (17.1)	4 (9.8)	0.9865
Number (%) of patients censored	65 (87.8)	55 (100.0)	16 (80.0)	23 (82.1)	5 (100.0)	7 (100.0)	15 (100.0)	19 (90.5)	29 (82.9)	37 (90.2)	
Kaplan-Meier estimates of TEAE in months											
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.1971 to NC)	NC (2.3655 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.1951 to NC)	NC (4.1396 to NC)	NC (10.9076 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.9671 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.9671 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd		0.0079		0.8213				0.3179		0.2668	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_greg_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=35)**	**IPd (N=41)**	**p-value of treatment-by-subgroup interaction[c]**
Hazard ratio (95% CI) vs Pd		NC (NC to NC)		0.8592 (0.2300 to 3.2103)		NC (NC to NC)		NC (NC to NC)		0.4943 (0.1390 to 1.7584)	
P-value		0.9926		0.8215				0.9980		0.2765	
probability (95% CI)[b]											
2 Months	0.8911 (0.7939 to 0.9440)	1.0000 (1.0000 to 1.0000)	0.8500 (0.6038 to 0.9490)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9429 (0.7903 to 0.9854)	0.9756 (0.8392 to 0.9965)	
4 Months	0.8911 (0.7939 to 0.9440)	1.0000 (1.0000 to 1.0000)	0.8500 (0.6038 to 0.9490)	0.8929 (0.7036 to 0.9641)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9134 (0.7549 to 0.9712)	0.9756 (0.8392 to 0.9965)	
6 Months	0.8760 (0.7750 to 0.9335)	1.0000 (1.0000 to 1.0000)	0.8500 (0.6038 to 0.9490)	0.8571 (0.6629 to 0.9438)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8534 (0.6828 to 0.9363)	0.9268 (0.7900 to 0.9758)	
8 Months	0.8760 (0.7750 to 0.9335)	1.0000 (1.0000 to 1.0000)	0.8500 (0.6038 to 0.9490)	0.8571 (0.6629 to 0.9438)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9444 (0.6664 to 0.9920)	0.8108 (0.6215 to 0.9116)	0.9268 (0.7900 to 0.9758)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_greg_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
10 Months	0.8760 (0.7750 to 0.9335)	1.0000 (1.0000 to 1.0000)	0.8500 (0.6038 to 0.9490)	0.8163 (0.6126 to 0.9194)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9444 (0.6664 to 0.9920)	0.8108 (0.6215 to 0.9116)	0.9268 (0.7900 to 0.9758)	
12 Months	0.8760 (0.7750 to 0.9335)	1.0000 (1.0000 to 1.0000)	0.8500 (0.6038 to 0.9490)	0.8163 (0.6126 to 0.9194)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9444 (0.6664 to 0.9920)	0.8108 (0.6215 to 0.9116)	0.8959 (0.7442 to 0.9600)	
14 Months	0.8760 (0.7750 to 0.9335)	1.0000 (1.0000 to 1.0000)	0.7846 (0.5181 to 0.9144)	0.8163 (0.6126 to 0.9194)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9444 (0.6664 to 0.9920)	0.8108 (0.6215 to 0.9116)	0.8959 (0.7442 to 0.9600)	
16 Months	0.8760 (0.7750 to 0.9335)	1.0000 (1.0000 to 1.0000)	0.7846 (0.5181 to 0.9144)	0.8163 (0.6126 to 0.9194)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.7556 (0.2447 to 0.9457)	0.8108 (0.6215 to 0.9116)	0.8959 (0.7442 to 0.9600)	
Number of patients at risk[b]											
2 Months	63	53	17	28	5	7	15	20	33	40	
4 Months	59	48	17	25	5	7	15	19	31	40	
6 Months	56	42	15	23	5	6	15	19	22	36	
8 Months	49	41	15	21	5	6	15	17	19	35	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_greg_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
10 Months	49	39	14	20	5	5	14	17	17	32	
12 Months	43	35	13	17	3	5	11	15	15	28	
14 Months	30	21	9	11	1	2	2	11	10	23	
16 Months	13	7	3	3	0	1	1	4	7	13	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_greg_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.4 Treatment emergent mild adverse event by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Number (%) of events	67 (90.5)	51 (92.7)	19 (95.0)	26 (92.9)	5 (100.0)	7 (100.0)	15 (100.0)	21 (100.0)	31 (88.6)	36 (87.8)	0.5348
Number (%) of patients censored	7 (9.5)	4 (7.3)	1 (5.0)	2 (7.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (11.4)	5 (12.2)	
Kaplan-Meier estimates of TEAE in months											
25% quantile (95% CI)	0.1314 (0.0657 to 0.2300)	0.0986 (0.0329 to 0.1643)	0.1478 (0.0329 to 0.2957)	0.1643 (0.0329 to 0.2628)	0.2628 (0.0657 to 0.8871)	0.0986 (0.0329 to 0.1971)	0.1971 (0.0657 to 0.2957)	0.0657 (0.0657 to 0.1314)	0.3285 (0.1314 to 0.3285)	0.1314 (0.0657 to 0.1643)	
Median (95% CI)	0.4928 (0.2628 to 0.8214)	0.2628 (0.1643 to 0.5257)	0.4600 (0.1314 to 0.8871)	0.3450 (0.1643 to 0.7228)	0.4600 (0.0657 to 0.8871)	0.1971 (0.0329 to 0.7228)	0.3285 (0.1643 to 0.8871)	0.1314 (0.0657 to 0.1971)	0.5914 (0.3285 to 1.4127)	0.1971 (0.1314 to 0.5585)	
75% quantile (95% CI)	1.7084 (0.8214 to 3.1540)	0.8214 (0.5257 to 3.2526)	1.3470 (0.4928 to 1.8727)	2.1684 (0.4928 to 5.9138)	0.8871 (0.0657 to 0.8871)	0.7228 (0.0986 to 4.4353)	0.9199 (0.3285 to 6.5051)	0.2300 (0.1643 to 0.8542)	1.6756 (0.8214 to 8.1807)	1.0185 (0.4928 to 6.4394)	
Comparison vs. Pd											

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_greg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.4 Treatment emergent mild adverse event by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Log-Rank test p-value[a] vs Pd		0.2524		0.2771		0.6780		0.0375		0.3007	
Hazard ratio (95% CI) vs Pd		1.2403 (0.8572 to 1.7946)		0.7079 (0.3785 to 1.3237)		1.2910 (0.3855 to 4.3230)		2.0632 (1.0295 to 4.1346)		1.2956 (0.7924 to 2.1184)	
P-value		0.2533		0.2793		0.6787		0.0411		0.3020	
Hazard ratio inverted (95% CI) vs IPd							0.4847 (0.2419 to 0.9713)				
probability (95% CI)[b]											
2 Months	0.2251 (0.1356 to 0.3285)	0.1852 (0.0954 to 0.2981)	0.0538 (0.0037 to 0.2182)	0.2857 (0.1354 to 0.4561)	0.4000 (0.0520 to 0.7528)	0.1429 (0.0071 to 0.4649)	0.0667 (0.0043 to 0.2603)	0.0476 (0.0033 to 0.1970)	0.2121 (0.0935 to 0.3625)	0.1951 (0.0916 to 0.3272)	
4 Months	0.1200 (0.0566 to 0.2091)	0.0988 (0.0355 to 0.2008)	0.0538 (0.0037 to 0.2182)	0.1714 (0.0590 to 0.3331)	0.4000 (0.0520 to 0.7528)	0.1429 (0.0071 to 0.4649)	0.0667 (0.0043 to 0.2603)	0.0476 (0.0033 to 0.1970)	0.1414 (0.0475 to 0.2850)	0.1707 (0.0751 to 0.2991)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_greg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.4 Treatment emergent mild adverse event by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
6 Months	0.0857 (0.0335 to 0.1692)	0.0988 (0.0355 to 0.2008)	0.0538 (0.0037 to 0.2182)	0.0857 (0.0158 to 0.2334)	0.4000 (0.0520 to 0.7528)	0.1429 (0.0071 to 0.4649)	0.0667 (0.0043 to 0.2603)	0.0476 (0.0033 to 0.1970)	0.1414 (0.0475 to 0.2850)	0.1463 (0.0594 to 0.2703)	
8 Months	0.0857 (0.0335 to 0.1692)	0.0658 (0.0154 to 0.1699)	0.0538 (0.0037 to 0.2182)	0.0429 (0.0032 to 0.1776)	0.4000 (0.0520 to 0.7528)	0.1429 (0.0071 to 0.4649)	0.0667 (0.0043 to 0.2603)	0.0476 (0.0033 to 0.1970)	0.1414 (0.0475 to 0.2850)	0.1171 (0.0407 to 0.2377)	
10 Months	0.0857 (0.0335 to 0.1692)	0.0658 (0.0154 to 0.1699)	0.0538 (0.0037 to 0.2182)	0.0429 (0.0032 to 0.1776)	0.4000 (0.0520 to 0.7528)	0.1429 (0.0071 to 0.4649)	0.0667 (0.0043 to 0.2603)	0.0476 (0.0033 to 0.1970)	0.0943 (0.0204 to 0.2387)	0.1171 (0.0407 to 0.2377)	
12 Months	0.0643 (0.0199 to 0.1463)	0.0658 (0.0154 to 0.1699)	0.0538 (0.0037 to 0.2182)	0.0429 (0.0032 to 0.1776)	0.4000 (0.0520 to 0.7528)	0.1429 (0.0071 to 0.4649)	0.0667 (0.0043 to 0.2603)	0.0476 (0.0033 to 0.1970)	0.0943 (0.0204 to 0.2387)	0.1171 (0.0407 to 0.2377)	
14 Months	0.0643 (0.0199 to 0.1463)	0.0658 (0.0154 to 0.1699)	0.0538 (0.0037 to 0.2182)	0.0429 (0.0032 to 0.1776)	0.4000 (0.0520 to 0.7528)	0.1429 (0.0071 to 0.4649)	0.0667 (0.0043 to 0.2603)	0.0476 (0.0033 to 0.1970)	0.0943 (0.0204 to 0.2387)	0.1171 (0.0407 to 0.2377)	
16 Months	0.0643 (0.0199 to 0.1463)	0.0658 (0.0154 to 0.1699)	0.0538 (0.0037 to 0.2182)	0.0429 (0.0032 to 0.1776)	0.4000 (0.0520 to 0.7528)	0.1429 (0.0071 to 0.4649)	0.0667 (0.0043 to 0.2603)	0.0476 (0.0033 to 0.1970)	0.0943 (0.0204 to 0.2387)	0.1171 (0.0407 to 0.2377)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_greg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.4 Treatment emergent mild adverse event by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Number of patients at risk[b]											
2 Months	15	9	1	8	0	1	1	1	6	8	
4 Months	8	4	0	4	0	1	1	0	4	7	
6 Months	4	3	0	2	0	0	1	0	3	5	
8 Months	4	2	0	1	0	0	0	0	3	4	
10 Months	4	2	0	1	0	0	0	0	1	4	
12 Months	3	1	0	1	0	0	0	0	1	4	
14 Months	3	1	0	1	0	0	0	0	1	4	
16 Months	0	0	0	1	0	0	0	0	1	1	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_greg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.5 Treatment emergent severe adverse event by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=35)**	**IPd (N=41)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	47 (63.5)	44 (80.0)	17 (85.0)	23 (82.1)	2 (40.0)	6 (85.7)	11 (73.3)	19 (90.5)	26 (74.3)	37 (90.2)	0.2820
Number (%) of patients censored	27 (36.5)	11 (20.0)	3 (15.0)	5 (17.9)	3 (60.0)	1 (14.3)	4 (26.7)	2 (9.5)	9 (25.7)	4 (9.8)	
Kaplan-Meier estimates of TEAE in months											
25% quantile (95% CI)	0.5914 (0.3285 to 0.7885)	0.4928 (0.2957 to 0.5585)	0.4928 (0.1314 to 0.7228)	0.4435 (0.1643 to 0.7885)	0.2957 (0.1971 to NC)	0.3614 (0.1971 to 0.5585)	1.1499 (0.1643 to 1.9384)	0.5914 (0.1314 to 0.7228)	0.5257 (0.2628 to 0.7885)	0.5421 (0.2957 to 0.7556)	
Median (95% CI)	2.6283 (0.8871 to 5.5852)	0.8542 (0.5585 to 1.4456)	0.7721 (0.4600 to 3.0883)	0.8542 (0.6571 to 1.9713)	NC (0.1971 to NC)	0.5585 (0.1971 to 1.0185)	2.8255 (1.1499 to 14.5544)	0.8542 (0.5914 to 2.3655)	1.5770 (0.7885 to 2.2669)	0.9363 (0.6242 to 2.8912)	
75% quantile (95% CI)	NC (NC to NC)	4.4353 (1.4456 to NC)	3.3511 (0.7885 to NC)	3.5318 (0.9199 to NC)	NC (0.1971 to NC)	1.0185 (0.4271 to NC)	14.5544 (2.8255 to 14.5544)	2.7926 (0.8871 to NC)	7.0308 (2.0370 to NC)	4.9117 (2.1355 to 10.9076)	
Comparison vs. Pd											

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_greg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.5 Treatment emergent severe adverse event by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=35)**	**IPd (N=41)**	**p-value of treatment-by-subgroup interaction[c]**
Log-Rank test p-value[a] vs Pd		0.0218		0.7540		0.2884		0.0623		0.4194	
Hazard ratio (95% CI) vs Pd		1.6216 (1.0689 to 2.4600)		0.9045 (0.4828 to 1.6947)		2.3437 (0.4651 to 11.8096)		2.0184 (0.9511 to 4.2836)		1.2308 (0.7428 to 2.0394)	
P-value		0.0230		0.7541		0.3019		0.0674		0.4203	
Hazard ratio inverted (95% CI) vs IPd	0.6167 (0.4065 to 0.9355)										
probability (95% CI)[b]											
2 Months	0.5294 (0.4084 to 0.6365)	0.2974 (0.1825 to 0.4212)	0.3000 (0.1225 to 0.5014)	0.3214 (0.1615 to 0.4934)	0.6000 (0.1257 to 0.8818)	0.1429 (0.0071 to 0.4649)	0.5333 (0.2632 to 0.7438)	0.3333 (0.1488 to 0.5307)	0.4286 (0.2643 to 0.5831)	0.4500 (0.2934 to 0.5946)	
4 Months	0.4458 (0.3291 to 0.5558)	0.2602 (0.1524 to 0.3815)	0.2000 (0.0624 to 0.3931)	0.2143 (0.0871 to 0.3783)	0.6000 (0.1257 to 0.8818)	0.1429 (0.0071 to 0.4649)	0.4667 (0.2123 to 0.6875)	0.1429 (0.0357 to 0.3212)	0.2857 (0.1491 to 0.4384)	0.2750 (0.1486 to 0.4172)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_greg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.5 Treatment emergent severe adverse event by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
6 Months	0.3739 (0.2632 to 0.4843)	0.1908 (0.0963 to 0.3096)	0.1500 (0.0373 to 0.3347)	0.2143 (0.0871 to 0.3783)	0.6000 (0.1257 to 0.8818)	0.1429 (0.0071 to 0.4649)	0.4000 (0.1649 to 0.6276)	0.1429 (0.0357 to 0.3212)	0.2857 (0.1491 to 0.4384)	0.2000 (0.0939 to 0.3345)	
8 Months	0.3595 (0.2503 to 0.4697)	0.1670 (0.0785 to 0.2839)	0.1500 (0.0373 to 0.3347)	0.1786 (0.0651 to 0.3375)	0.6000 (0.1257 to 0.8818)	0.1429 (0.0071 to 0.4649)	0.3333 (0.1215 to 0.5640)	0.1429 (0.0357 to 0.3212)	0.2449 (0.1150 to 0.4004)	0.1500 (0.0609 to 0.2764)	
10 Months	0.3595 (0.2503 to 0.4697)	0.1670 (0.0785 to 0.2839)	0.1500 (0.0373 to 0.3347)	0.1786 (0.0651 to 0.3375)	0.6000 (0.1257 to 0.8818)	0.1429 (0.0071 to 0.4649)	0.3333 (0.1215 to 0.5640)	0.0952 (0.0163 to 0.2612)	0.2449 (0.1150 to 0.4004)	0.1500 (0.0609 to 0.2764)	
12 Months	0.3595 (0.2503 to 0.4697)	0.1670 (0.0785 to 0.2839)	0.1500 (0.0373 to 0.3347)	0.1786 (0.0651 to 0.3375)	0.6000 (0.1257 to 0.8818)	0.1429 (0.0071 to 0.4649)	0.3333 (0.1215 to 0.5640)	0.0952 (0.0163 to 0.2612)	0.2449 (0.1150 to 0.4004)	0.1250 (0.0458 to 0.2461)	
14 Months	0.3595 (0.2503 to 0.4697)	0.1670 (0.0785 to 0.2839)	0.1500 (0.0373 to 0.3347)	0.1786 (0.0651 to 0.3375)	0.6000 (0.1257 to 0.8818)	0.1429 (0.0071 to 0.4649)	0.3333 (0.1215 to 0.5640)	0.0952 (0.0163 to 0.2612)	0.2449 (0.1150 to 0.4004)	0.1000 (0.0318 to 0.2149)	
16 Months	0.3595 (0.2503 to 0.4697)	0.1670 (0.0785 to 0.2839)	0.1500 (0.0373 to 0.3347)	0.1786 (0.0651 to 0.3375)	0.6000 (0.1257 to 0.8818)	0.1429 (0.0071 to 0.4649)	0.3333 (0.1215 to 0.5640)	0.0952 (0.0163 to 0.2612)	0.2449 (0.1150 to 0.4004)	0.1000 (0.0318 to 0.2149)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_greg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.5 Treatment emergent severe adverse event by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Number of patients at risk[b]											
2 Months	38	16	6	9	3	1	8	7	15	18	
4 Months	32	12	4	6	3	1	7	3	10	11	
6 Months	26	8	3	6	3	1	6	3	9	8	
8 Months	23	7	3	5	3	1	5	3	6	6	
10 Months	23	7	3	4	3	1	5	2	6	6	
12 Months	19	5	3	4	1	1	5	1	6	5	
14 Months	14	4	2	2	0	0	1	1	3	4	
16 Months	8	1	1	0	0	0	0	0	3	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_greg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.6 Treatment emergent severe adverse event including death by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Number (%) of events	48 (64.9)	46 (83.6)	17 (85.0)	24 (85.7)	2 (40.0)	6 (85.7)	11 (73.3)	19 (90.5)	27 (77.1)	37 (90.2)	0.2637
Number (%) of patients censored	26 (35.1)	9 (16.4)	3 (15.0)	4 (14.3)	3 (60.0)	1 (14.3)	4 (26.7)	2 (9.5)	8 (22.9)	4 (9.8)	
Kaplan-Meier estimates of TEAE in months											
25% quantile (95% CI)	0.5585 (0.2957 to 0.7556)	0.4928 (0.2957 to 0.5585)	0.4928 (0.1314 to 0.7228)	0.4435 (0.1643 to 0.7885)	0.2957 (0.1971 to NC)	0.3614 (0.1971 to 0.5585)	1.1499 (0.1643 to 1.9384)	0.5914 (0.1314 to 0.7228)	0.5257 (0.2628 to 0.7885)	0.5421 (0.2957 to 0.7556)	
Median (95% CI)	2.2669 (0.8214 to 5.5852)	0.8214 (0.5585 to 1.4456)	0.7721 (0.4600 to 3.0883)	0.8542 (0.6571 to 1.9713)	NC (0.1971 to NC)	0.5585 (0.1971 to 1.0185)	2.8255 (1.1499 to 14.5544)	0.8542 (0.5914 to 2.3655)	1.5770 (0.7885 to 2.2669)	0.9363 (0.6242 to 2.8912)	
75% quantile (95% CI)	NC (6.0452 to NC)	2.2669 (1.4456 to NC)	3.3511 (0.7885 to NC)	3.5318 (0.9199 to NC)	NC (0.1971 to NC)	1.0185 (0.4271 to NC)	14.5544 (2.8255 to 14.5544)	2.7926 (0.8871 to NC)	7.0308 (2.0370 to NC)	4.9117 (2.1355 to 10.9076)	
Comparison vs. Pd											

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.6 Treatment emergent severe adverse event including death by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=35)**	**IPd (N=41)**	**p-value of treatment-by-subgroup interaction[c]**
Log-Rank test p-value[a] vs Pd		0.0140		0.8494		0.2884		0.0623		0.5000	
Hazard ratio (95% CI) vs Pd		1.6632 (1.1037 to 2.5064)		0.9412 (0.5052 to 1.7535)		2.3437 (0.4651 to 11.8096)		2.0184 (0.9511 to 4.2836)		1.1873 (0.7205 to 1.9567)	
P-value		0.0150		0.8486		0.3019		0.0674		0.5005	
Hazard ratio inverted (95% CI) vs IPd	0.6012 (0.3990 to 0.9060)										
probability (95% CI)[b]											
2 Months	0.5205 (0.4006 to 0.6275)	0.2727 (0.1635 to 0.3937)	0.3000 (0.1225 to 0.5014)	0.3214 (0.1615 to 0.4934)	0.6000 (0.1257 to 0.8818)	0.1429 (0.0071 to 0.4649)	0.5333 (0.2632 to 0.7438)	0.3333 (0.1488 to 0.5307)	0.4286 (0.2643 to 0.5831)	0.4500 (0.2934 to 0.5946)	
4 Months	0.4384 (0.3231 to 0.5477)	0.2364 (0.1347 to 0.3543)	0.2000 (0.0624 to 0.3931)	0.2143 (0.0871 to 0.3783)	0.6000 (0.1257 to 0.8818)	0.1429 (0.0071 to 0.4649)	0.4667 (0.2123 to 0.6875)	0.1429 (0.0357 to 0.3212)	0.2857 (0.1491 to 0.4384)	0.2750 (0.1486 to 0.4172)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_greg_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.6 Treatment emergent severe adverse event including death by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
6 Months	0.3677 (0.2584 to 0.4772)	0.1733 (0.0857 to 0.2865)	0.1500 (0.0373 to 0.3347)	0.2143 (0.0871 to 0.3783)	0.6000 (0.1257 to 0.8818)	0.1429 (0.0071 to 0.4649)	0.4000 (0.1649 to 0.6276)	0.1429 (0.0357 to 0.3212)	0.2571 (0.1280 to 0.4077)	0.2000 (0.0939 to 0.3345)	
8 Months	0.3535 (0.2458 to 0.4628)	0.1517 (0.0700 to 0.2624)	0.1500 (0.0373 to 0.3347)	0.1786 (0.0651 to 0.3375)	0.6000 (0.1257 to 0.8818)	0.1429 (0.0071 to 0.4649)	0.3333 (0.1215 to 0.5640)	0.1429 (0.0357 to 0.3212)	0.2204 (0.0995 to 0.3712)	0.1500 (0.0609 to 0.2764)	
10 Months	0.3535 (0.2458 to 0.4628)	0.1517 (0.0700 to 0.2624)	0.1500 (0.0373 to 0.3347)	0.1429 (0.0450 to 0.2950)	0.6000 (0.1257 to 0.8818)	0.1429 (0.0071 to 0.4649)	0.3333 (0.1215 to 0.5640)	0.0952 (0.0163 to 0.2612)	0.2204 (0.0995 to 0.3712)	0.1500 (0.0609 to 0.2764)	
12 Months	0.3535 (0.2458 to 0.4628)	0.1517 (0.0700 to 0.2624)	0.1500 (0.0373 to 0.3347)	0.1429 (0.0450 to 0.2950)	0.6000 (0.1257 to 0.8818)	0.1429 (0.0071 to 0.4649)	0.3333 (0.1215 to 0.5640)	0.0952 (0.0163 to 0.2612)	0.2204 (0.0995 to 0.3712)	0.1250 (0.0458 to 0.2461)	
14 Months	0.3535 (0.2458 to 0.4628)	0.1517 (0.0700 to 0.2624)	0.1500 (0.0373 to 0.3347)	0.1429 (0.0450 to 0.2950)	0.6000 (0.1257 to 0.8818)	0.1429 (0.0071 to 0.4649)	0.3333 (0.1215 to 0.5640)	0.0952 (0.0163 to 0.2612)	0.2204 (0.0995 to 0.3712)	0.1000 (0.0318 to 0.2149)	
16 Months	0.3535 (0.2458 to 0.4628)	0.1517 (0.0700 to 0.2624)	0.1500 (0.0373 to 0.3347)	0.1429 (0.0450 to 0.2950)	0.6000 (0.1257 to 0.8818)	0.1429 (0.0071 to 0.4649)	0.3333 (0.1215 to 0.5640)	0.0952 (0.0163 to 0.2612)	0.2204 (0.0995 to 0.3712)	0.1000 (0.0318 to 0.2149)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_greg_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.7 Subgroup analyses by geographical region
16.2.7.1.1.7.6 Treatment emergent severe adverse event including death by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Number of patients at risk[b]											
2 Months	38	15	6	9	3	1	8	7	15	18	
4 Months	32	12	4	6	3	1	7	3	10	11	
6 Months	26	8	3	6	3	1	6	3	9	8	
8 Months	23	7	3	5	3	1	5	3	6	6	
10 Months	23	7	3	4	3	1	5	2	6	6	
12 Months	19	5	3	4	1	1	5	1	6	5	
14 Months	14	4	2	2	0	0	1	1	3	4	
16 Months	8	1	1	0	0	0	0	0	3	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_greg_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.8 Subgroup analyses by regulatory region
16.2.7.1.1.8.1 Treatment emergent adverse event by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	91 (96.8)	76 (98.7)	55 (100.0)	75 (100.0)	0.4019
Number (%) of patients censored	3 (3.2)	1 (1.3)	0 (0.0)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0657 to 0.1314)	0.0986 (0.0657 to 0.1314)	0.1643 (0.1314 to 0.2957)	0.1314 (0.0657 to 0.1314)	
Median (95% CI)	0.3285 (0.1971 to 0.4928)	0.1971 (0.1314 to 0.2628)	0.3943 (0.2957 to 0.7228)	0.1971 (0.1643 to 0.2957)	
75% quantile (95% CI)	0.8214 (0.5585 to 1.8398)	0.4928 (0.2957 to 0.7228)	0.9528 (0.7228 to 1.4456)	0.6242 (0.3614 to 0.9528)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0076		0.1230	
Hazard ratio (95% CI) vs Pd		1.5326 (1.1176 to 2.1018)		1.3218 (0.9262 to 1.8863)	
P-value		0.0081		0.1241	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_rreg_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.8 Subgroup analyses by regulatory region
16.2.7.1.1.8.1 Treatment emergent adverse event by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6525 (0.4758 to 0.8948)				
probability (95% CI)[b]					
2 Months	0.1444 (0.0813 to 0.2249)	0.0263 (0.0050 to 0.0823)	0.0556 (0.0146 to 0.1387)	0.0946 (0.0416 to 0.1740)	
4 Months	0.0556 (0.0206 to 0.1162)	0.0132 (0.0011 to 0.0631)	0.0370 (0.0069 to 0.1129)	0.0270 (0.0051 to 0.0843)	
6 Months	0.0417 (0.0125 to 0.0999)	0.0132 (0.0011 to 0.0631)	0.0370 (0.0069 to 0.1129)	0.0135 (0.0012 to 0.0647)	
8 Months	0.0417 (0.0125 to 0.0999)	0.0132 (0.0011 to 0.0631)	0.0185 (0.0015 to 0.0862)	0.0135 (0.0012 to 0.0647)	
10 Months	0.0417 (0.0125 to 0.0999)	0.0132 (0.0011 to 0.0631)	0.0185 (0.0015 to 0.0862)	0.0135 (0.0012 to 0.0647)	
12 Months	0.0278 (0.0058 to 0.0826)	0.0132 (0.0011 to 0.0631)	0.0185 (0.0015 to 0.0862)	0.0135 (0.0012 to 0.0647)	
14 Months	0.0278 (0.0058 to 0.0826)	0.0132 (0.0011 to 0.0631)	0.0185 (0.0015 to 0.0862)	0.0135 (0.0012 to 0.0647)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_rreg_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.8 Subgroup analyses by regulatory region
16.2.7.1.1.8.1 Treatment emergent adverse event by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0278 (0.0058 to 0.0826)	0.0132 (0.0011 to 0.0631)	0.0185 (0.0015 to 0.0862)	0.0135 (0.0012 to 0.0647)	
Number of patients at risk[b]					
2 Months	13	2	3	7	
4 Months	5	1	2	2	
6 Months	3	1	2	1	
8 Months	3	1	1	0	
10 Months	3	1	0	0	
12 Months	2	0	0	0	
14 Months	2	0	0	0	
16 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.8 Subgroup analyses by regulatory region
16.2.7.1.1.8.2 Treatment emergent serious adverse event by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	53 (56.4)	49 (63.6)	27 (49.1)	45 (60.0)	0.9683
Number (%) of patients censored	41 (43.6)	28 (36.4)	28 (50.9)	30 (40.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.0842 (0.5257 to 2.0370)	0.6571 (0.4271 to 1.2156)	1.5770 (0.7228 to 2.8255)	1.5113 (0.3285 to 2.7926)	
Median (95% CI)	5.5852 (3.0883 to NC)	4.4353 (1.4127 to 9.9548)	14.5544 (2.8255 to NC)	6.9651 (3.3840 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (11.0390 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.3342		0.3960	
Hazard ratio (95% CI) vs Pd		1.2107 (0.8208 to 1.7856)		1.2302 (0.7618 to 1.9866)	
P-value		0.3350		0.3969	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.8 Subgroup analyses by regulatory region
16.2.7.1.1.8.2 Treatment emergent serious adverse event by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.6702 (0.5653 to 0.7552)	0.5844 (0.4664 to 0.6850)	0.6909 (0.5508 to 0.7951)	0.7162 (0.5987 to 0.8048)	
4 Months	0.5638 (0.4577 to 0.6570)	0.5325 (0.4154 to 0.6363)	0.6162 (0.4742 to 0.7304)	0.5927 (0.4717 to 0.6948)	
6 Months	0.4870 (0.3824 to 0.5836)	0.4655 (0.3511 to 0.5721)	0.5602 (0.4189 to 0.6798)	0.5376 (0.4173 to 0.6435)	
8 Months	0.4524 (0.3490 to 0.5501)	0.4518 (0.3381 to 0.5588)	0.5402 (0.3992 to 0.6617)	0.4962 (0.3775 to 0.6041)	
10 Months	0.4524 (0.3490 to 0.5501)	0.3834 (0.2747 to 0.4910)	0.5402 (0.3992 to 0.6617)	0.4549 (0.3385 to 0.5639)	
12 Months	0.4399 (0.3368 to 0.5380)	0.3539 (0.2476 to 0.4616)	0.5402 (0.3992 to 0.6617)	0.3997 (0.2877 to 0.5092)	
14 Months	0.4252 (0.3221 to 0.5244)	0.3539 (0.2476 to 0.4616)	0.5167 (0.3751 to 0.6410)	0.3997 (0.2877 to 0.5092)	
16 Months	0.4252 (0.3221 to 0.5244)	0.3539 (0.2476 to 0.4616)	0.4650 (0.3065 to 0.6092)	0.3997 (0.2877 to 0.5092)	
Number of patients at risk[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_rreg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.8 Subgroup analyses by regulatory region
16.2.7.1.1.8.2 Treatment emergent serious adverse event by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	63	45	37	53	
4 Months	53	40	33	43	
6 Months	44	34	28	39	
8 Months	36	33	27	36	
10 Months	36	28	26	33	
12 Months	30	23	23	27	
14 Months	19	17	10	18	
16 Months	9	6	6	8	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.8 Subgroup analyses by regulatory region
16.2.7.1.1.8.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (11.7)	1 (1.3)	8 (14.5)	10 (13.3)	0.0632
Number (%) of patients censored	83 (88.3)	76 (98.7)	47 (85.5)	65 (86.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.1622 to NC)	NC (15.9671 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0081		0.7157	
Hazard ratio (95% CI) vs Pd		0.1049 (0.0135 to 0.8124)		0.8414 (0.3319 to 2.1333)	
P-value		0.0309		0.7160	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.8 Subgroup analyses by regulatory region
16.2.7.1.1.8.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9144 (0.8361 to 0.9562)	1.0000 (1.0000 to 1.0000)	0.9091 (0.7953 to 0.9611)	0.9867 (0.9091 to 0.9981)	
4 Months	0.9032 (0.8222 to 0.9485)	1.0000 (1.0000 to 1.0000)	0.9091 (0.7953 to 0.9611)	0.9461 (0.8628 to 0.9794)	
6 Months	0.8801 (0.7938 to 0.9318)	0.9857 (0.9029 to 0.9980)	0.8902 (0.7716 to 0.9491)	0.9187 (0.8279 to 0.9626)	
8 Months	0.8801 (0.7938 to 0.9318)	0.9857 (0.9029 to 0.9980)	0.8684 (0.7431 to 0.9352)	0.9041 (0.8092 to 0.9531)	
10 Months	0.8801 (0.7938 to 0.9318)	0.9857 (0.9029 to 0.9980)	0.8684 (0.7431 to 0.9352)	0.8888 (0.7896 to 0.9429)	
12 Months	0.8801 (0.7938 to 0.9318)	0.9857 (0.9029 to 0.9980)	0.8684 (0.7431 to 0.9352)	0.8729 (0.7695 to 0.9319)	
14 Months	0.8801 (0.7938 to 0.9318)	0.9857 (0.9029 to 0.9980)	0.8374 (0.6957 to 0.9169)	0.8729 (0.7695 to 0.9319)	
16 Months	0.8801 (0.7938 to 0.9318)	0.9857 (0.9029 to 0.9980)	0.8374 (0.6957 to 0.9169)	0.8270 (0.6744 to 0.9125)	
Number of patients at risk[b]					
2 Months	83	75	50	73	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.8 Subgroup analyses by regulatory region
16.2.7.1.1.8.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	78	70	49	69	
6 Months	72	61	41	65	
8 Months	63	59	40	61	
10 Months	61	56	38	57	
12 Months	53	50	32	50	
14 Months	35	31	17	37	
16 Months	15	12	9	16	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.8 Subgroup analyses by regulatory region
16.2.7.1.1.8.4 Treatment emergent mild adverse event by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	86 (91.5)	73 (94.8)	51 (92.7)	68 (90.7)	0.6609
Number (%) of patients censored	8 (8.5)	4 (5.2)	4 (7.3)	7 (9.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0986 to 0.1971)	0.0986 (0.0657 to 0.1643)	0.2628 (0.1314 to 0.3285)	0.1314 (0.0657 to 0.1314)	
Median (95% CI)	0.4928 (0.3285 to 0.6899)	0.2300 (0.1643 to 0.3943)	0.4928 (0.3285 to 0.9199)	0.1971 (0.1643 to 0.4600)	
75% quantile (95% CI)	1.1170 (0.8214 to 2.2998)	0.8049 (0.5257 to 1.1499)	1.4456 (0.9199 to 2.0370)	0.8542 (0.4928 to 3.8439)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.1325		0.4798	
Hazard ratio (95% CI) vs Pd		1.2741 (0.9285 to 1.7483)		1.1425 (0.7894 to 1.6535)	
P-value		0.1335		0.4801	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.8 Subgroup analyses by regulatory region
16.2.7.1.1.8.4 Treatment emergent mild adverse event by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.1882 (0.1148 to 0.2757)	0.1447 (0.0770 to 0.2330)	0.1519 (0.0711 to 0.2609)	0.2267 (0.1399 to 0.3263)	
4 Months	0.1059 (0.0524 to 0.1809)	0.0844 (0.0343 to 0.1635)	0.0868 (0.0290 to 0.1848)	0.1579 (0.0859 to 0.2497)	
6 Months	0.0794 (0.0340 to 0.1498)	0.0675 (0.0237 to 0.1436)	0.0868 (0.0290 to 0.1848)	0.1117 (0.0518 to 0.1973)	
8 Months	0.0794 (0.0340 to 0.1498)	0.0450 (0.0105 to 0.1212)	0.0578 (0.0129 to 0.1548)	0.0798 (0.0308 to 0.1593)	
10 Months	0.0794 (0.0340 to 0.1498)	0.0450 (0.0105 to 0.1212)	0.0289 (0.0026 to 0.1214)	0.0798 (0.0308 to 0.1593)	
12 Months	0.0595 (0.0199 to 0.1310)	0.0450 (0.0105 to 0.1212)	0.0289 (0.0026 to 0.1214)	0.0798 (0.0308 to 0.1593)	
14 Months	0.0595 (0.0199 to 0.1310)	0.0450 (0.0105 to 0.1212)	0.0289 (0.0026 to 0.1214)	0.0798 (0.0308 to 0.1593)	
16 Months	0.0595 (0.0199 to 0.1310)	0.0450 (0.0105 to 0.1212)	0.0289 (0.0026 to 0.1214)	0.0798 (0.0308 to 0.1593)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.8 Subgroup analyses by regulatory region
16.2.7.1.1.8.4 Treatment emergent mild adverse event by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	16	10	7	17	
4 Months	9	5	4	11	
6 Months	5	3	3	7	
8 Months	5	2	2	5	
10 Months	4	2	1	5	
12 Months	3	1	1	5	
14 Months	3	1	1	5	
16 Months	0	0	1	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.8 Subgroup analyses by regulatory region
16.2.7.1.1.8.5 Treatment emergent severe adverse event by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	59 (62.8)	64 (83.1)	44 (80.0)	65 (86.7)	0.0914
Number (%) of patients censored	35 (37.2)	13 (16.9)	11 (20.0)	10 (13.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.5914 (0.3285 to 0.7885)	0.4928 (0.2957 to 0.5585)	0.5257 (0.2628 to 0.7885)	0.5585 (0.2957 to 0.7228)	
Median (95% CI)	2.2669 (0.9856 to 5.5852)	0.8214 (0.5914 to 1.3142)	1.2813 (0.7885 to 2.2669)	0.8706 (0.7556 to 1.9713)	
75% quantile (95% CI)	NC (NC to NC)	4.4353 (1.5113 to 7.4251)	7.0308 (2.2669 to NC)	3.7782 (2.3655 to 10.9076)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0020		0.4224	
Hazard ratio (95% CI) vs Pd		1.7452 (1.2197 to 2.4971)		1.1702 (0.7968 to 1.7185)	
P-value		0.0023		0.4229	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.8 Subgroup analyses by regulatory region
16.2.7.1.1.8.5 Treatment emergent severe adverse event by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.5730 (0.4005 to 0.8199)				
probability (95% CI)[b]					
2 Months	0.5339 (0.4272 to 0.6294)	0.3036 (0.2046 to 0.4083)	0.3818 (0.2553 to 0.5071)	0.3784 (0.2691 to 0.4869)	
4 Months	0.4358 (0.3333 to 0.5338)	0.2508 (0.1601 to 0.3520)	0.2909 (0.1782 to 0.4131)	0.2162 (0.1309 to 0.3155)	
6 Months	0.3800 (0.2813 to 0.4779)	0.1888 (0.1084 to 0.2863)	0.2532 (0.1476 to 0.3731)	0.1892 (0.1097 to 0.2853)	
8 Months	0.3688 (0.2711 to 0.4666)	0.1416 (0.0721 to 0.2339)	0.2143 (0.1169 to 0.3310)	0.1757 (0.0993 to 0.2700)	
10 Months	0.3688 (0.2711 to 0.4666)	0.1416 (0.0721 to 0.2339)	0.2143 (0.1169 to 0.3310)	0.1622 (0.0891 to 0.2545)	
12 Months	0.3688 (0.2711 to 0.4666)	0.1416 (0.0721 to 0.2339)	0.2143 (0.1169 to 0.3310)	0.1474 (0.0779 to 0.2379)	
14 Months	0.3688 (0.2711 to 0.4666)	0.1416 (0.0721 to 0.2339)	0.2143 (0.1169 to 0.3310)	0.1264 (0.0607 to 0.2172)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_rreg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.8 Subgroup analyses by regulatory region
16.2.7.1.1.8.5 Treatment emergent severe adverse event by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3688 (0.2711 to 0.4666)	0.1416 (0.0721 to 0.2339)	0.1714 (0.0755 to 0.3000)	0.1264 (0.0607 to 0.2172)	
Number of patients at risk[b]					
2 Months	49	23	21	28	
4 Months	40	17	16	16	
6 Months	34	12	13	14	
8 Months	29	9	11	13	
10 Months	29	9	11	11	
12 Months	23	7	11	9	
14 Months	15	5	5	6	
16 Months	9	2	3	1	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.8 Subgroup analyses by regulatory region
16.2.7.1.1.8.6 Treatment emergent severe adverse event including death by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	60 (63.8)	66 (85.7)	45 (81.8)	66 (88.0)	0.0695
Number (%) of patients censored	34 (36.2)	11 (14.3)	10 (18.2)	9 (12.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.5585 (0.2957 to 0.7556)	0.4600 (0.2957 to 0.5257)	0.5257 (0.2628 to 0.7885)	0.5585 (0.2957 to 0.7228)	
Median (95% CI)	2.0698 (0.9528 to 4.9610)	0.8214 (0.5585 to 1.2156)	1.2813 (0.7885 to 2.2669)	0.8706 (0.7556 to 1.9713)	
75% quantile (95% CI)	NC (NC to NC)	2.2669 (1.4456 to 6.9651)	4.6653 (2.2669 to NC)	3.7782 (2.3655 to 9.1335)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0013		0.4291	
Hazard ratio (95% CI) vs Pd		1.7732 (1.2443 to 2.5268)		1.1658 (0.7968 to 1.7057)	
P-value		0.0015		0.4296	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.8 Subgroup analyses by regulatory region
16.2.7.1.1.8.6 Treatment emergent severe adverse event including death by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.5640 (0.3958 to 0.8036)				
probability (95% CI)[b]					
2 Months	0.5269 (0.4209 to 0.6222)	0.2857 (0.1900 to 0.3887)	0.3818 (0.2553 to 0.5071)	0.3784 (0.2691 to 0.4869)	
4 Months	0.4301 (0.3285 to 0.5276)	0.2338 (0.1467 to 0.3327)	0.2909 (0.1782 to 0.4131)	0.2162 (0.1309 to 0.3155)	
6 Months	0.3750 (0.2773 to 0.4723)	0.1760 (0.0997 to 0.2701)	0.2364 (0.1347 to 0.3543)	0.1892 (0.1097 to 0.2853)	
8 Months	0.3639 (0.2672 to 0.4611)	0.1320 (0.0665 to 0.2203)	0.2000 (0.1070 to 0.3138)	0.1757 (0.0993 to 0.2700)	
10 Months	0.3639 (0.2672 to 0.4611)	0.1320 (0.0665 to 0.2203)	0.2000 (0.1070 to 0.3138)	0.1486 (0.0791 to 0.2388)	
12 Months	0.3639 (0.2672 to 0.4611)	0.1320 (0.0665 to 0.2203)	0.2000 (0.1070 to 0.3138)	0.1351 (0.0693 to 0.2230)	
14 Months	0.3639 (0.2672 to 0.4611)	0.1320 (0.0665 to 0.2203)	0.2000 (0.1070 to 0.3138)	0.1158 (0.0542 to 0.2032)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.8 Subgroup analyses by regulatory region
16.2.7.1.1.8.6 Treatment emergent severe adverse event including death by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3639 (0.2672 to 0.4611)	0.1320 (0.0665 to 0.2203)	0.1600 (0.0696 to 0.2837)	0.1158 (0.0542 to 0.2032)	
Number of patients at risk[b]					
2 Months	49	22	21	28	
4 Months	40	17	16	16	
6 Months	34	12	13	14	
8 Months	29	9	11	13	
10 Months	29	9	11	11	
12 Months	23	7	11	9	
14 Months	15	5	5	6	
16 Months	9	2	3	1	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_rreg_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.1 Treatment emergent adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	132 (97.8)	135 (99.3)	14 (100.0)	16 (100.0)	0.5323
Number (%) of patients censored	3 (2.2)	1 (0.7)	0 (0.0)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0986 to 0.1643)	0.0986 (0.0657 to 0.1314)	0.1643 (0.0657 to 0.2300)	0.0657 (0.0000 to 0.0986)	
Median (95% CI)	0.3285 (0.2957 to 0.5257)	0.1971 (0.1643 to 0.2628)	0.2300 (0.1314 to 0.3943)	0.0986 (0.0657 to 0.1643)	
75% quantile (95% CI)	0.9528 (0.7885 to 1.4456)	0.5585 (0.4600 to 0.7556)	0.3943 (0.1971 to 3.1540)	0.2300 (0.0986 to 0.7885)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0081		0.2149	
Hazard ratio (95% CI) vs Pd		1.3888 (1.0880 to 1.7726)		1.6234 (0.7498 to 3.5147)	
P-value		0.0084		0.2189	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.1 Treatment emergent adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.7201 (0.5641 to 0.9191)				
probability (95% CI)[b]					
2 Months	0.1145 (0.0672 to 0.1756)	0.0667 (0.0328 to 0.1171)	0.0769 (0.0048 to 0.2920)	0.1333 (0.0219 to 0.3457)	
4 Months	0.0534 (0.0236 to 0.1012)	0.0222 (0.0061 to 0.0586)	0.0769 (0.0048 to 0.2920)	0.1333 (0.0219 to 0.3457)	
6 Months	0.0445 (0.0178 to 0.0905)	0.0148 (0.0029 to 0.0479)	0.0769 (0.0048 to 0.2920)	0.1333 (0.0219 to 0.3457)	
8 Months	0.0356 (0.0124 to 0.0794)	0.0074 (0.0007 to 0.0371)	0.0769 (0.0048 to 0.2920)	0.1333 (0.0219 to 0.3457)	
10 Months	0.0267 (0.0076 to 0.0678)	0.0074 (0.0007 to 0.0371)	0.0769 (0.0048 to 0.2920)	0.1333 (0.0219 to 0.3457)	
12 Months	0.0178 (0.0036 to 0.0558)	0.0074 (0.0007 to 0.0371)	0.0769 (0.0048 to 0.2920)	0.1333 (0.0219 to 0.3457)	
14 Months	0.0178 (0.0036 to 0.0558)	0.0074 (0.0007 to 0.0371)	0.0769 (0.0048 to 0.2920)	0.1333 (0.0219 to 0.3457)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.1 Treatment emergent adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0178 (0.0036 to 0.0558)	0.0074 (0.0007 to 0.0371)	0.0769 (0.0048 to 0.2920)	0.1333 (0.0219 to 0.3457)	
Number of patients at risk[b]					
2 Months	15	9	1	0	
4 Months	7	3	0	0	
6 Months	5	2	0	0	
8 Months	4	1	0	0	
10 Months	3	1	0	0	
12 Months	2	0	0	0	
14 Months	2	0	0	0	
16 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.2 Treatment emergent serious adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	72 (53.3)	78 (57.4)	8 (57.1)	16 (100.0)	0.0009
Number (%) of patients censored	63 (46.7)	58 (42.6)	6 (42.9)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.3142 (0.5914 to 1.9384)	1.3799 (0.5585 to 2.2669)	1.7741 (0.4271 to 6.5708)	0.1314 (0.0657 to 0.4271)	
Median (95% CI)	6.0452 (3.6140 to NC)	8.8049 (4.3039 to NC)	6.5708 (0.7556 to NC)	0.4271 (0.1314 to 1.0185)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.5708 to NC)	1.1499 (0.4271 to 8.6078)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.8051		0.0005	
Hazard ratio (95% CI) vs Pd		1.0411 (0.7557 to 1.4343)		4.4859 (1.8233 to 11.0365)	
P-value		0.8053		0.0011	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.2 Treatment emergent serious adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.2229 (0.0906 to 0.5484)		
probability (95% CI)[b]					
2 Months	0.6741 (0.5880 to 0.7461)	0.7059 (0.6215 to 0.7748)	0.7143 (0.4063 to 0.8819)	0.1333 (0.0219 to 0.3457)	
4 Months	0.5767 (0.4887 to 0.6550)	0.6093 (0.5218 to 0.6856)	0.6429 (0.3433 to 0.8331)	0.1333 (0.0219 to 0.3457)	
6 Months	0.5076 (0.4200 to 0.5887)	0.5489 (0.4611 to 0.6283)	0.5625 (0.2718 to 0.7756)	0.0667 (0.0043 to 0.2603)	
8 Months	0.4918 (0.4043 to 0.5733)	0.5184 (0.4309 to 0.5989)	0.3750 (0.1254 to 0.6292)	0.0667 (0.0043 to 0.2603)	
10 Months	0.4918 (0.4043 to 0.5733)	0.4650 (0.3788 to 0.5467)	0.3750 (0.1254 to 0.6292)	0.0667 (0.0043 to 0.2603)	
12 Months	0.4833 (0.3959 to 0.5651)	0.4179 (0.3334 to 0.5000)	0.3750 (0.1254 to 0.6292)	0.0667 (0.0043 to 0.2603)	
14 Months	0.4639 (0.3764 to 0.5469)	0.4179 (0.3334 to 0.5000)	0.3750 (0.1254 to 0.6292)	0.0667 (0.0043 to 0.2603)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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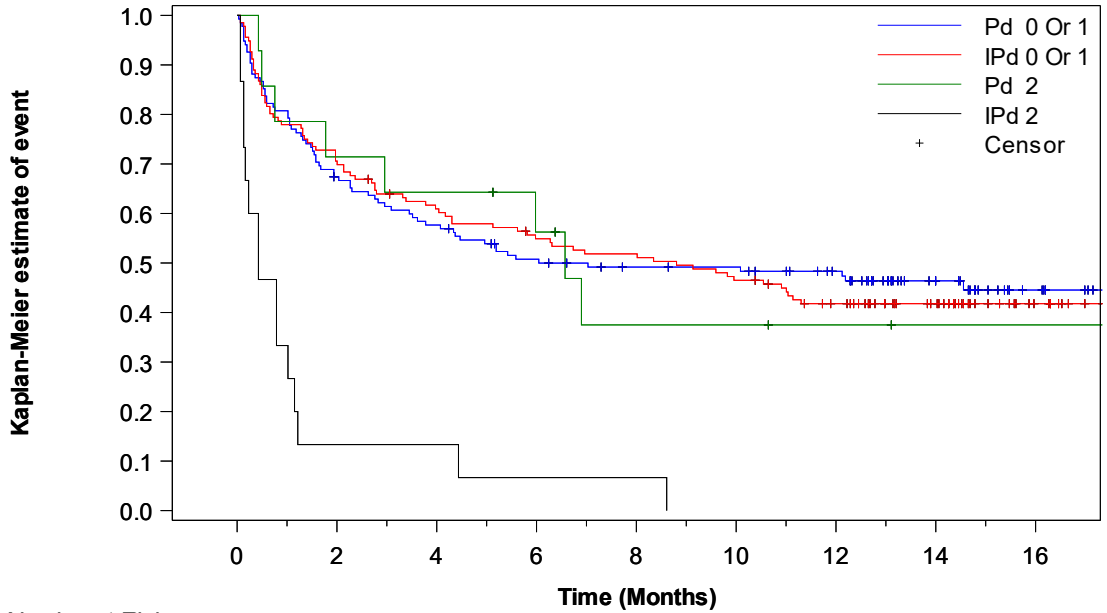
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.2 Treatment emergent serious adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.4454 (0.3542 to 0.5324)	0.4179 (0.3334 to 0.5000)	0.3750 (0.1254 to 0.6292)	0.0667 (0.0043 to 0.2603)	
Number of patients at risk[b]					
2 Months	90	96	10	2	
4 Months	77	81	9	2	
6 Months	65	72	7	1	
8 Months	59	68	4	1	
10 Months	58	61	4	0	
12 Months	50	50	3	0	
14 Months	27	35	2	0	
16 Months	13	14	2	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_ecog_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.3 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event by treatment group according to baseline ECOG PS - Safety population



Number at Risk

Pd 0 Or 1	135	90	77	65	59	58	50	27	13
IPd 0 Or 1	136	96	81	72	68	61	50	35	14
Pd 2	14	10	9	7	4	4	3	2	2
IPd 2	15	2	2	1	1	0	0	0	0

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (11.1)	11 (8.1)	4 (28.6)	0 (0.0)	0.9889
Number (%) of patients censored	120 (88.9)	125 (91.9)	10 (71.4)	16 (100.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	2.3326 (0.1643 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.6756 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.3032		0.0296	
Hazard ratio (95% CI) vs Pd		0.6663 (0.3059 to 1.4510)		NC (NC to NC)	
P-value		0.3065		0.9967	

probability (95% CI)[b]

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9253 (0.8656 to 0.9591)	0.9926 (0.9490 to 0.9990)	0.7857 (0.4725 to 0.9254)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9253 (0.8656 to 0.9591)	0.9704 (0.9231 to 0.9888)	0.7143 (0.4063 to 0.8819)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9014 (0.8362 to 0.9416)	0.9477 (0.8934 to 0.9747)	0.7143 (0.4063 to 0.8819)	1.0000 (1.0000 to 1.0000)	
8 Months	0.8924 (0.8248 to 0.9349)	0.9394 (0.8823 to 0.9692)	0.7143 (0.4063 to 0.8819)	1.0000 (1.0000 to 1.0000)	
10 Months	0.8924 (0.8248 to 0.9349)	0.9306 (0.8706 to 0.9633)	0.7143 (0.4063 to 0.8819)	1.0000 (1.0000 to 1.0000)	
12 Months	0.8924 (0.8248 to 0.9349)	0.9214 (0.8584 to 0.9570)	0.7143 (0.4063 to 0.8819)	1.0000 (1.0000 to 1.0000)	
14 Months	0.8791 (0.8055 to 0.9261)	0.9214 (0.8584 to 0.9570)	0.7143 (0.4063 to 0.8819)	1.0000 (1.0000 to 1.0000)	
16 Months	0.8791 (0.8055 to 0.9261)	0.8885 (0.7802 to 0.9452)	0.7143 (0.4063 to 0.8819)	1.0000 (1.0000 to 1.0000)	
Number of patients at risk[b]					
2 Months	122	134	11	14	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	117	128	10	11	
6 Months	104	118	9	8	
8 Months	94	112	9	8	
10 Months	91	105	8	8	
12 Months	79	92	6	8	
14 Months	48	63	4	5	
16 Months	21	25	3	3	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.5 Treatment emergent mild adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	123 (91.1)	127 (93.4)	14 (100.0)	14 (87.5)	0.6729
Number (%) of patients censored	12 (8.9)	9 (6.6)	0 (0.0)	2 (12.5)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1643 (0.1314 to 0.2957)	0.1314 (0.0657 to 0.1314)	0.1971 (0.0657 to 0.2628)	0.0821 (0.0000 to 0.1314)	
Median (95% CI)	0.4928 (0.3285 to 0.8214)	0.2300 (0.1643 to 0.3285)	0.2628 (0.1314 to 0.3943)	0.1807 (0.0657 to 0.4928)	
75% quantile (95% CI)	1.4456 (0.9528 to 1.8727)	0.8542 (0.6571 to 2.1684)	0.3943 (0.2628 to 3.1540)	0.6407 (0.1314 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.1454		0.8597	
Hazard ratio (95% CI) vs Pd		1.2048 (0.9372 to 1.5487)		0.9330 (0.4327 to 2.0117)	
P-value		0.1460		0.8595	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.5 Treatment emergent mild adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.1758 (0.1155 to 0.2464)	0.1926 (0.1311 to 0.2630)	0.1538 (0.0248 to 0.3878)	0.1250 (0.0207 to 0.3280)	
4 Months	0.1088 (0.0618 to 0.1707)	0.1244 (0.0753 to 0.1865)	0.0769 (0.0048 to 0.2920)	0.1250 (0.0207 to 0.3280)	
6 Months	0.0907 (0.0480 to 0.1499)	0.0914 (0.0496 to 0.1487)	0.0769 (0.0048 to 0.2920)	0.1250 (0.0207 to 0.3280)	
8 Months	0.0793 (0.0392 to 0.1377)	0.0640 (0.0296 to 0.1167)	0.0769 (0.0048 to 0.2920)	0.1250 (0.0207 to 0.3280)	
10 Months	0.0680 (0.0309 to 0.1251)	0.0640 (0.0296 to 0.1167)	0.0769 (0.0048 to 0.2920)	0.1250 (0.0207 to 0.3280)	
12 Months	0.0544 (0.0211 to 0.1110)	0.0640 (0.0296 to 0.1167)	0.0769 (0.0048 to 0.2920)	0.1250 (0.0207 to 0.3280)	
14 Months	0.0544 (0.0211 to 0.1110)	0.0640 (0.0296 to 0.1167)	0.0769 (0.0048 to 0.2920)	0.1250 (0.0207 to 0.3280)	
16 Months	0.0544 (0.0211 to 0.1110)	0.0533 (0.0222 to 0.1047)	0.0769 (0.0048 to 0.2920)	0.1250 (0.0207 to 0.3280)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.5 Treatment emergent mild adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	21	26	2	1	
4 Months	13	16	0	0	
6 Months	8	10	0	0	
8 Months	7	7	0	0	
10 Months	5	7	0	0	
12 Months	4	6	0	0	
14 Months	4	6	0	0	
16 Months	1	2	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.6 Treatment emergent severe adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	92 (68.1)	115 (84.6)	11 (78.6)	14 (87.5)	0.8043
Number (%) of patients censored	43 (31.9)	21 (15.4)	3 (21.4)	2 (12.5)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.6242 (0.4928 to 0.7885)	0.5257 (0.3614 to 0.5914)	0.2628 (0.1643 to 0.4928)	0.1643 (0.0657 to 0.5257)	
Median (95% CI)	1.9384 (1.1499 to 3.5154)	0.8542 (0.7556 to 1.4127)	0.5092 (0.2300 to 2.9569)	0.7885 (0.1314 to 1.1499)	
75% quantile (95% CI)	NC (7.0308 to NC)	3.7782 (2.3655 to 7.4251)	2.9569 (0.4928 to NC)	1.1499 (0.5257 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0023		0.5968	
Hazard ratio (95% CI) vs Pd		1.5307 (1.1613 to 2.0176)		1.2426 (0.5542 to 2.7863)	
P-value		0.0025		0.5980	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.6 Treatment emergent severe adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6533 (0.4956 to 0.8611)				
probability (95% CI)[b]					
2 Months	0.4969 (0.4094 to 0.5783)	0.3603 (0.2805 to 0.4405)	0.2857 (0.0883 to 0.5237)	0.1467 (0.0239 to 0.3726)	
4 Months	0.3991 (0.3157 to 0.4809)	0.2406 (0.1723 to 0.3154)	0.2143 (0.0521 to 0.4479)	0.1467 (0.0239 to 0.3726)	
6 Months	0.3446 (0.2648 to 0.4256)	0.2007 (0.1375 to 0.2726)	0.2143 (0.0521 to 0.4479)	0.0733 (0.0046 to 0.2808)	
8 Months	0.3201 (0.2421 to 0.4005)	0.1686 (0.1104 to 0.2375)	0.2143 (0.0521 to 0.4479)	0.0733 (0.0046 to 0.2808)	
10 Months	0.3201 (0.2421 to 0.4005)	0.1606 (0.1037 to 0.2286)	0.2143 (0.0521 to 0.4479)	0.0733 (0.0046 to 0.2808)	
12 Months	0.3201 (0.2421 to 0.4005)	0.1517 (0.0962 to 0.2189)	0.2143 (0.0521 to 0.4479)	0.0733 (0.0046 to 0.2808)	
14 Months	0.3201 (0.2421 to 0.4005)	0.1390 (0.0847 to 0.2066)	0.2143 (0.0521 to 0.4479)	0.0733 (0.0046 to 0.2808)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.6 Treatment emergent severe adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3013 (0.2207 to 0.3856)	0.1390 (0.0847 to 0.2066)	0.2143 (0.0521 to 0.4479)	0.0733 (0.0046 to 0.2808)	
Number of patients at risk[b]					
2 Months	66	49	4	2	
4 Months	53	31	3	2	
6 Months	44	25	3	1	
8 Months	37	21	3	1	
10 Months	37	19	3	1	
12 Months	32	15	2	1	
14 Months	18	10	2	1	
16 Months	10	3	2	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.7 Treatment emergent severe adverse event including death by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	94 (69.6)	117 (86.0)	11 (78.6)	15 (93.8)	0.9785
Number (%) of patients censored	41 (30.4)	19 (14.0)	3 (21.4)	1 (6.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.6242 (0.4600 to 0.7885)	0.5257 (0.3614 to 0.5914)	0.2628 (0.1643 to 0.4928)	0.1643 (0.0657 to 0.4271)	
Median (95% CI)	1.9384 (1.1499 to 3.4497)	0.8542 (0.7556 to 1.4127)	0.5092 (0.2300 to 2.9569)	0.5257 (0.1314 to 1.0185)	
75% quantile (95% CI)	NC (6.0452 to NC)	3.7782 (2.2669 to 6.9651)	2.9569 (0.4928 to NC)	1.1499 (0.5257 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0021		0.4549	
Hazard ratio (95% CI) vs Pd		1.5309 (1.1645 to 2.0125)		1.3520 (0.6112 to 2.9906)	
P-value		0.0023		0.4566	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.7 Treatment emergent severe adverse event including death by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6532 (0.4969 to 0.8587)				
probability (95% CI)[b]					
2 Months	0.4925 (0.4055 to 0.5737)	0.3529 (0.2737 to 0.4330)	0.2857 (0.0883 to 0.5237)	0.1333 (0.0219 to 0.3457)	
4 Months	0.3955 (0.3127 to 0.4770)	0.2341 (0.1668 to 0.3082)	0.2143 (0.0521 to 0.4479)	0.1333 (0.0219 to 0.3457)	
6 Months	0.3347 (0.2561 to 0.4149)	0.1953 (0.1332 to 0.2663)	0.2143 (0.0521 to 0.4479)	0.0667 (0.0043 to 0.2603)	
8 Months	0.3109 (0.2343 to 0.3904)	0.1641 (0.1069 to 0.2319)	0.2143 (0.0521 to 0.4479)	0.0667 (0.0043 to 0.2603)	
10 Months	0.3109 (0.2343 to 0.3904)	0.1484 (0.0941 to 0.2144)	0.2143 (0.0521 to 0.4479)	0.0667 (0.0043 to 0.2603)	
12 Months	0.3109 (0.2343 to 0.3904)	0.1402 (0.0874 to 0.2052)	0.2143 (0.0521 to 0.4479)	0.0667 (0.0043 to 0.2603)	
14 Months	0.3109 (0.2343 to 0.3904)	0.1285 (0.0771 to 0.1935)	0.2143 (0.0521 to 0.4479)	0.0667 (0.0043 to 0.2603)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_ecog_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.1.9.7 Treatment emergent severe adverse event including death by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.2926 (0.2137 to 0.3758)	0.1285 (0.0771 to 0.1935)	0.2143 (0.0521 to 0.4479)	0.0667 (0.0043 to 0.2603)	
Number of patients at risk[b]					
2 Months	66	48	4	2	
4 Months	53	31	3	2	
6 Months	44	25	3	1	
8 Months	37	21	3	1	
10 Months	37	19	3	1	
12 Months	32	15	2	1	
14 Months	18	10	2	1	
16 Months	10	3	2	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_ecog_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.10 Subgroup analyses by ISS staging
16.2.7.1.1.10.1 Treatment emergent adverse event by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (98.0)	62 (98.4)	53 (96.4)	53 (100.0)	40 (100.0)	33 (100.0)	0.2580
Number (%) of patients censored	1 (2.0)	1 (1.6)	2 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	0.1314 (0.0657 to 0.2957)	0.0986 (0.0657 to 0.1314)	0.1314 (0.0986 to 0.1971)	0.0657 (0.0657 to 0.1314)	0.1314 (0.0986 to 0.1971)	0.1314 (0.0329 to 0.1314)	
Median (95% CI)	0.3943 (0.2300 to 0.6899)	0.1971 (0.1314 to 0.2957)	0.3450 (0.1971 to 0.6242)	0.1971 (0.1314 to 0.2628)	0.2793 (0.1643 to 0.5257)	0.2300 (0.1314 to 0.4928)	
75% quantile (95% CI)	0.8871 (0.4928 to 1.5441)	0.6242 (0.3285 to 0.8214)	1.4456 (0.6242 to 2.2998)	0.3943 (0.2628 to 0.6242)	0.8214 (0.3943 to 1.1170)	0.5914 (0.4928 to 0.9528)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd		0.1462		0.0027		0.5541	
Hazard ratio (95% CI) vs Pd		1.3232 (0.9054 to 1.9337)		1.8318 (1.2265 to 2.7359)		1.1512 (0.7218 to 1.8361)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_seiss_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.10 Subgroup analyses by ISS staging
16.2.7.1.1.10.1 Treatment emergent adverse event by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
P-value		0.1480		0.0031		0.5544	
Hazard ratio inverted (95% CI) vs IPd			0.5459 (0.3655 to 0.8153)				
probability (95% CI)[b]							
2 Months	0.1000 (0.0367 to 0.2010)	0.0820 (0.0302 to 0.1673)	0.1731 (0.0853 to 0.2865)	0.0189 (0.0015 to 0.0876)	0.0500 (0.0091 to 0.1483)	0.0909 (0.0233 to 0.2167)	
4 Months	0.0800 (0.0256 to 0.1754)	0.0328 (0.0061 to 0.1009)	0.0385 (0.0071 to 0.1168)	0.0189 (0.0015 to 0.0876)	0.0250 (0.0020 to 0.1127)	0.0303 (0.0023 to 0.1335)	
6 Months	0.0600 (0.0157 to 0.1488)	0.0328 (0.0061 to 0.1009)	0.0385 (0.0071 to 0.1168)	0.0189 (0.0015 to 0.0876)	0.0250 (0.0020 to 0.1127)	0.0303 (0.0023 to 0.1335)	
8 Months	0.0400 (0.0074 to 0.1211)	0.0164 (0.0014 to 0.0772)	0.0385 (0.0071 to 0.1168)	0.0189 (0.0015 to 0.0876)	0.0250 (0.0020 to 0.1127)	0.0303 (0.0023 to 0.1335)	
10 Months	0.0200 (0.0016 to 0.0923)	0.0164 (0.0014 to 0.0772)	0.0385 (0.0071 to 0.1168)	0.0189 (0.0015 to 0.0876)	0.0250 (0.0020 to 0.1127)	0.0303 (0.0023 to 0.1335)	
12 Months	0.0200 (0.0016 to 0.0923)	0.0164 (0.0014 to 0.0772)	0.0385 (0.0071 to 0.1168)	0.0189 (0.0015 to 0.0876)	0.0250 (0.0020 to 0.1127)	0.0303 (0.0023 to 0.1335)	
14 Months	0.0200 (0.0016 to 0.0923)	0.0164 (0.0014 to 0.0772)	0.0385 (0.0071 to 0.1168)	0.0189 (0.0015 to 0.0876)	0.0250 (0.0020 to 0.1127)	0.0303 (0.0023 to 0.1335)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_seiss_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.10 Subgroup analyses by ISS staging
16.2.7.1.1.10.1 Treatment emergent adverse event by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0200 (0.0016 to 0.0923)	0.0164 (0.0014 to 0.0772)	0.0385 (0.0071 to 0.1168)	0.0189 (0.0015 to 0.0876)	0.0250 (0.0020 to 0.1127)	0.0303 (0.0023 to 0.1335)	
Number of patients at risk[b]							
2 Months	5	5	9	1	2	3	
4 Months	4	2	2	1	1	0	
6 Months	3	2	1	0	1	0	
8 Months	2	1	1	0	1	0	
10 Months	1	1	1	0	1	0	
12 Months	1	0	1	0	0	0	
14 Months	1	0	1	0	0	0	
16 Months	0	0	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_seiss_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.10 Subgroup analyses by ISS staging
16.2.7.1.1.10.2 Treatment emergent serious adverse event by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (41.2)	29 (46.0)	33 (60.0)	35 (66.0)	24 (60.0)	28 (84.8)	0.6252
Number (%) of patients censored	30 (58.8)	34 (54.0)	22 (40.0)	18 (34.0)	16 (40.0)	5 (15.2)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	4.3368 (1.7741 to 6.8994)	2.3655 (0.5585 to 5.1253)	1.0842 (0.2957 to 1.6756)	0.7228 (0.2957 to 1.9713)	0.6571 (0.2628 to 1.4784)	0.4928 (0.1314 to 0.7885)	
Median (95% CI)	NC (6.0452 to NC)	NC (9.1335 to NC)	5.1910 (1.6756 to NC)	4.4353 (1.3142 to 11.0390)	2.7598 (1.1828 to NC)	1.5770 (0.4928 to 4.3039)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.8049 to NC)	NC (5.4209 to NC)	8.3450 (3.3840 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd		0.5113		0.6568		0.1080	
Hazard ratio (95% CI) vs Pd		1.2085 (0.6862 to 2.1284)		1.1139 (0.6922 to 1.7926)		1.5587 (0.9032 to 2.6900)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_seiss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.10 Subgroup analyses by ISS staging
16.2.7.1.1.10.2 Treatment emergent serious adverse event by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
P-value		0.5119		0.6568		0.1109	
probability (95% CI)[b]							
2 Months	0.8627 (0.7335 to 0.9321)	0.7742 (0.6487 to 0.8595)	0.6182 (0.4768 to 0.7318)	0.5849 (0.4410 to 0.7037)	0.5500 (0.3846 to 0.6879)	0.4848 (0.3083 to 0.6406)	
4 Months	0.7647 (0.6230 to 0.8589)	0.6760 (0.5440 to 0.7774)	0.5273 (0.3882 to 0.6486)	0.5283 (0.3865 to 0.6516)	0.4452 (0.2879 to 0.5911)	0.3571 (0.1990 to 0.5186)	
6 Months	0.6667 (0.5198 to 0.7778)	0.6430 (0.5100 to 0.7485)	0.4699 (0.3337 to 0.5947)	0.4717 (0.3336 to 0.5979)	0.3891 (0.2379 to 0.5377)	0.2922 (0.1482 to 0.4525)	
8 Months	0.6275 (0.4801 to 0.7437)	0.6430 (0.5100 to 0.7485)	0.4308 (0.2974 to 0.5571)	0.4151 (0.2823 to 0.5426)	0.3891 (0.2379 to 0.5377)	0.2597 (0.1243 to 0.4182)	
10 Months	0.6275 (0.4801 to 0.7437)	0.5753 (0.4418 to 0.6879)	0.4308 (0.2974 to 0.5571)	0.3774 (0.2492 to 0.5049)	0.3891 (0.2379 to 0.5377)	0.1948 (0.0800 to 0.3468)	
12 Months	0.6275 (0.4801 to 0.7437)	0.5410 (0.4080 to 0.6563)	0.4103 (0.2786 to 0.5374)	0.3376 (0.2146 to 0.4648)	0.3891 (0.2379 to 0.5377)	0.1299 (0.0413 to 0.2704)	
14 Months	0.6050 (0.4568 to 0.7245)	0.5410 (0.4080 to 0.6563)	0.3846 (0.2537 to 0.5140)	0.3376 (0.2146 to 0.4648)	0.3891 (0.2379 to 0.5377)	0.1299 (0.0413 to 0.2704)	
16 Months	0.5618 (0.4005 to 0.6954)	0.5410 (0.4080 to 0.6563)	0.3846 (0.2537 to 0.5140)	0.3376 (0.2146 to 0.4648)	0.3891 (0.2379 to 0.5377)	0.1299 (0.0413 to 0.2704)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_seiss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.10 Subgroup analyses by ISS staging
16.2.7.1.1.10.2 Treatment emergent serious adverse event by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	44	48	34	31	21	16	
4 Months	39	41	29	28	17	11	
6 Months	34	38	24	25	13	9	
8 Months	31	38	21	22	10	8	
10 Months	31	34	21	20	9	6	
12 Months	28	28	16	17	8	4	
14 Months	15	17	8	13	6	4	
16 Months	9	10	3	3	3	1	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_seiss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.10 Subgroup analyses by ISS staging
16.2.7.1.1.10.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (3.9)	4 (6.3)	4 (7.3)	2 (3.8)	12 (30.0)	4 (12.1)	0.2995
Number (%) of patients censored	49 (96.1)	59 (93.7)	51 (92.7)	51 (96.2)	28 (70.0)	29 (87.9)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	4.1396 (0.3614 to NC)	15.9671 (10.9076 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.8789 to NC)	NC (15.9671 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd		0.5689		0.4177		0.0391	
Hazard ratio (95% CI) vs Pd		1.6300 (0.2985 to 8.9017)		0.5024 (0.0920 to 2.7439)		0.3219 (0.1035 to 1.0009)	
P-value		0.5727		0.4268		0.0502	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_seiss_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.10 Subgroup analyses by ISS staging
16.2.7.1.1.10.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]							
2 Months	0.9608 (0.8522 to 0.9900)	0.9841 (0.8926 to 0.9977)	0.9629 (0.8598 to 0.9906)	1.0000 (1.0000 to 1.0000)	0.7727 (0.6085 to 0.8747)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9608 (0.8522 to 0.9900)	0.9841 (0.8926 to 0.9977)	0.9629 (0.8598 to 0.9906)	0.9804 (0.8689 to 0.9972)	0.7727 (0.6085 to 0.8747)	0.9375 (0.7725 to 0.9840)	
6 Months	0.9608 (0.8522 to 0.9900)	0.9683 (0.8790 to 0.9920)	0.9441 (0.8364 to 0.9816)	0.9600 (0.8492 to 0.9898)	0.7096 (0.5347 to 0.8286)	0.9375 (0.7725 to 0.9840)	
8 Months	0.9608 (0.8522 to 0.9900)	0.9506 (0.8545 to 0.9838)	0.9216 (0.8035 to 0.9700)	0.9600 (0.8492 to 0.9898)	0.7096 (0.5347 to 0.8286)	0.9375 (0.7725 to 0.9840)	
10 Months	0.9608 (0.8522 to 0.9900)	0.9327 (0.8302 to 0.9743)	0.9216 (0.8035 to 0.9700)	0.9600 (0.8492 to 0.9898)	0.7096 (0.5347 to 0.8286)	0.9375 (0.7725 to 0.9840)	
12 Months	0.9608 (0.8522 to 0.9900)	0.9327 (0.8302 to 0.9743)	0.9216 (0.8035 to 0.9700)	0.9600 (0.8492 to 0.9898)	0.7096 (0.5347 to 0.8286)	0.8854 (0.6735 to 0.9632)	
14 Months	0.9608 (0.8522 to 0.9900)	0.9327 (0.8302 to 0.9743)	0.9216 (0.8035 to 0.9700)	0.9600 (0.8492 to 0.9898)	0.6504 (0.4486 to 0.7939)	0.8854 (0.6735 to 0.9632)	
16 Months	0.9608 (0.8522 to 0.9900)	0.9327 (0.8302 to 0.9743)	0.9216 (0.8035 to 0.9700)	0.9600 (0.8492 to 0.9898)	0.6504 (0.4486 to 0.7939)	0.7378 (0.3395 to 0.9180)	
Number of patients at risk[b]							

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_seiss_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.10 Subgroup analyses by ISS staging
16.2.7.1.1.10.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	49	62	51	51	30	32	
4 Months	49	62	51	48	25	26	
6 Months	49	56	44	45	18	23	
8 Months	46	54	38	44	17	20	
10 Months	45	52	36	40	16	19	
12 Months	41	47	28	35	14	16	
14 Months	25	31	17	24	10	11	
16 Months	14	16	6	8	4	4	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_seiss_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.10 Subgroup analyses by ISS staging
16.2.7.1.1.10.4 Treatment emergent mild adverse event by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (96.1)	61 (96.8)	49 (89.1)	48 (90.6)	36 (90.0)	29 (87.9)	0.5385
Number (%) of patients censored	2 (3.9)	2 (3.2)	6 (10.9)	5 (9.4)	4 (10.0)	4 (12.1)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	0.1314 (0.0657 to 0.2957)	0.0986 (0.0657 to 0.1643)	0.2300 (0.0986 to 0.3285)	0.0986 (0.0657 to 0.1643)	0.1643 (0.0986 to 0.2628)	0.1314 (0.0329 to 0.1314)	
Median (95% CI)	0.4435 (0.2300 to 0.7228)	0.1971 (0.1643 to 0.3614)	0.6242 (0.3285 to 0.8871)	0.2628 (0.1643 to 0.3943)	0.4600 (0.2628 to 0.9528)	0.2628 (0.1314 to 0.7228)	
75% quantile (95% CI)	0.9199 (0.6899 to 1.8727)	0.8214 (0.4928 to 3.3183)	1.7084 (0.8871 to 3.1540)	0.7228 (0.3285 to 2.7269)	1.3470 (0.7228 to 2.5626)	0.8542 (0.5585 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd		0.5111		0.0967		0.9072	
Hazard ratio (95% CI) vs Pd		1.1362 (0.7761 to 1.6634)		1.4062 (0.9387 to 2.1064)		1.0299 (0.6284 to 1.6879)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_seiss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.10 Subgroup analyses by ISS staging
16.2.7.1.1.10.4 Treatment emergent mild adverse event by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
P-value		0.5114		0.0983		0.9071	
probability (95% CI)[b]							
2 Months	0.1400 (0.0615 to 0.2500)	0.1935 (0.1067 to 0.2996)	0.2147 (0.1154 to 0.3342)	0.1887 (0.0972 to 0.3032)	0.1731 (0.0728 to 0.3091)	0.1818 (0.0738 to 0.3279)	
4 Months	0.1200 (0.0488 to 0.2258)	0.1129 (0.0496 to 0.2051)	0.0976 (0.0359 to 0.1964)	0.1258 (0.0528 to 0.2319)	0.0692 (0.0133 to 0.1919)	0.1515 (0.0553 to 0.2922)	
6 Months	0.0800 (0.0256 to 0.1754)	0.0941 (0.0371 to 0.1834)	0.0976 (0.0359 to 0.1964)	0.0629 (0.0136 to 0.1685)	0.0692 (0.0133 to 0.1919)	0.1212 (0.0383 to 0.2553)	
8 Months	0.0600 (0.0157 to 0.1488)	0.0376 (0.0073 to 0.1123)	0.0976 (0.0359 to 0.1964)	0.0629 (0.0136 to 0.1685)	0.0692 (0.0133 to 0.1919)	0.1212 (0.0383 to 0.2553)	
10 Months	0.0400 (0.0074 to 0.1211)	0.0376 (0.0073 to 0.1123)	0.0976 (0.0359 to 0.1964)	0.0629 (0.0136 to 0.1685)	0.0692 (0.0133 to 0.1919)	0.1212 (0.0383 to 0.2553)	
12 Months	0.0400 (0.0074 to 0.1211)	0.0376 (0.0073 to 0.1123)	0.0976 (0.0359 to 0.1964)	0.0629 (0.0136 to 0.1685)	0.0692 (0.0133 to 0.1919)	0.1212 (0.0383 to 0.2553)	
14 Months	0.0400 (0.0074 to 0.1211)	0.0376 (0.0073 to 0.1123)	0.0976 (0.0359 to 0.1964)	0.0629 (0.0136 to 0.1685)	0.0692 (0.0133 to 0.1919)	0.1212 (0.0383 to 0.2553)	
16 Months	0.0400 (0.0074 to 0.1211)	0.0376 (0.0073 to 0.1123)	0.0976 (0.0359 to 0.1964)	0.0629 (0.0136 to 0.1685)	0.0692 (0.0133 to 0.1919)	0.1212 (0.0383 to 0.2553)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_seiss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.10 Subgroup analyses by ISS staging
16.2.7.1.1.10.4 Treatment emergent mild adverse event by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	7	12	11	9	5	6	
4 Months	6	7	5	4	2	5	
6 Months	4	5	3	2	1	3	
8 Months	3	2	3	2	1	3	
10 Months	2	2	2	2	1	3	
12 Months	2	1	2	2	0	3	
14 Months	2	1	2	2	0	3	
16 Months	1	0	0	1	0	1	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_seiss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.10 Subgroup analyses by ISS staging
16.2.7.1.1.10.5 Treatment emergent severe adverse event by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (56.9)	50 (79.4)	38 (69.1)	47 (88.7)	34 (85.0)	29 (87.9)	0.1703
Number (%) of patients censored	22 (43.1)	13 (20.6)	17 (30.9)	6 (11.3)	6 (15.0)	4 (12.1)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	0.7885 (0.5914 to 2.2669)	0.5585 (0.3285 to 0.7556)	0.5257 (0.1643 to 0.7885)	0.4928 (0.2300 to 0.6242)	0.3285 (0.1643 to 0.6242)	0.4928 (0.1643 to 0.5257)	
Median (95% CI)	5.5852 (2.0370 to NC)	1.0021 (0.7556 to 1.9055)	1.5606 (0.7885 to 2.8255)	0.8542 (0.5914 to 1.3142)	0.8542 (0.5257 to 1.5441)	0.7556 (0.4928 to 2.3655)	
75% quantile (95% CI)	NC (NC to NC)	3.7782 (1.9384 to NC)	NC (2.8255 to NC)	2.2669 (1.1499 to 5.8152)	3.6140 (1.2813 to 5.5852)	3.3183 (0.7885 to 8.3450)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd		0.0029		0.0387		0.9443	
Hazard ratio (95% CI) vs Pd		1.9941 (1.2544 to 3.1700)		1.5746 (1.0202 to 2.4303)		1.0179 (0.6189 to 1.6741)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_seiss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.10 Subgroup analyses by ISS staging
16.2.7.1.1.10.5 Treatment emergent severe adverse event by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
P-value		0.0035		0.0403		0.9443	
Hazard ratio inverted (95% CI) vs IPd	0.5015 (0.3155 to 0.7972)		0.6351 (0.4115 to 0.9802)				
probability (95% CI)[b]							
2 Months	0.6667 (0.5198 to 0.7778)	0.3548 (0.2387 to 0.4727)	0.4259 (0.2932 to 0.5522)	0.3019 (0.1853 to 0.4270)	0.3107 (0.1747 to 0.4570)	0.3467 (0.1900 to 0.5088)	
4 Months	0.5490 (0.4034 to 0.6730)	0.2419 (0.1443 to 0.3533)	0.3519 (0.2283 to 0.4778)	0.2058 (0.1094 to 0.3233)	0.2071 (0.0975 to 0.3449)	0.2101 (0.0883 to 0.3668)	
6 Months	0.4902 (0.3479 to 0.6179)	0.2419 (0.1443 to 0.3533)	0.3323 (0.2114 to 0.4579)	0.1235 (0.0513 to 0.2293)	0.1208 (0.0408 to 0.2476)	0.1751 (0.0658 to 0.3277)	
8 Months	0.4510 (0.3120 to 0.5802)	0.2074 (0.1167 to 0.3159)	0.3115 (0.1935 to 0.4369)	0.1235 (0.0513 to 0.2293)	0.1208 (0.0408 to 0.2476)	0.1401 (0.0453 to 0.2869)	
10 Months	0.4510 (0.3120 to 0.5802)	0.2074 (0.1167 to 0.3159)	0.3115 (0.1935 to 0.4369)	0.1235 (0.0513 to 0.2293)	0.1208 (0.0408 to 0.2476)	0.1051 (0.0273 to 0.2441)	
12 Months	0.4510 (0.3120 to 0.5802)	0.2074 (0.1167 to 0.3159)	0.3115 (0.1935 to 0.4369)	0.1235 (0.0513 to 0.2293)	0.1208 (0.0408 to 0.2476)	0.0700 (0.0126 to 0.1988)	
14 Months	0.4510 (0.3120 to 0.5802)	0.2074 (0.1167 to 0.3159)	0.3115 (0.1935 to 0.4369)	0.0926 (0.0298 to 0.1996)	0.1208 (0.0408 to 0.2476)	0.0700 (0.0126 to 0.1988)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_seiss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.10 Subgroup analyses by ISS staging
16.2.7.1.1.10.5 Treatment emergent severe adverse event by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.4163 (0.2744 to 0.5522)	0.2074 (0.1167 to 0.3159)	0.3115 (0.1935 to 0.4369)	0.0926 (0.0298 to 0.1996)	0.1208 (0.0408 to 0.2476)	0.0700 (0.0126 to 0.1988)	
Number of patients at risk[b]							
2 Months	34	22	23	16	12	11	
4 Months	28	15	19	10	8	6	
6 Months	25	14	17	6	4	5	
8 Months	22	12	14	6	3	4	
10 Months	22	11	14	6	3	3	
12 Months	20	8	11	6	2	2	
14 Months	13	6	6	3	1	2	
16 Months	9	2	2	1	1	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_seiss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.10 Subgroup analyses by ISS staging
16.2.7.1.1.10.6 Treatment emergent severe adverse event including death by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (56.9)	51 (81.0)	38 (69.1)	48 (90.6)	36 (90.0)	30 (90.9)	0.1166
Number (%) of patients censored	22 (43.1)	12 (19.0)	17 (30.9)	5 (9.4)	4 (10.0)	3 (9.1)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	0.7885 (0.5914 to 2.2669)	0.5585 (0.3285 to 0.7556)	0.5257 (0.1643 to 0.7885)	0.4928 (0.2300 to 0.6242)	0.3121 (0.1643 to 0.5585)	0.4600 (0.1643 to 0.5257)	
Median (95% CI)	5.5852 (2.0370 to NC)	1.0021 (0.7556 to 1.9055)	1.5606 (0.7885 to 2.8255)	0.8542 (0.5914 to 1.3142)	0.8214 (0.4600 to 1.4456)	0.7556 (0.4928 to 1.2156)	
75% quantile (95% CI)	NC (NC to NC)	3.7782 (1.9384 to NC)	NC (2.8255 to NC)	2.1355 (1.1499 to 5.6181)	2.9405 (1.1170 to 4.6653)	3.3183 (0.7885 to 8.3450)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd		0.0019		0.0274		0.9855	
Hazard ratio (95% CI) vs Pd		2.0477 (1.2903 to 3.2497)		1.6192 (1.0511 to 2.4945)		0.9955 (0.6120 to 1.6192)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_seiss_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.10 Subgroup analyses by ISS staging
16.2.7.1.1.10.6 Treatment emergent severe adverse event including death by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
P-value		0.0024		0.0288		0.9855	
Hazard ratio inverted (95% CI) vs IPd	0.4884 (0.3077 to 0.7750)		0.6176 (0.4009 to 0.9514)				
probability (95% CI)[b]							
2 Months	0.6667 (0.5198 to 0.7778)	0.3548 (0.2387 to 0.4727)	0.4259 (0.2932 to 0.5522)	0.2830 (0.1699 to 0.4070)	0.3000 (0.1680 to 0.4437)	0.3333 (0.1819 to 0.4926)	
4 Months	0.5490 (0.4034 to 0.6730)	0.2419 (0.1443 to 0.3533)	0.3519 (0.2283 to 0.4778)	0.1887 (0.0972 to 0.3032)	0.2000 (0.0939 to 0.3345)	0.2020 (0.0848 to 0.3547)	
6 Months	0.4902 (0.3479 to 0.6179)	0.2419 (0.1443 to 0.3533)	0.3323 (0.2114 to 0.4579)	0.1132 (0.0460 to 0.2141)	0.1000 (0.0318 to 0.2149)	0.1684 (0.0632 to 0.3167)	
8 Months	0.4510 (0.3120 to 0.5802)	0.2074 (0.1167 to 0.3159)	0.3115 (0.1935 to 0.4369)	0.1132 (0.0460 to 0.2141)	0.1000 (0.0318 to 0.2149)	0.1347 (0.0436 to 0.2772)	
10 Months	0.4510 (0.3120 to 0.5802)	0.1901 (0.1034 to 0.2968)	0.3115 (0.1935 to 0.4369)	0.1132 (0.0460 to 0.2141)	0.1000 (0.0318 to 0.2149)	0.1010 (0.0263 to 0.2359)	
12 Months	0.4510 (0.3120 to 0.5802)	0.1901 (0.1034 to 0.2968)	0.3115 (0.1935 to 0.4369)	0.1132 (0.0460 to 0.2141)	0.1000 (0.0318 to 0.2149)	0.0673 (0.0121 to 0.1921)	
14 Months	0.4510 (0.3120 to 0.5802)	0.1901 (0.1034 to 0.2968)	0.3115 (0.1935 to 0.4369)	0.0849 (0.0269 to 0.1858)	0.1000 (0.0318 to 0.2149)	0.0673 (0.0121 to 0.1921)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_seiss_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.10 Subgroup analyses by ISS staging
16.2.7.1.1.10.6 Treatment emergent severe adverse event including death by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.4163 (0.2744 to 0.5522)	0.1901 (0.1034 to 0.2968)	0.3115 (0.1935 to 0.4369)	0.0849 (0.0269 to 0.1858)	0.1000 (0.0318 to 0.2149)	0.0673 (0.0121 to 0.1921)	
Number of patients at risk[b]							
2 Months	34	22	23	15	12	11	
4 Months	28	15	19	10	8	6	
6 Months	25	14	17	6	4	5	
8 Months	22	12	14	6	3	4	
10 Months	22	11	14	6	3	3	
12 Months	20	8	11	6	2	2	
14 Months	13	6	6	3	1	2	
16 Months	9	2	2	1	1	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_seiss_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.1 Treatment emergent adverse event by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (96.8)	39 (100.0)	95 (97.9)	97 (99.0)	21 (100.0)	15 (100.0)	0.3352
Number (%) of patients censored	1 (3.2)	0 (0.0)	2 (2.1)	1 (1.0)	0 (0.0)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	0.2300 (0.0657 to 0.4600)	0.0986 (0.0657 to 0.0986)	0.1314 (0.0986 to 0.1643)	0.1314 (0.0657 to 0.1314)	0.1314 (0.0329 to 0.1971)	0.0657 (0.0329 to 0.1314)	
Median (95% CI)	0.4928 (0.2957 to 0.8214)	0.1643 (0.0986 to 0.3614)	0.3285 (0.2300 to 0.4600)	0.1971 (0.1643 to 0.2628)	0.1971 (0.1314 to 0.5585)	0.1314 (0.0329 to 0.5585)	
75% quantile (95% CI)	0.9199 (0.6899 to 5.0595)	0.7228 (0.1971 to 1.3470)	0.9199 (0.5914 to 1.5441)	0.4928 (0.3285 to 0.7228)	0.6242 (0.2300 to 1.3470)	0.7885 (0.1314 to 3.9754)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd		0.0337		0.0135		0.8516	
Hazard ratio (95% CI) vs Pd		1.6843 (1.0358 to 2.7388)		1.4435 (1.0771 to 1.9347)		0.9355 (0.4650 to 1.8819)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_seriss_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.1 Treatment emergent adverse event by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
P-value		0.0356		0.0140		0.8516	
Hazard ratio inverted (95% CI) vs IPd	0.5937 (0.3651 to 0.9654)		0.6928 (0.5169 to 0.9285)				
probability (95% CI)[b]							
2 Months	0.1290 (0.0407 to 0.2698)	0.0769 (0.0199 to 0.1866)	0.1304 (0.0714 to 0.2076)	0.0417 (0.0136 to 0.0954)	0.0476 (0.0033 to 0.1970)	0.1333 (0.0219 to 0.3457)	
4 Months	0.1290 (0.0407 to 0.2698)	0.0256 (0.0020 to 0.1153)	0.0326 (0.0088 to 0.0843)	0.0208 (0.0040 to 0.0661)	0.0476 (0.0033 to 0.1970)	0.0667 (0.0043 to 0.2603)	
6 Months	0.0968 (0.0247 to 0.2291)	0.0256 (0.0020 to 0.1153)	0.0326 (0.0088 to 0.0843)	0.0104 (0.0009 to 0.0509)	0.0476 (0.0033 to 0.1970)	0.0667 (0.0043 to 0.2603)	
8 Months	0.0645 (0.0115 to 0.1862)	0.0256 (0.0020 to 0.1153)	0.0326 (0.0088 to 0.0843)	0.0104 (0.0009 to 0.0509)	0.0476 (0.0033 to 0.1970)	0.0667 (0.0043 to 0.2603)	
10 Months	0.0323 (0.0024 to 0.1411)	0.0256 (0.0020 to 0.1153)	0.0326 (0.0088 to 0.0843)	0.0104 (0.0009 to 0.0509)	0.0476 (0.0033 to 0.1970)	0.0667 (0.0043 to 0.2603)	
12 Months	0.0323 (0.0024 to 0.1411)	0.0256 (0.0020 to 0.1153)	0.0163 (0.0018 to 0.0691)	0.0104 (0.0009 to 0.0509)	0.0476 (0.0033 to 0.1970)	0.0667 (0.0043 to 0.2603)	
14 Months	0.0323 (0.0024 to 0.1411)	0.0256 (0.0020 to 0.1153)	0.0163 (0.0018 to 0.0691)	0.0104 (0.0009 to 0.0509)	0.0476 (0.0033 to 0.1970)	0.0667 (0.0043 to 0.2603)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_seriss_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.1 Treatment emergent adverse event by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0323 (0.0024 to 0.1411)	0.0256 (0.0020 to 0.1153)	0.0163 (0.0018 to 0.0691)	0.0104 (0.0009 to 0.0509)	0.0476 (0.0033 to 0.1970)	0.0667 (0.0043 to 0.2603)	
Number of patients at risk[b]							
2 Months	4	3	12	4	0	2	
4 Months	4	1	3	2	0	0	
6 Months	3	1	2	1	0	0	
8 Months	2	0	2	1	0	0	
10 Months	1	0	2	1	0	0	
12 Months	1	0	1	0	0	0	
14 Months	1	0	1	0	0	0	
16 Months	0	0	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_seriss_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.2 Treatment emergent serious adverse event by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (32.3)	14 (35.9)	54 (55.7)	68 (69.4)	16 (76.2)	12 (80.0)	0.5960
Number (%) of patients censored	21 (67.7)	25 (64.1)	43 (44.3)	30 (30.6)	5 (23.8)	3 (20.0)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	6.0452 (2.0370 to NC)	2.7926 (0.5585 to NC)	1.4784 (0.5914 to 1.9384)	0.7228 (0.3285 to 1.3142)	0.2957 (0.0657 to 1.0185)	0.4600 (0.1314 to 0.7885)	
Median (95% CI)	NC (12.1889 to NC)	NC (9.8234 to NC)	5.9795 (3.4497 to NC)	4.3039 (1.9713 to 8.3450)	1.1828 (0.2957 to 2.7598)	1.2813 (0.2628 to 6.9651)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.0062 to NC)	5.4209 (1.2813 to NC)	6.9651 (1.2813 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd		0.6124		0.1098		0.7446	
Hazard ratio (95% CI) vs Pd		1.2330 (0.5475 to 2.7767)		1.3385 (0.9352 to 1.9157)		0.8822 (0.4149 to 1.8761)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_seriss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.2 Treatment emergent serious adverse event by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
P-value		0.6131		0.1110		0.7448	
probability (95% CI)[b]							
2 Months	0.9355 (0.7659 to 0.9835)	0.8462 (0.6892 to 0.9278)	0.6598 (0.5564 to 0.7446)	0.5979 (0.4935 to 0.6877)	0.3810 (0.1831 to 0.5778)	0.4667 (0.2123 to 0.6875)	
4 Months	0.8387 (0.6550 to 0.9295)	0.7146 (0.5440 to 0.8308)	0.5670 (0.4626 to 0.6586)	0.5361 (0.4321 to 0.6292)	0.2721 (0.1042 to 0.4727)	0.3111 (0.1020 to 0.5503)	
6 Months	0.7742 (0.5840 to 0.8854)	0.6882 (0.5164 to 0.8095)	0.4924 (0.3892 to 0.5874)	0.4532 (0.3522 to 0.5486)	0.2041 (0.0592 to 0.4091)	0.3111 (0.1020 to 0.5503)	
8 Months	0.7097 (0.5162 to 0.8371)	0.6882 (0.5164 to 0.8095)	0.4697 (0.3671 to 0.5656)	0.4215 (0.3224 to 0.5173)	0.2041 (0.0592 to 0.4091)	0.2333 (0.0592 to 0.4727)	
10 Months	0.7097 (0.5162 to 0.8371)	0.6352 (0.4628 to 0.7655)	0.4697 (0.3671 to 0.5656)	0.3688 (0.2736 to 0.4642)	0.2041 (0.0592 to 0.4091)	0.1556 (0.0260 to 0.3874)	
12 Months	0.7097 (0.5162 to 0.8371)	0.6352 (0.4628 to 0.7655)	0.4574 (0.3550 to 0.5539)	0.3038 (0.2148 to 0.3973)	0.2041 (0.0592 to 0.4091)	0.1556 (0.0260 to 0.3874)	
14 Months	0.6742 (0.4786 to 0.8098)	0.6352 (0.4628 to 0.7655)	0.4431 (0.3405 to 0.5406)	0.3038 (0.2148 to 0.3973)	0.2041 (0.0592 to 0.4091)	0.1556 (0.0260 to 0.3874)	
16 Months	0.6742 (0.4786 to 0.8098)	0.6352 (0.4628 to 0.7655)	0.4185 (0.3115 to 0.5217)	0.3038 (0.2148 to 0.3973)	0.2041 (0.0592 to 0.4091)	0.1556 (0.0260 to 0.3874)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_seriss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.2 Treatment emergent serious adverse event by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	29	33	64	58	7	7	
4 Months	26	27	55	52	5	4	
6 Months	24	26	45	43	3	4	
8 Months	22	26	39	40	2	3	
10 Months	22	24	38	35	2	2	
12 Months	20	21	32	27	1	2	
14 Months	9	12	19	21	1	2	
16 Months	5	7	10	7	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_seriss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (3.2)	3 (7.7)	11 (11.3)	8 (8.2)	7 (33.3)	0 (0.0)	0.5951
Number (%) of patients censored	30 (96.8)	36 (92.3)	86 (88.7)	90 (91.8)	14 (66.7)	15 (100.0)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.9671 to NC)	1.2156 (0.1643 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.2156 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd		0.4363		0.3963		0.0150	
Hazard ratio (95% CI) vs Pd		2.3897 (0.2485 to 22.9773)		0.6759 (0.2718 to 1.6808)		NC (NC to NC)	
P-value		0.4506		0.3993		0.9958	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_seriss_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]							
2 Months	0.9677 (0.7923 to 0.9954)	0.9744 (0.8316 to 0.9963)	0.9377 (0.8665 to 0.9715)	1.0000 (1.0000 to 1.0000)	0.7083 (0.4619 to 0.8573)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9677 (0.7923 to 0.9954)	0.9744 (0.8316 to 0.9963)	0.9272 (0.8532 to 0.9646)	0.9686 (0.9059 to 0.9898)	0.7083 (0.4619 to 0.8573)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9677 (0.7923 to 0.9954)	0.9487 (0.8102 to 0.9869)	0.9057 (0.8266 to 0.9498)	0.9471 (0.8776 to 0.9776)	0.6375 (0.3784 to 0.8118)	1.0000 (1.0000 to 1.0000)	
8 Months	0.9677 (0.7923 to 0.9954)	0.9224 (0.7782 to 0.9743)	0.8933 (0.8105 to 0.9412)	0.9471 (0.8776 to 0.9776)	0.6375 (0.3784 to 0.8118)	1.0000 (1.0000 to 1.0000)	
10 Months	0.9677 (0.7923 to 0.9954)	0.9224 (0.7782 to 0.9743)	0.8933 (0.8105 to 0.9412)	0.9341 (0.8588 to 0.9700)	0.6375 (0.3784 to 0.8118)	1.0000 (1.0000 to 1.0000)	
12 Months	0.9677 (0.7923 to 0.9954)	0.9224 (0.7782 to 0.9743)	0.8933 (0.8105 to 0.9412)	0.9206 (0.8398 to 0.9616)	0.6375 (0.3784 to 0.8118)	1.0000 (1.0000 to 1.0000)	
14 Months	0.9677 (0.7923 to 0.9954)	0.9224 (0.7782 to 0.9743)	0.8735 (0.7791 to 0.9293)	0.9206 (0.8398 to 0.9616)	0.6375 (0.3784 to 0.8118)	1.0000 (1.0000 to 1.0000)	
16 Months	0.9677 (0.7923 to 0.9954)	0.9224 (0.7782 to 0.9743)	0.8735 (0.7791 to 0.9293)	0.8664 (0.6942 to 0.9452)	0.6375 (0.3784 to 0.8118)	1.0000 (1.0000 to 1.0000)	
Number of patients at risk[b]							

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_seriss_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	30	38	89	96	14	14	
4 Months	30	38	87	90	10	11	
6 Months	30	36	77	81	6	9	
8 Months	29	35	68	78	6	7	
10 Months	29	35	64	72	6	6	
12 Months	27	32	53	62	5	6	
14 Months	15	19	33	43	4	6	
16 Months	9	11	14	15	1	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_seriss_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.4 Treatment emergent mild adverse event by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (93.5)	39 (100.0)	90 (92.8)	88 (89.8)	18 (85.7)	14 (93.3)	0.5705
Number (%) of patients censored	2 (6.5)	0 (0.0)	7 (7.2)	10 (10.2)	3 (14.3)	1 (6.7)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	0.2300 (0.0657 to 0.4928)	0.0986 (0.0657 to 0.1314)	0.1314 (0.0986 to 0.2628)	0.1314 (0.0657 to 0.1643)	0.1971 (0.0329 to 0.2628)	0.0657 (0.0329 to 0.1314)	
Median (95% CI)	0.6899 (0.2957 to 0.8871)	0.1971 (0.0986 to 0.6571)	0.3943 (0.3285 to 0.7228)	0.2628 (0.1971 to 0.3285)	0.4928 (0.1971 to 1.0513)	0.1314 (0.0329 to 0.9528)	
75% quantile (95% CI)	1.8727 (0.8214 to 6.5051)	0.8214 (0.3614 to 3.7454)	1.5441 (0.8542 to 2.2341)	0.7556 (0.4928 to 2.2669)	1.1170 (0.4928 to NC)	1.4456 (0.1314 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd		0.0911		0.4479		0.9953	
Hazard ratio (95% CI) vs Pd		1.5136 (0.9328 to 2.4560)		1.1231 (0.8325 to 1.5152)		1.0022 (0.4762 to 2.1092)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_seriss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.4 Treatment emergent mild adverse event by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
P-value		0.0933		0.4473		0.9953	
probability (95% CI)[b]							
2 Months	0.1935 (0.0786 to 0.3464)	0.1538 (0.0624 to 0.2827)	0.1869 (0.1148 to 0.2725)	0.1959 (0.1240 to 0.2800)	0.0680 (0.0050 to 0.2555)	0.2000 (0.0489 to 0.4239)	
4 Months	0.1613 (0.0588 to 0.3088)	0.0769 (0.0199 to 0.1866)	0.0879 (0.0411 to 0.1569)	0.1406 (0.0798 to 0.2183)	0.0680 (0.0050 to 0.2555)	0.1333 (0.0219 to 0.3457)	
6 Months	0.1290 (0.0407 to 0.2698)	0.0769 (0.0199 to 0.1866)	0.0754 (0.0326 to 0.1420)	0.0974 (0.0458 to 0.1723)	0.0680 (0.0050 to 0.2555)	0.0667 (0.0043 to 0.2603)	
8 Months	0.0968 (0.0247 to 0.2291)	0.0256 (0.0020 to 0.1153)	0.0754 (0.0326 to 0.1420)	0.0812 (0.0341 to 0.1547)	0.0680 (0.0050 to 0.2555)	0.0667 (0.0043 to 0.2603)	
10 Months	0.0645 (0.0115 to 0.1862)	0.0256 (0.0020 to 0.1153)	0.0754 (0.0326 to 0.1420)	0.0812 (0.0341 to 0.1547)	0.0680 (0.0050 to 0.2555)	0.0667 (0.0043 to 0.2603)	
12 Months	0.0645 (0.0115 to 0.1862)	0.0256 (0.0020 to 0.1153)	0.0502 (0.0137 to 0.1245)	0.0812 (0.0341 to 0.1547)	0.0680 (0.0050 to 0.2555)	0.0667 (0.0043 to 0.2603)	
14 Months	0.0645 (0.0115 to 0.1862)	0.0256 (0.0020 to 0.1153)	0.0502 (0.0137 to 0.1245)	0.0812 (0.0341 to 0.1547)	0.0680 (0.0050 to 0.2555)	0.0667 (0.0043 to 0.2603)	
16 Months	0.0645 (0.0115 to 0.1862)	0.0256 (0.0020 to 0.1153)	0.0502 (0.0137 to 0.1245)	0.0812 (0.0341 to 0.1547)	0.0680 (0.0050 to 0.2555)	0.0667 (0.0043 to 0.2603)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_seriss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.4 Treatment emergent mild adverse event by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	6	6	17	18	0	3	
4 Months	5	3	8	11	0	2	
6 Months	4	3	4	6	0	1	
8 Months	3	1	4	5	0	1	
10 Months	2	1	3	5	0	1	
12 Months	2	1	2	4	0	1	
14 Months	2	1	2	4	0	1	
16 Months	1	0	0	2	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_seriss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.5 Treatment emergent severe adverse event by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (48.4)	29 (74.4)	67 (69.1)	88 (89.8)	21 (100.0)	12 (80.0)	0.0192
Number (%) of patients censored	16 (51.6)	10 (25.6)	30 (30.9)	10 (10.2)	0 (0.0)	3 (20.0)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	0.7885 (0.5257 to 4.3368)	0.5585 (0.2957 to 0.7556)	0.5585 (0.2957 to 0.7885)	0.5257 (0.2957 to 0.5914)	0.2300 (0.0657 to 0.3285)	0.4600 (0.1314 to 0.5257)	
Median (95% CI)	NC (2.0370 to NC)	1.8398 (0.7228 to 3.6468)	1.9384 (0.9528 to 3.4497)	0.8542 (0.7228 to 0.9856)	0.5585 (0.2300 to 1.1170)	0.5257 (0.2957 to 3.9754)	
75% quantile (95% CI)	NC (NC to NC)	NC (2.6940 to NC)	NC (5.5852 to NC)	2.3655 (1.3142 to 5.6181)	1.2813 (0.6242 to 3.7454)	3.9754 (0.5257 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd		0.0191		0.0009		0.1207	
Hazard ratio (95% CI) vs Pd		2.0801 (1.1122 to 3.8905)		1.7200 (1.2452 to 2.3757)		0.5597 (0.2664 to 1.1759)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.5 Treatment emergent severe adverse event by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
P-value		0.0219		0.0010		0.1255	
Hazard ratio inverted (95% CI) vs IPd	0.4807 (0.2570 to 0.8991)		0.5814 (0.4209 to 0.8031)				
probability (95% CI)[b]							
2 Months	0.7097 (0.5162 to 0.8371)	0.4615 (0.3016 to 0.6073)	0.4748 (0.3718 to 0.5707)	0.2887 (0.2024 to 0.3805)	0.1429 (0.0357 to 0.3212)	0.3636 (0.1339 to 0.6012)	
4 Months	0.6129 (0.4202 to 0.7585)	0.3077 (0.1725 to 0.4536)	0.3798 (0.2830 to 0.4760)	0.2057 (0.1319 to 0.2910)	0.0476 (0.0033 to 0.1970)	0.1818 (0.0318 to 0.4306)	
6 Months	0.5806 (0.3896 to 0.7309)	0.3077 (0.1725 to 0.4536)	0.3240 (0.2320 to 0.4191)	0.1380 (0.0774 to 0.2159)	0.0476 (0.0033 to 0.1970)	0.1818 (0.0318 to 0.4306)	
8 Months	0.5161 (0.3304 to 0.6736)	0.2564 (0.1332 to 0.3989)	0.3120 (0.2211 to 0.4069)	0.1265 (0.0687 to 0.2027)	0.0476 (0.0033 to 0.1970)	0.0909 (0.0058 to 0.3276)	
10 Months	0.5161 (0.3304 to 0.6736)	0.2564 (0.1332 to 0.3989)	0.3120 (0.2211 to 0.4069)	0.1150 (0.0602 to 0.1894)	0.0476 (0.0033 to 0.1970)	0.0909 (0.0058 to 0.3276)	
12 Months	0.5161 (0.3304 to 0.6736)	0.2564 (0.1332 to 0.3989)	0.3120 (0.2211 to 0.4069)	0.1022 (0.0507 to 0.1749)	0.0476 (0.0033 to 0.1970)	0.0909 (0.0058 to 0.3276)	
14 Months	0.5161 (0.3304 to 0.6736)	0.2564 (0.1332 to 0.3989)	0.3120 (0.2211 to 0.4069)	0.0818 (0.0340 to 0.1567)	0.0476 (0.0033 to 0.1970)	0.0909 (0.0058 to 0.3276)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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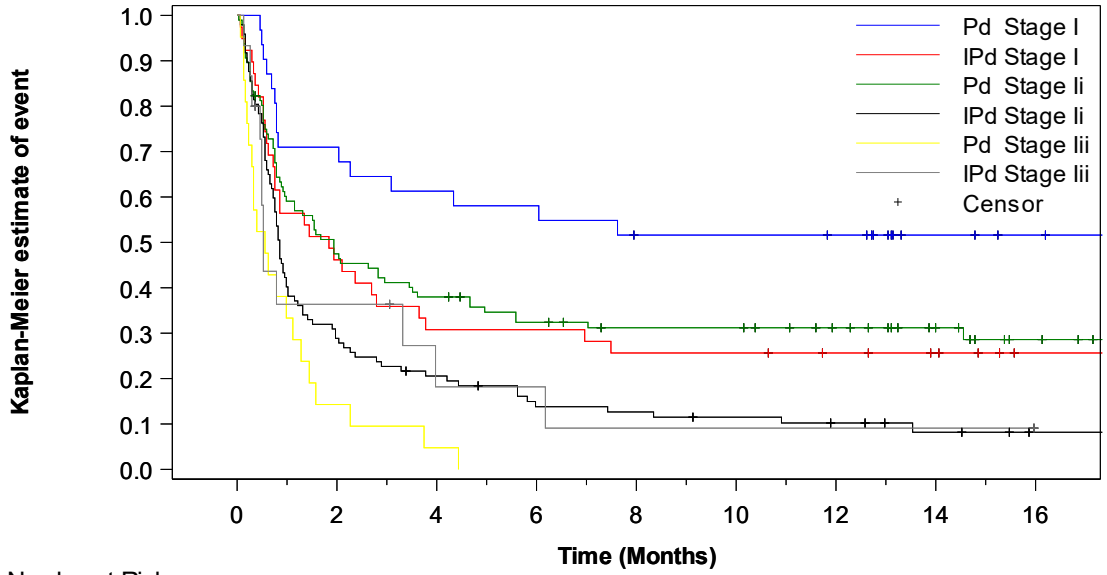
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.5 Treatment emergent severe adverse event by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5161 (0.3304 to 0.6736)	0.2564 (0.1332 to 0.3989)	0.2860 (0.1918 to 0.3871)	0.0818 (0.0340 to 0.1567)	0.0476 (0.0033 to 0.1970)	0.0909 (0.0058 to 0.3276)	
Number of patients at risk[b]							
2 Months	22	18	45	28	3	5	
4 Months	19	12	36	19	1	2	
6 Months	18	12	29	12	0	2	
8 Months	15	10	25	11	0	1	
10 Months	15	10	25	9	0	1	
12 Months	14	8	20	7	0	1	
14 Months	7	6	13	4	0	1	
16 Months	5	2	7	1	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_seriss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.6 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event by treatment group according to R-ISS stage - Safety population



Number at Risk									
Pd Stage I	31	22	19	18	15	15	14	7	5
IPd Stage I	39	18	12	12	10	10	8	6	2
Pd Stage Ii	96	45	36	29	25	25	20	13	7
IPd Stage Ii	97	28	19	12	11	9	7	4	1
Pd Stage Iii	21	3	1	0	0	0	0	0	0
IPd Stage Iii	15	5	2	2	1	1	1	1	0

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.7 Treatment emergent severe adverse event including death by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (48.4)	29 (74.4)	69 (71.1)	90 (91.8)	21 (100.0)	13 (86.7)	0.0271
Number (%) of patients censored	16 (51.6)	10 (25.6)	28 (28.9)	8 (8.2)	0 (0.0)	2 (13.3)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	0.7885 (0.5257 to 4.3368)	0.5585 (0.2957 to 0.7556)	0.5421 (0.2957 to 0.7885)	0.5257 (0.2957 to 0.5914)	0.2300 (0.0657 to 0.3285)	0.2957 (0.1314 to 0.4928)	
Median (95% CI)	NC (2.0370 to NC)	1.8398 (0.7228 to 3.6468)	1.8070 (0.9199 to 3.4497)	0.8542 (0.7228 to 0.9856)	0.5585 (0.2300 to 1.1170)	0.5257 (0.2628 to 3.3183)	
75% quantile (95% CI)	NC (NC to NC)	NC (2.6940 to NC)	NC (4.6653 to NC)	2.2669 (1.3142 to 5.6181)	1.2813 (0.6242 to 3.7454)	3.6468 (0.5257 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd		0.0191		0.0007		0.1858	
Hazard ratio (95% CI) vs Pd		2.0801 (1.1122 to 3.8905)		1.7248 (1.2538 to 2.3726)		0.6171 (0.2999 to 1.2696)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.7 Treatment emergent severe adverse event including death by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
P-value		0.0219		0.0008		0.1897	
Hazard ratio inverted (95% CI) vs IPd	0.4807 (0.2570 to 0.8991)		0.5798 (0.4215 to 0.7976)				
probability (95% CI)[b]							
2 Months	0.7097 (0.5162 to 0.8371)	0.4615 (0.3016 to 0.6073)	0.4688 (0.3666 to 0.5644)	0.2784 (0.1934 to 0.3696)	0.1429 (0.0357 to 0.3212)	0.3333 (0.1215 to 0.5640)	
4 Months	0.6129 (0.4202 to 0.7585)	0.3077 (0.1725 to 0.4536)	0.3750 (0.2791 to 0.4706)	0.1959 (0.1240 to 0.2800)	0.0476 (0.0033 to 0.1970)	0.1667 (0.0294 to 0.4024)	
6 Months	0.5806 (0.3896 to 0.7309)	0.3077 (0.1725 to 0.4536)	0.3107 (0.2210 to 0.4045)	0.1314 (0.0730 to 0.2073)	0.0476 (0.0033 to 0.1970)	0.1667 (0.0294 to 0.4024)	
8 Months	0.5161 (0.3304 to 0.6736)	0.2564 (0.1332 to 0.3989)	0.2992 (0.2107 to 0.3927)	0.1205 (0.0648 to 0.1946)	0.0476 (0.0033 to 0.1970)	0.0833 (0.0054 to 0.3060)	
10 Months	0.5161 (0.3304 to 0.6736)	0.2564 (0.1332 to 0.3989)	0.2992 (0.2107 to 0.3927)	0.0986 (0.0490 to 0.1687)	0.0476 (0.0033 to 0.1970)	0.0833 (0.0054 to 0.3060)	
12 Months	0.5161 (0.3304 to 0.6736)	0.2564 (0.1332 to 0.3989)	0.2992 (0.2107 to 0.3927)	0.0876 (0.0414 to 0.1554)	0.0476 (0.0033 to 0.1970)	0.0833 (0.0054 to 0.3060)	
14 Months	0.5161 (0.3304 to 0.6736)	0.2564 (0.1332 to 0.3989)	0.2992 (0.2107 to 0.3927)	0.0701 (0.0281 to 0.1385)	0.0476 (0.0033 to 0.1970)	0.0833 (0.0054 to 0.3060)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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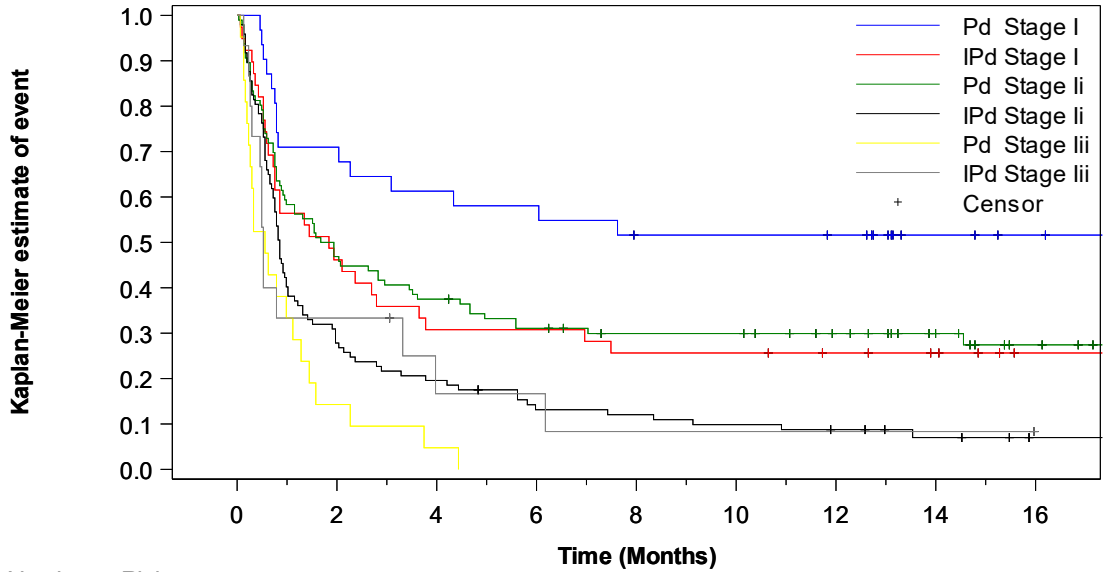
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.7 Treatment emergent severe adverse event including death by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5161 (0.3304 to 0.6736)	0.2564 (0.1332 to 0.3989)	0.2743 (0.1830 to 0.3733)	0.0701 (0.0281 to 0.1385)	0.0476 (0.0033 to 0.1970)	0.0833 (0.0054 to 0.3060)	
Number of patients at risk[b]							
2 Months	22	18	45	27	3	5	
4 Months	19	12	36	19	1	2	
6 Months	18	12	29	12	0	2	
8 Months	15	10	25	11	0	1	
10 Months	15	10	25	9	0	1	
12 Months	14	8	20	7	0	1	
14 Months	7	6	13	4	0	1	
16 Months	5	2	7	1	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_seriss_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.11 Subgroup analyses by R-ISS stage
16.2.7.1.1.11.8 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death by treatment group according to R-ISS stage - Safety population



Number at Risk									
Pd Stage I	31	22	19	18	15	15	14	7	5
IPd Stage I	39	18	12	12	10	10	8	6	2
Pd Stage Ii	96	45	36	29	25	25	20	13	7
IPd Stage Ii	97	27	19	12	11	9	7	4	1
Pd Stage Iii	21	3	1	0	0	0	0	0	0
IPd Stage Iii	15	5	2	2	1	1	1	1	0

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.1.12.1 Treatment emergent adverse event by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (90.5)	14 (100.0)	92 (98.9)	115 (99.1)	0.2217
Number (%) of patients censored	2 (9.5)	0 (0.0)	1 (1.1)	1 (0.9)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0657 to 0.3285)	0.0657 (0.0329 to 0.1314)	0.1643 (0.1314 to 0.2300)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.3285 (0.1314 to 1.1170)	0.1314 (0.0657 to 0.1643)	0.3943 (0.2957 to 0.6242)	0.1971 (0.1643 to 0.2957)	
75% quantile (95% CI)	1.2813 (0.3285 to NC)	0.1643 (0.1314 to 3.3183)	0.9528 (0.7885 to 1.7741)	0.5914 (0.4600 to 0.7885)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0804		0.0166	
Hazard ratio (95% CI) vs Pd		1.8874 (0.9162 to 3.8880)		1.4064 (1.0627 to 1.8613)	
P-value		0.0850		0.0171	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.1.12.1 Treatment emergent adverse event by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.7110 (0.5373 to 0.9410)		
probability (95% CI)[b]					
2 Months	0.1500 (0.0373 to 0.3347)	0.0714 (0.0045 to 0.2752)	0.1236 (0.0656 to 0.2010)	0.0609 (0.0269 to 0.1147)	
4 Months	0.1000 (0.0170 to 0.2723)	0.0714 (0.0045 to 0.2752)	0.0449 (0.0146 to 0.1025)	0.0261 (0.0071 to 0.0683)	
6 Months	0.1000 (0.0170 to 0.2723)	0.0714 (0.0045 to 0.2752)	0.0337 (0.0090 to 0.0870)	0.0174 (0.0034 to 0.0558)	
8 Months	0.1000 (0.0170 to 0.2723)	0.0714 (0.0045 to 0.2752)	0.0225 (0.0043 to 0.0710)	0.0087 (0.0008 to 0.0431)	
10 Months	0.1000 (0.0170 to 0.2723)	0.0714 (0.0045 to 0.2752)	0.0225 (0.0043 to 0.0710)	0.0087 (0.0008 to 0.0431)	
12 Months	0.1000 (0.0170 to 0.2723)	0.0714 (0.0045 to 0.2752)	0.0112 (0.0010 to 0.0546)	0.0087 (0.0008 to 0.0431)	
14 Months	0.1000 (0.0170 to 0.2723)	0.0714 (0.0045 to 0.2752)	0.0112 (0.0010 to 0.0546)	0.0087 (0.0008 to 0.0431)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.1.12.1 Treatment emergent adverse event by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.1000 (0.0170 to 0.2723)	0.0714 (0.0045 to 0.2752)	0.0112 (0.0010 to 0.0546)	0.0087 (0.0008 to 0.0431)	
Number of patients at risk[b]					
2 Months	3	1	11	7	
4 Months	2	0	4	3	
6 Months	1	0	3	2	
8 Months	1	0	2	1	
10 Months	1	0	2	1	
12 Months	1	0	1	0	
14 Months	1	0	1	0	
16 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.1.12.2 Treatment emergent serious adverse event by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (66.7)	10 (71.4)	52 (55.9)	69 (59.5)	0.5985
Number (%) of patients censored	7 (33.3)	4 (28.6)	41 (44.1)	47 (40.5)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.5585 (0.0657 to 1.3799)	0.1643 (0.0657 to 0.3285)	1.5441 (0.7228 to 2.8255)	1.3142 (0.6571 to 2.2669)	
Median (95% CI)	3.4497 (0.5585 to NC)	0.3943 (0.1314 to NC)	6.0452 (3.7782 to NC)	8.0164 (3.9754 to 11.1376)	
75% quantile (95% CI)	NC (3.4497 to NC)	NC (0.3285 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.5176		0.7221	
Hazard ratio (95% CI) vs Pd		1.3099 (0.5770 to 2.9737)		1.0675 (0.7439 to 1.5318)	
P-value		0.5188		0.7231	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.1.12.2 Treatment emergent serious adverse event by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.5714 (0.3380 to 0.7492)	0.3571 (0.1303 to 0.5944)	0.7097 (0.6059 to 0.7908)	0.6870 (0.5936 to 0.7631)	
4 Months	0.4675 (0.2469 to 0.6615)	0.3571 (0.1303 to 0.5944)	0.6022 (0.4953 to 0.6933)	0.5899 (0.4941 to 0.6736)	
6 Months	0.4091 (0.1976 to 0.6110)	0.3571 (0.1303 to 0.5944)	0.5021 (0.3962 to 0.5989)	0.5452 (0.4494 to 0.6312)	
8 Months	0.2922 (0.1120 to 0.5009)	0.3571 (0.1303 to 0.5944)	0.4790 (0.3737 to 0.5767)	0.5088 (0.4136 to 0.5963)	
10 Months	0.2922 (0.1120 to 0.5009)	0.2857 (0.0883 to 0.5237)	0.4790 (0.3737 to 0.5767)	0.4543 (0.3608 to 0.5431)	
12 Months	0.2922 (0.1120 to 0.5009)	0.2857 (0.0883 to 0.5237)	0.4670 (0.3621 to 0.5652)	0.3989 (0.3081 to 0.4879)	
14 Months	0.2922 (0.1120 to 0.5009)	0.2857 (0.0883 to 0.5237)	0.4387 (0.3338 to 0.5387)	0.3989 (0.3081 to 0.4879)	
16 Months	0.2922 (0.1120 to 0.5009)	0.2857 (0.0883 to 0.5237)	0.4168 (0.3093 to 0.5206)	0.3989 (0.3081 to 0.4879)	
Number of patients at risk[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.1.12.2 Treatment emergent serious adverse event by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	11	5	66	79	
4 Months	9	5	56	66	
6 Months	7	5	44	60	
8 Months	5	5	41	56	
10 Months	5	4	40	50	
12 Months	5	4	33	40	
14 Months	4	3	20	28	
16 Months	2	1	10	11	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.1.12.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (28.6)	2 (14.3)	9 (9.7)	9 (7.8)	0.6202
Number (%) of patients censored	15 (71.4)	12 (85.7)	84 (90.3)	107 (92.2)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.3799 (0.1971 to NC)	9.1335 (4.3368 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (1.3799 to NC)	NC (4.3368 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.3348		0.5406	
Hazard ratio (95% CI) vs Pd		0.4634 (0.0934 to 2.2991)		0.7500 (0.2976 to 1.8904)	
P-value		0.3466		0.5419	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.1.12.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.7143 (0.4715 to 0.8602)	1.0000 (1.0000 to 1.0000)	0.9461 (0.8754 to 0.9772)	0.9914 (0.9404 to 0.9988)	
4 Months	0.7143 (0.4715 to 0.8602)	1.0000 (1.0000 to 1.0000)	0.9352 (0.8615 to 0.9704)	0.9654 (0.9105 to 0.9869)	
6 Months	0.7143 (0.4715 to 0.8602)	0.8889 (0.4330 to 0.9836)	0.9018 (0.8198 to 0.9477)	0.9477 (0.8873 to 0.9762)	
8 Months	0.7143 (0.4715 to 0.8602)	0.8889 (0.4330 to 0.9836)	0.9018 (0.8198 to 0.9477)	0.9382 (0.8747 to 0.9701)	
10 Months	0.7143 (0.4715 to 0.8602)	0.7407 (0.2892 to 0.9300)	0.9018 (0.8198 to 0.9477)	0.9382 (0.8747 to 0.9701)	
12 Months	0.7143 (0.4715 to 0.8602)	0.7407 (0.2892 to 0.9300)	0.9018 (0.8198 to 0.9477)	0.9277 (0.8603 to 0.9633)	
14 Months	0.7143 (0.4715 to 0.8602)	0.7407 (0.2892 to 0.9300)	0.9018 (0.8198 to 0.9477)	0.9277 (0.8603 to 0.9633)	
16 Months	0.7143 (0.4715 to 0.8602)	0.7407 (0.2892 to 0.9300)	0.9018 (0.8198 to 0.9477)	0.8920 (0.7728 to 0.9506)	
Number of patients at risk[b]					
2 Months	15	12	87	115	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.1.12.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	13	9	84	109	
6 Months	10	7	74	101	
8 Months	10	6	67	98	
10 Months	10	5	64	92	
12 Months	10	5	53	80	
14 Months	9	4	35	56	
16 Months	4	1	16	23	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.1.12.4 Treatment emergent mild adverse event by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (76.2)	12 (85.7)	87 (93.5)	108 (93.1)	0.7920
Number (%) of patients censored	5 (23.8)	2 (14.3)	6 (6.5)	8 (6.9)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.2300 (0.0657 to 0.4928)	0.1314 (0.0329 to 0.1643)	0.1971 (0.1314 to 0.2957)	0.0986 (0.0657 to 0.1643)	
Median (95% CI)	0.5585 (0.1971 to 1.4784)	0.2464 (0.0657 to 2.2998)	0.5421 (0.3285 to 0.8214)	0.2464 (0.1643 to 0.3614)	
75% quantile (95% CI)	3.1704 (0.7228 to NC)	2.2998 (0.1643 to NC)	1.5770 (0.9199 to 2.5626)	0.7885 (0.5914 to 2.0698)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.4322		0.1568	
Hazard ratio (95% CI) vs Pd		1.3617 (0.6283 to 2.9511)		1.2297 (0.9232 to 1.6379)	
P-value		0.4340		0.1575	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.1.12.4 Treatment emergent mild adverse event by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.2500 (0.0830 to 0.4621)	0.2857 (0.0883 to 0.5237)	0.2000 (0.1249 to 0.2879)	0.1810 (0.1172 to 0.2560)	
4 Months	0.2500 (0.0830 to 0.4621)	0.0952 (0.0063 to 0.3353)	0.1000 (0.0491 to 0.1722)	0.1369 (0.0817 to 0.2062)	
6 Months	0.1250 (0.0111 to 0.3827)	0.0952 (0.0063 to 0.3353)	0.0889 (0.0415 to 0.1586)	0.0996 (0.0531 to 0.1632)	
8 Months	0.1250 (0.0111 to 0.3827)	0.0952 (0.0063 to 0.3353)	0.0741 (0.0310 to 0.1423)	0.0697 (0.0318 to 0.1279)	
10 Months	0.1250 (0.0111 to 0.3827)	0.0952 (0.0063 to 0.3353)	0.0741 (0.0310 to 0.1423)	0.0697 (0.0318 to 0.1279)	
12 Months	0.1250 (0.0111 to 0.3827)	0.0952 (0.0063 to 0.3353)	0.0556 (0.0183 to 0.1240)	0.0697 (0.0318 to 0.1279)	
14 Months	0.1250 (0.0111 to 0.3827)	0.0952 (0.0063 to 0.3353)	0.0556 (0.0183 to 0.1240)	0.0697 (0.0318 to 0.1279)	
16 Months	0.1250 (0.0111 to 0.3827)	0.0952 (0.0063 to 0.3353)	0.0556 (0.0183 to 0.1240)	0.0581 (0.0238 to 0.1146)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.1.12.4 Treatment emergent mild adverse event by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	3	3	18	21	
4 Months	3	0	9	15	
6 Months	1	0	6	10	
8 Months	1	0	5	7	
10 Months	1	0	4	7	
12 Months	1	0	3	6	
14 Months	1	0	3	6	
16 Months	0	0	1	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.1.12.5 Treatment emergent severe adverse event by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (71.4)	11 (78.6)	66 (71.0)	99 (85.3)	0.5037
Number (%) of patients censored	6 (28.6)	3 (21.4)	27 (29.0)	17 (14.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.3285 (0.0657 to 0.7885)	0.1643 (0.0657 to 0.4600)	0.5914 (0.4600 to 0.7885)	0.5257 (0.4271 to 0.6571)	
Median (95% CI)	2.2669 (0.3285 to 7.0308)	0.4600 (0.1314 to 0.8542)	1.9384 (0.9856 to 3.5154)	0.9199 (0.7885 to 1.3470)	
75% quantile (95% CI)	NC (3.4497 to NC)	0.8542 (0.4600 to NC)	NC (4.6653 to NC)	3.6468 (2.1355 to 7.4251)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.2347		0.0147	
Hazard ratio (95% CI) vs Pd		1.6067 (0.7301 to 3.5355)		1.4764 (1.0774 to 2.0231)	
P-value		0.2387		0.0154	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.1.12.5 Treatment emergent severe adverse event by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.6773 (0.4943 to 0.9282)		
probability (95% CI)[b]					
2 Months	0.5238 (0.2967 to 0.7088)	0.2449 (0.0608 to 0.4931)	0.4954 (0.3892 to 0.5928)	0.3478 (0.2622 to 0.4346)	
4 Months	0.4286 (0.2192 to 0.6231)	0.1633 (0.0267 to 0.4040)	0.3743 (0.2759 to 0.4724)	0.2236 (0.1522 to 0.3038)	
6 Months	0.3214 (0.1371 to 0.5229)	0.1633 (0.0267 to 0.4040)	0.3179 (0.2250 to 0.4145)	0.1864 (0.1207 to 0.2632)	
8 Months	0.2679 (0.1011 to 0.4690)	0.1633 (0.0267 to 0.4040)	0.2943 (0.2040 to 0.3901)	0.1584 (0.0978 to 0.2321)	
10 Months	0.2679 (0.1011 to 0.4690)	0.1633 (0.0267 to 0.4040)	0.2943 (0.2040 to 0.3901)	0.1491 (0.0904 to 0.2216)	
12 Months	0.2679 (0.1011 to 0.4690)	0.1633 (0.0267 to 0.4040)	0.2943 (0.2040 to 0.3901)	0.1392 (0.0824 to 0.2105)	
14 Months	0.2679 (0.1011 to 0.4690)	0.1633 (0.0267 to 0.4040)	0.2943 (0.2040 to 0.3901)	0.1392 (0.0824 to 0.2105)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.1.12.5 Treatment emergent severe adverse event by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.2679 (0.1011 to 0.4690)	0.1633 (0.0267 to 0.4040)	0.2716 (0.1802 to 0.3711)	0.1392 (0.0824 to 0.2105)	
Number of patients at risk[b]					
2 Months	11	3	45	40	
4 Months	9	2	34	24	
6 Months	6	2	28	20	
8 Months	5	2	23	17	
10 Months	5	1	23	16	
12 Months	5	1	20	12	
14 Months	4	1	13	9	
16 Months	3	0	6	3	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.1.12.6 Treatment emergent severe adverse event including death by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (71.4)	13 (92.9)	68 (73.1)	100 (86.2)	0.2407
Number (%) of patients censored	6 (28.6)	1 (7.1)	25 (26.9)	16 (13.8)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.3285 (0.0657 to 0.7885)	0.1643 (0.0657 to 0.2957)	0.5914 (0.4600 to 0.7885)	0.5257 (0.4271 to 0.6571)	
Median (95% CI)	2.2669 (0.3285 to 7.0308)	0.3778 (0.1314 to 0.8542)	1.7577 (0.9856 to 3.5154)	0.9199 (0.7885 to 1.3470)	
75% quantile (95% CI)	NC (3.4497 to NC)	0.8542 (0.2957 to NC)	NC (4.6653 to NC)	3.3183 (2.0370 to 6.1766)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0789		0.0178	
Hazard ratio (95% CI) vs Pd		1.9405 (0.9146 to 4.1173)		1.4545 (1.0651 to 1.9864)	
P-value		0.0841		0.0185	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.1.12.6 Treatment emergent severe adverse event including death by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.6875 (0.5034 to 0.9389)		
probability (95% CI)[b]					
2 Months	0.5238 (0.2967 to 0.7088)	0.2143 (0.0521 to 0.4479)	0.4891 (0.3838 to 0.5862)	0.3391 (0.2543 to 0.4257)	
4 Months	0.4286 (0.2192 to 0.6231)	0.1429 (0.0232 to 0.3655)	0.3696 (0.2721 to 0.4670)	0.2159 (0.1458 to 0.2951)	
6 Months	0.3214 (0.1371 to 0.5229)	0.1429 (0.0232 to 0.3655)	0.3043 (0.2139 to 0.3995)	0.1799 (0.1157 to 0.2556)	
8 Months	0.2679 (0.1011 to 0.4690)	0.1429 (0.0232 to 0.3655)	0.2817 (0.1940 to 0.3758)	0.1529 (0.0939 to 0.2253)	
10 Months	0.2679 (0.1011 to 0.4690)	0.0714 (0.0045 to 0.2752)	0.2817 (0.1940 to 0.3758)	0.1439 (0.0868 to 0.2150)	
12 Months	0.2679 (0.1011 to 0.4690)	0.0714 (0.0045 to 0.2752)	0.2817 (0.1940 to 0.3758)	0.1343 (0.0791 to 0.2042)	
14 Months	0.2679 (0.1011 to 0.4690)	0.0714 (0.0045 to 0.2752)	0.2817 (0.1940 to 0.3758)	0.1343 (0.0791 to 0.2042)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.1.12.6 Treatment emergent severe adverse event including death by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.2679 (0.1011 to 0.4690)	0.0714 (0.0045 to 0.2752)	0.2601 (0.1715 to 0.3574)	0.1343 (0.0791 to 0.2042)	
Number of patients at risk[b]					
2 Months	11	3	45	39	
4 Months	9	2	34	24	
6 Months	6	2	28	20	
8 Months	5	2	23	17	
10 Months	5	1	23	16	
12 Months	5	1	20	12	
14 Months	4	1	13	9	
16 Months	3	0	6	3	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.1 Treatment emergent adverse event by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (94.1)	23 (100.0)	75 (98.7)	102 (99.0)	0.1679
Number (%) of patients censored	2 (5.9)	0 (0.0)	1 (1.3)	1 (1.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0657 to 0.3285)	0.0657 (0.0329 to 0.1314)	0.1314 (0.0986 to 0.2300)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.3450 (0.1643 to 1.0513)	0.1643 (0.1314 to 0.2957)	0.3778 (0.2957 to 0.6242)	0.1971 (0.1643 to 0.3285)	
75% quantile (95% CI)	1.2813 (0.5585 to 3.1540)	0.4600 (0.1643 to 0.5585)	0.8871 (0.6899 to 1.5113)	0.7228 (0.4928 to 0.7885)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0206		0.0701	
Hazard ratio (95% CI) vs Pd		1.9264 (1.0966 to 3.3844)		1.3213 (0.9765 to 1.7878)	
P-value		0.0226		0.0710	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.1 Treatment emergent adverse event by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.5191 (0.2955 to 0.9119)				
probability (95% CI)[b]					
2 Months	0.1250 (0.0395 to 0.2623)	0.0435 (0.0031 to 0.1824)	0.1081 (0.0505 to 0.1906)	0.0686 (0.0302 to 0.1285)	
4 Months	0.0625 (0.0111 to 0.1811)	0.0435 (0.0031 to 0.1824)	0.0541 (0.0175 to 0.1219)	0.0294 (0.0079 to 0.0765)	
6 Months	0.0625 (0.0111 to 0.1811)	0.0435 (0.0031 to 0.1824)	0.0405 (0.0108 to 0.1035)	0.0196 (0.0038 to 0.0624)	
8 Months	0.0625 (0.0111 to 0.1811)	0.0435 (0.0031 to 0.1824)	0.0270 (0.0051 to 0.0843)	0.0098 (0.0009 to 0.0481)	
10 Months	0.0625 (0.0111 to 0.1811)	0.0435 (0.0031 to 0.1824)	0.0270 (0.0051 to 0.0843)	0.0098 (0.0009 to 0.0481)	
12 Months	0.0625 (0.0111 to 0.1811)	0.0435 (0.0031 to 0.1824)	0.0135 (0.0012 to 0.0647)	0.0098 (0.0009 to 0.0481)	
14 Months	0.0625 (0.0111 to 0.1811)	0.0435 (0.0031 to 0.1824)	0.0135 (0.0012 to 0.0647)	0.0098 (0.0009 to 0.0481)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.1 Treatment emergent adverse event by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0625 (0.0111 to 0.1811)	0.0435 (0.0031 to 0.1824)	0.0135 (0.0012 to 0.0647)	0.0098 (0.0009 to 0.0481)	
Number of patients at risk[b]					
2 Months	4	1	8	7	
4 Months	2	0	4	3	
6 Months	1	0	3	2	
8 Months	1	0	2	1	
10 Months	1	0	2	1	
12 Months	1	0	1	0	
14 Months	1	0	1	0	
16 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.2 Treatment emergent serious adverse event by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (50.0)	17 (73.9)	47 (61.8)	60 (58.3)	0.0389
Number (%) of patients censored	17 (50.0)	6 (26.1)	29 (38.2)	43 (41.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.1828 (0.1314 to 4.0739)	0.2628 (0.0657 to 0.4600)	1.4949 (0.5914 to 2.6283)	1.3470 (0.6571 to 2.3655)	
Median (95% CI)	7.0308 (2.2669 to NC)	0.4928 (0.3285 to 9.1335)	5.1910 (2.8255 to 12.1889)	8.3450 (3.7782 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.7228 to NC)	NC (14.5544 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0475		0.6349	
Hazard ratio (95% CI) vs Pd		1.9569 (0.9951 to 3.8482)		0.9113 (0.6211 to 1.3372)	
P-value		0.0517		0.6351	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.2 Treatment emergent serious adverse event by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.7059 (0.5224 to 0.8296)	0.3913 (0.1988 to 0.5798)	0.6842 (0.5669 to 0.7759)	0.6961 (0.5968 to 0.7755)	
4 Months	0.6138 (0.4291 to 0.7546)	0.3913 (0.1988 to 0.5798)	0.5658 (0.4472 to 0.6683)	0.5864 (0.4843 to 0.6751)	
6 Months	0.5507 (0.3681 to 0.7005)	0.3913 (0.1988 to 0.5798)	0.4588 (0.3441 to 0.5661)	0.5460 (0.4440 to 0.6370)	
8 Months	0.4773 (0.2971 to 0.6372)	0.3478 (0.1663 to 0.5371)	0.4314 (0.3184 to 0.5393)	0.5151 (0.4135 to 0.6075)	
10 Months	0.4773 (0.2971 to 0.6372)	0.2609 (0.1062 to 0.4469)	0.4314 (0.3184 to 0.5393)	0.4636 (0.3636 to 0.5575)	
12 Months	0.4773 (0.2971 to 0.6372)	0.2609 (0.1062 to 0.4469)	0.4170 (0.3049 to 0.5252)	0.4111 (0.3138 to 0.5057)	
14 Months	0.4773 (0.2971 to 0.6372)	0.2609 (0.1062 to 0.4469)	0.3850 (0.2744 to 0.4943)	0.4111 (0.3138 to 0.5057)	
16 Months	0.4773 (0.2971 to 0.6372)	0.2609 (0.1062 to 0.4469)	0.3609 (0.2491 to 0.4737)	0.4111 (0.3138 to 0.5057)	
Number of patients at risk[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.2 Treatment emergent serious adverse event by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	23	9	52	71	
4 Months	20	9	43	58	
6 Months	15	9	34	53	
8 Months	13	8	31	50	
10 Months	13	6	30	45	
12 Months	10	6	26	36	
14 Months	7	4	16	25	
16 Months	4	1	8	10	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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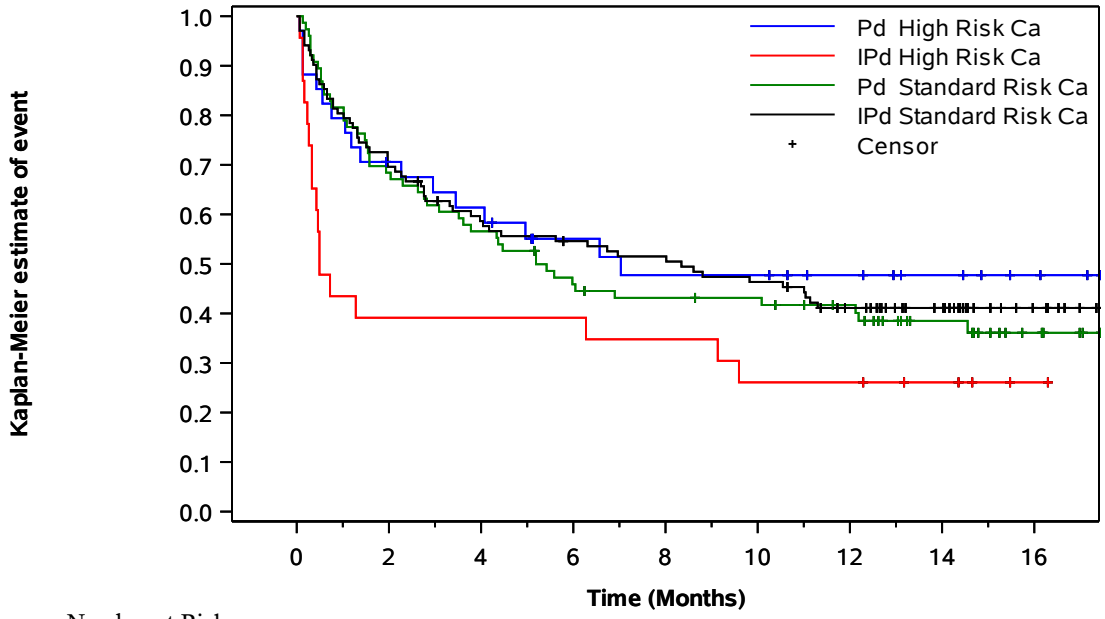
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.3 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event by treatment group according to cytogenetic abnormality - Safety population



Number at Risk									
Pd High Risk Ca	34	23	20	15	13	13	10	7	4
IPd High Risk Ca	23	9	9	9	8	6	6	4	1
Pd Standard Risk Ca	76	52	43	34	31	30	26	16	8
IPd Standard Risk Ca	102	71	58	53	50	45	36	25	10

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (23.5)	2 (8.7)	6 (7.9)	7 (6.8)	0.3618
Number (%) of patients censored	26 (76.5)	21 (91.3)	70 (92.1)	96 (93.2)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (0.4271 to NC)	NC (4.3368 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.1538		0.7306	
Hazard ratio (95% CI) vs Pd		0.3412 (0.0724 to 1.6071)		0.8258 (0.2774 to 2.4584)	
P-value		0.1738		0.7310	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.7941 (0.6161 to 0.8961)	1.0000 (1.0000 to 1.0000)	0.9472 (0.8654 to 0.9798)	0.9903 (0.9331 to 0.9986)	
4 Months	0.7941 (0.6161 to 0.8961)	1.0000 (1.0000 to 1.0000)	0.9472 (0.8654 to 0.9798)	0.9611 (0.8996 to 0.9852)	
6 Months	0.7624 (0.5802 to 0.8735)	0.9444 (0.6664 to 0.9920)	0.9201 (0.8308 to 0.9633)	0.9410 (0.8734 to 0.9731)	
8 Months	0.7624 (0.5802 to 0.8735)	0.9444 (0.6664 to 0.9920)	0.9201 (0.8308 to 0.9633)	0.9410 (0.8734 to 0.9731)	
10 Months	0.7624 (0.5802 to 0.8735)	0.8770 (0.5880 to 0.9681)	0.9201 (0.8308 to 0.9633)	0.9410 (0.8734 to 0.9731)	
12 Months	0.7624 (0.5802 to 0.8735)	0.8770 (0.5880 to 0.9681)	0.9201 (0.8308 to 0.9633)	0.9410 (0.8734 to 0.9731)	
14 Months	0.7624 (0.5802 to 0.8735)	0.8770 (0.5880 to 0.9681)	0.9201 (0.8308 to 0.9633)	0.9410 (0.8734 to 0.9731)	
16 Months	0.7624 (0.5802 to 0.8735)	0.8770 (0.5880 to 0.9681)	0.9201 (0.8308 to 0.9633)	0.9018 (0.7687 to 0.9602)	
Number of patients at risk[b]					
2 Months	27	21	71	102	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	25	18	70	96	
6 Months	19	16	63	88	
8 Months	19	14	56	87	
10 Months	19	13	53	81	
12 Months	16	11	45	72	
14 Months	12	8	31	50	
16 Months	6	2	14	21	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.5 Treatment emergent mild adverse event by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (82.4)	21 (91.3)	71 (93.4)	95 (92.2)	0.8583
Number (%) of patients censored	6 (17.6)	2 (8.7)	5 (6.6)	8 (7.8)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.2628 (0.0657 to 0.3614)	0.1314 (0.0329 to 0.1971)	0.1643 (0.0986 to 0.2957)	0.0986 (0.0657 to 0.1643)	
Median (95% CI)	0.5914 (0.3285 to 1.4456)	0.2957 (0.1314 to 1.1499)	0.4271 (0.3285 to 0.8214)	0.2300 (0.1643 to 0.4271)	
75% quantile (95% CI)	1.5441 (0.7228 to NC)	2.2998 (0.3285 to 7.6550)	1.4456 (0.8542 to 2.5626)	0.7885 (0.5914 to 2.0698)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.4107		0.2127	
Hazard ratio (95% CI) vs Pd		1.2710 (0.7169 to 2.2535)		1.2184 (0.8926 to 1.6632)	
P-value		0.4118		0.2134	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.5 Treatment emergent mild adverse event by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.2083 (0.0869 to 0.3652)	0.2609 (0.1062 to 0.4469)	0.1892 (0.1097 to 0.2853)	0.1748 (0.1087 to 0.2538)	
4 Months	0.1667 (0.0588 to 0.3221)	0.1043 (0.0188 to 0.2765)	0.1081 (0.0505 to 0.1906)	0.1346 (0.0771 to 0.2083)	
6 Months	0.1111 (0.0247 to 0.2715)	0.1043 (0.0188 to 0.2765)	0.0946 (0.0416 to 0.1740)	0.0921 (0.0454 to 0.1589)	
8 Months	0.1111 (0.0247 to 0.2715)	0.1043 (0.0188 to 0.2765)	0.0788 (0.0312 to 0.1555)	0.0690 (0.0295 to 0.1315)	
10 Months	0.1111 (0.0247 to 0.2715)	0.1043 (0.0188 to 0.2765)	0.0788 (0.0312 to 0.1555)	0.0690 (0.0295 to 0.1315)	
12 Months	0.1111 (0.0247 to 0.2715)	0.1043 (0.0188 to 0.2765)	0.0591 (0.0185 to 0.1346)	0.0690 (0.0295 to 0.1315)	
14 Months	0.1111 (0.0247 to 0.2715)	0.1043 (0.0188 to 0.2765)	0.0591 (0.0185 to 0.1346)	0.0690 (0.0295 to 0.1315)	
16 Months	0.1111 (0.0247 to 0.2715)	0.1043 (0.0188 to 0.2765)	0.0591 (0.0185 to 0.1346)	0.0690 (0.0295 to 0.1315)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.5 Treatment emergent mild adverse event by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	5	5	14	18	
4 Months	4	1	8	13	
6 Months	1	1	6	8	
8 Months	1	0	5	6	
10 Months	1	0	4	6	
12 Months	1	0	3	5	
14 Months	1	0	3	5	
16 Months	0	0	1	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.6 Treatment emergent severe adverse event by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (67.6)	20 (87.0)	56 (73.7)	87 (84.5)	0.0376
Number (%) of patients censored	11 (32.4)	3 (13.0)	20 (26.3)	16 (15.5)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.3285 (0.1314 to 0.7885)	0.2957 (0.0657 to 0.4928)	0.6242 (0.5257 to 0.7885)	0.5914 (0.4271 to 0.7556)	
Median (95% CI)	2.2669 (0.6242 to 7.0308)	0.5585 (0.2957 to 0.7885)	1.5770 (0.9199 to 3.5154)	1.0185 (0.8214 to 1.9055)	
75% quantile (95% CI)	NC (4.4353 to NC)	0.8214 (0.5585 to NC)	14.5544 (4.3368 to NC)	3.7782 (2.3655 to 7.4251)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0119		0.0798	
Hazard ratio (95% CI) vs Pd		2.2023 (1.1743 to 4.1302)		1.3508 (0.9637 to 1.8933)	
P-value		0.0139		0.0809	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.6 Treatment emergent severe adverse event by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.4541 (0.2421 to 0.8516)				
probability (95% CI)[b]					
2 Months	0.5455 (0.3630 to 0.6959)	0.1391 (0.0349 to 0.3136)	0.4809 (0.3644 to 0.5880)	0.3725 (0.2796 to 0.4653)	
4 Months	0.4242 (0.2559 to 0.5831)	0.0928 (0.0159 to 0.2552)	0.3606 (0.2540 to 0.4682)	0.2323 (0.1554 to 0.3185)	
6 Months	0.3590 (0.2008 to 0.5200)	0.0928 (0.0159 to 0.2552)	0.2917 (0.1935 to 0.3969)	0.1901 (0.1200 to 0.2726)	
8 Months	0.3263 (0.1747 to 0.4874)	0.0928 (0.0159 to 0.2552)	0.2624 (0.1682 to 0.3663)	0.1584 (0.0944 to 0.2372)	
10 Months	0.3263 (0.1747 to 0.4874)	0.0928 (0.0159 to 0.2552)	0.2624 (0.1682 to 0.3663)	0.1478 (0.0862 to 0.2252)	
12 Months	0.3263 (0.1747 to 0.4874)	0.0928 (0.0159 to 0.2552)	0.2624 (0.1682 to 0.3663)	0.1478 (0.0862 to 0.2252)	
14 Months	0.3263 (0.1747 to 0.4874)	0.0928 (0.0159 to 0.2552)	0.2624 (0.1682 to 0.3663)	0.1478 (0.0862 to 0.2252)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.6 Treatment emergent severe adverse event by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3263 (0.1747 to 0.4874)	0.0928 (0.0159 to 0.2552)	0.2332 (0.1380 to 0.3430)	0.1478 (0.0862 to 0.2252)	
Number of patients at risk[b]					
2 Months	18	3	36	38	
4 Months	14	2	27	22	
6 Months	11	2	21	18	
8 Months	10	2	16	15	
10 Months	10	1	16	14	
12 Months	9	1	14	11	
14 Months	7	1	9	8	
16 Months	5	0	4	3	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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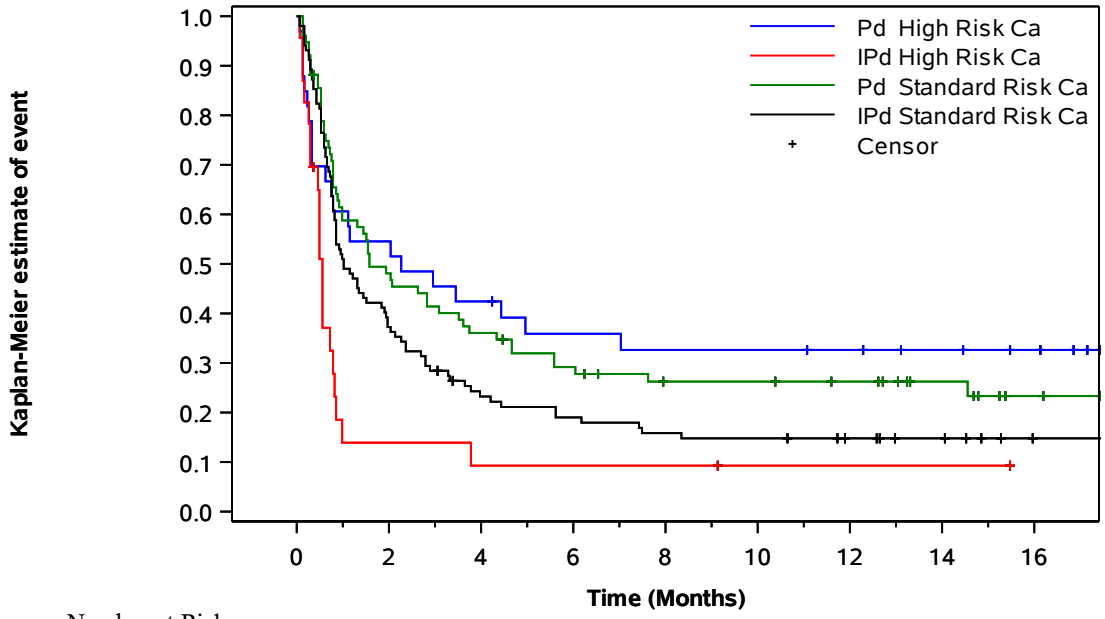
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.7 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event by treatment group according to cytogenetic abnormality - Safety population



Number at Risk									
Pd High Risk Ca	33	18	14	11	10	10	9	7	5
IPd High Risk Ca	23	3	2	2	2	1	1	1	0
Pd Standard Risk Ca	76	36	27	21	16	16	14	9	4
IPd Standard Risk Ca	102	38	22	18	15	14	11	8	3

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.8 Treatment emergent severe adverse event including death by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (67.6)	22 (95.7)	58 (76.3)	88 (85.4)	0.0129
Number (%) of patients censored	11 (32.4)	1 (4.3)	18 (23.7)	15 (14.6)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.3285 (0.1314 to 0.7885)	0.2628 (0.0657 to 0.4928)	0.6078 (0.4600 to 0.7885)	0.5914 (0.4271 to 0.7556)	
Median (95% CI)	2.2669 (0.6242 to 7.0308)	0.4928 (0.2957 to 0.7228)	1.5770 (0.8871 to 3.5154)	1.0185 (0.8214 to 1.9055)	
75% quantile (95% CI)	NC (4.4353 to NC)	0.8214 (0.5585 to 3.7782)	7.6222 (3.7454 to NC)	3.6468 (2.2669 to 7.4251)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0029		0.0955	
Hazard ratio (95% CI) vs Pd		2.4758 (1.3403 to 4.5736)		1.3266 (0.9505 to 1.8516)	
P-value		0.0038		0.0966	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_care_s_t_x.rtf (20APR2021 10:26)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.8 Treatment emergent severe adverse event including death by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.4039 (0.2186 to 0.7461)				
probability (95% CI)[b]					
2 Months	0.5455 (0.3630 to 0.6959)	0.1304 (0.0327 to 0.2972)	0.4737 (0.3584 to 0.5803)	0.3627 (0.2707 to 0.4553)	
4 Months	0.4242 (0.2559 to 0.5831)	0.0870 (0.0150 to 0.2417)	0.3553 (0.2499 to 0.4619)	0.2237 (0.1483 to 0.3088)	
6 Months	0.3590 (0.2008 to 0.5200)	0.0870 (0.0150 to 0.2417)	0.2763 (0.1815 to 0.3793)	0.1830 (0.1146 to 0.2641)	
8 Months	0.3263 (0.1747 to 0.4874)	0.0870 (0.0150 to 0.2417)	0.2485 (0.1579 to 0.3499)	0.1525 (0.0903 to 0.2297)	
10 Months	0.3263 (0.1747 to 0.4874)	0.0435 (0.0031 to 0.1824)	0.2485 (0.1579 to 0.3499)	0.1423 (0.0825 to 0.2180)	
12 Months	0.3263 (0.1747 to 0.4874)	0.0435 (0.0031 to 0.1824)	0.2485 (0.1579 to 0.3499)	0.1423 (0.0825 to 0.2180)	
14 Months	0.3263 (0.1747 to 0.4874)	0.0435 (0.0031 to 0.1824)	0.2485 (0.1579 to 0.3499)	0.1423 (0.0825 to 0.2180)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_care_s_t_x.rtf (20APR2021 10:26)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.8 Treatment emergent severe adverse event including death by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3263 (0.1747 to 0.4874)	0.0435 (0.0031 to 0.1824)	0.2209 (0.1298 to 0.3273)	0.1423 (0.0825 to 0.2180)	
Number of patients at risk[b]					
2 Months	18	3	36	37	
4 Months	14	2	27	22	
6 Months	11	2	21	18	
8 Months	10	2	16	15	
10 Months	10	1	16	14	
12 Months	9	1	14	11	
14 Months	7	1	9	8	
16 Months	5	0	4	3	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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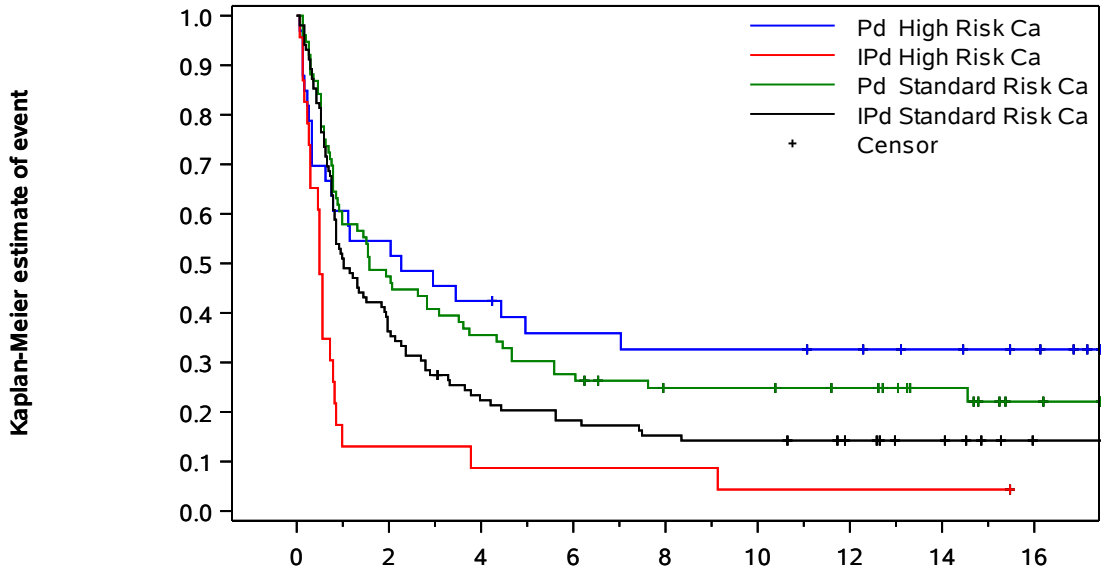
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.1.13.9 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death by treatment group according to cytogenetic abnormality - Safety population



Number at Risk									
Pd High Risk Ca	33	18	14	11	10	10	9	7	5
IPd High Risk Ca	23	3	2	2	2	1	1	1	0
Pd Standard Risk Ca	76	36	27	21	16	16	14	9	4
IPd Standard Risk Ca	102	37	22	18	15	14	11	8	3

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.1.14.1 Treatment emergent adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	86 (97.7)	80 (98.8)	60 (98.4)	71 (100.0)	0.8036
Number (%) of patients censored	2 (2.3)	1 (1.2)	1 (1.6)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0986 to 0.1643)	0.0986 (0.0657 to 0.1314)	0.1314 (0.0657 to 0.2628)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.3285 (0.1971 to 0.4600)	0.1807 (0.1314 to 0.2628)	0.4600 (0.2628 to 0.6242)	0.1971 (0.1643 to 0.2957)	
75% quantile (95% CI)	0.9199 (0.4928 to 1.4127)	0.5421 (0.2957 to 0.7556)	0.8542 (0.6242 to 1.7084)	0.5585 (0.3614 to 0.8542)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0526		0.0254	
Hazard ratio (95% CI) vs Pd		1.3550 (0.9955 to 1.8442)		1.5005 (1.0490 to 2.1464)	
P-value		0.0534		0.0263	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.1.14.1 Treatment emergent adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.6664 (0.4659 to 0.9533)		
probability (95% CI)[b]					
2 Months	0.1264 (0.0671 to 0.2053)	0.0625 (0.0232 to 0.1298)	0.0877 (0.0323 to 0.1781)	0.0571 (0.0185 to 0.1284)	
4 Months	0.0460 (0.0150 to 0.1047)	0.0250 (0.0048 to 0.0784)	0.0526 (0.0138 to 0.1319)	0.0143 (0.0012 to 0.0681)	
6 Months	0.0307 (0.0068 to 0.0875)	0.0250 (0.0048 to 0.0784)	0.0526 (0.0138 to 0.1319)	0.0143 (0.0012 to 0.0681)	
8 Months	0.0307 (0.0068 to 0.0875)	0.0125 (0.0011 to 0.0602)	0.0351 (0.0065 to 0.1074)	0.0143 (0.0012 to 0.0681)	
10 Months	0.0307 (0.0068 to 0.0875)	0.0125 (0.0011 to 0.0602)	0.0175 (0.0014 to 0.0820)	0.0143 (0.0012 to 0.0681)	
12 Months	0.0153 (0.0015 to 0.0690)	0.0125 (0.0011 to 0.0602)	0.0175 (0.0014 to 0.0820)	0.0143 (0.0012 to 0.0681)	
14 Months	0.0153 (0.0015 to 0.0690)	0.0125 (0.0011 to 0.0602)	0.0175 (0.0014 to 0.0820)	0.0143 (0.0012 to 0.0681)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.1.14.1 Treatment emergent adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0153 (0.0015 to 0.0690)	0.0125 (0.0011 to 0.0602)	0.0175 (0.0014 to 0.0820)	0.0143 (0.0012 to 0.0681)	
Number of patients at risk[b]					
2 Months	11	5	5	4	
4 Months	4	2	3	1	
6 Months	2	2	3	0	
8 Months	2	1	2	0	
10 Months	2	1	1	0	
12 Months	1	0	1	0	
14 Months	1	0	1	0	
16 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.1.14.2 Treatment emergent serious adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (56.8)	48 (59.3)	30 (49.2)	46 (64.8)	0.3400
Number (%) of patients censored	38 (43.2)	33 (40.7)	31 (50.8)	25 (35.2)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.4292 (0.5914 to 2.2669)	0.6242 (0.3285 to 2.1355)	1.3142 (0.4928 to 2.8255)	1.0185 (0.4271 to 1.5770)	
Median (95% CI)	5.5852 (3.0883 to NC)	6.3080 (3.3183 to NC)	12.1889 (2.9569 to NC)	4.4353 (2.0041 to 10.5462)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.0062 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.8273		0.1447	
Hazard ratio (95% CI) vs Pd		1.0454 (0.7018 to 1.5572)		1.4061 (0.8875 to 2.2278)	
P-value		0.8272		0.1466	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.1.14.2 Treatment emergent serious adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.6705 (0.5617 to 0.7579)	0.6625 (0.5477 to 0.7546)	0.6885 (0.5562 to 0.7887)	0.6338 (0.5107 to 0.7338)	
4 Months	0.5664 (0.4562 to 0.6625)	0.5995 (0.4836 to 0.6974)	0.6066 (0.4728 to 0.7163)	0.5194 (0.3974 to 0.6281)	
6 Months	0.4958 (0.3871 to 0.5954)	0.5230 (0.4081 to 0.6257)	0.5365 (0.4031 to 0.6527)	0.4757 (0.3556 to 0.5863)	
8 Months	0.4592 (0.3518 to 0.5601)	0.4974 (0.3835 to 0.6013)	0.5180 (0.3849 to 0.6357)	0.4460 (0.3276 to 0.5575)	
10 Months	0.4592 (0.3518 to 0.5601)	0.4337 (0.3233 to 0.5390)	0.5180 (0.3849 to 0.6357)	0.4014 (0.2864 to 0.5135)	
12 Months	0.4464 (0.3395 to 0.5477)	0.4074 (0.2988 to 0.5130)	0.5180 (0.3849 to 0.6357)	0.3396 (0.2306 to 0.4516)	
14 Months	0.4320 (0.3253 to 0.5341)	0.4074 (0.2988 to 0.5130)	0.4945 (0.3602 to 0.6152)	0.3396 (0.2306 to 0.4516)	
16 Months	0.4066 (0.2961 to 0.5141)	0.4074 (0.2988 to 0.5130)	0.4945 (0.3602 to 0.6152)	0.3396 (0.2306 to 0.4516)	
Number of patients at risk[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.1.14.2 Treatment emergent serious adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	58	53	42	45	
4 Months	49	47	37	36	
6 Months	42	41	30	32	
8 Months	36	39	27	30	
10 Months	36	34	26	27	
12 Months	31	28	22	22	
14 Months	18	18	11	17	
16 Months	10	7	5	7	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.1.14.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (12.5)	5 (6.2)	8 (13.1)	6 (8.5)	0.7927
Number (%) of patients censored	77 (87.5)	76 (93.8)	53 (86.9)	65 (91.5)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.8789 to NC)	NC (15.9671 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.1501		0.2706	
Hazard ratio (95% CI) vs Pd		0.4687 (0.1628 to 1.3489)		0.5556 (0.1923 to 1.6047)	
P-value		0.1600		0.2774	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.1.14.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9202 (0.8398 to 0.9611)	1.0000 (1.0000 to 1.0000)	0.9002 (0.7911 to 0.9539)	0.9859 (0.9042 to 0.9980)	
4 Months	0.9202 (0.8398 to 0.9611)	0.9873 (0.9135 to 0.9982)	0.8829 (0.7698 to 0.9424)	0.9573 (0.8735 to 0.9860)	
6 Months	0.8840 (0.7950 to 0.9359)	0.9610 (0.8839 to 0.9873)	0.8829 (0.7698 to 0.9424)	0.9424 (0.8536 to 0.9780)	
8 Months	0.8704 (0.7778 to 0.9262)	0.9460 (0.8621 to 0.9794)	0.8829 (0.7698 to 0.9424)	0.9424 (0.8536 to 0.9780)	
10 Months	0.8704 (0.7778 to 0.9262)	0.9300 (0.8391 to 0.9704)	0.8829 (0.7698 to 0.9424)	0.9424 (0.8536 to 0.9780)	
12 Months	0.8704 (0.7778 to 0.9262)	0.9300 (0.8391 to 0.9704)	0.8829 (0.7698 to 0.9424)	0.9249 (0.8283 to 0.9682)	
14 Months	0.8704 (0.7778 to 0.9262)	0.9300 (0.8391 to 0.9704)	0.8489 (0.7109 to 0.9244)	0.9249 (0.8283 to 0.9682)	
16 Months	0.8704 (0.7778 to 0.9262)	0.9300 (0.8391 to 0.9704)	0.8489 (0.7109 to 0.9244)	0.8671 (0.6761 to 0.9494)	
Number of patients at risk[b]					
2 Months	80	79	53	69	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_auto_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.1.14.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	77	75	50	64	
6 Months	68	68	45	58	
8 Months	63	62	40	58	
10 Months	61	58	38	55	
12 Months	54	51	31	49	
14 Months	33	33	19	35	
16 Months	15	15	9	13	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_auto_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.1.14.4 Treatment emergent mild adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	83 (94.3)	76 (93.8)	54 (88.5)	65 (91.5)	0.8206
Number (%) of patients censored	5 (5.7)	5 (6.2)	7 (11.5)	6 (8.5)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0986 to 0.2628)	0.0986 (0.0657 to 0.1314)	0.1971 (0.0986 to 0.3285)	0.0986 (0.0657 to 0.1643)	
Median (95% CI)	0.3943 (0.2957 to 0.7228)	0.2300 (0.1643 to 0.3285)	0.6242 (0.3285 to 0.8214)	0.2464 (0.1643 to 0.4600)	
75% quantile (95% CI)	1.0513 (0.8871 to 1.8727)	0.7556 (0.4928 to 2.0698)	1.7741 (0.8214 to 2.5626)	0.8542 (0.5257 to 3.7454)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.3198		0.2483	
Hazard ratio (95% CI) vs Pd		1.1721 (0.8569 to 1.6032)		1.2427 (0.8587 to 1.7983)	
P-value		0.3203		0.2492	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.1.14.4 Treatment emergent mild adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.1609 (0.0930 to 0.2454)	0.1728 (0.1000 to 0.2623)	0.1929 (0.1008 to 0.3072)	0.2000 (0.1161 to 0.3003)	
4 Months	0.0866 (0.0388 to 0.1587)	0.0960 (0.0438 to 0.1729)	0.1157 (0.0475 to 0.2173)	0.1523 (0.0791 to 0.2476)	
6 Months	0.0578 (0.0201 to 0.1247)	0.0800 (0.0327 to 0.1549)	0.1157 (0.0475 to 0.2173)	0.1015 (0.0431 to 0.1894)	
8 Months	0.0578 (0.0201 to 0.1247)	0.0480 (0.0137 to 0.1165)	0.0868 (0.0278 to 0.1888)	0.0812 (0.0296 to 0.1670)	
10 Months	0.0578 (0.0201 to 0.1247)	0.0480 (0.0137 to 0.1165)	0.0579 (0.0124 to 0.1572)	0.0812 (0.0296 to 0.1670)	
12 Months	0.0385 (0.0090 to 0.1052)	0.0480 (0.0137 to 0.1165)	0.0579 (0.0124 to 0.1572)	0.0812 (0.0296 to 0.1670)	
14 Months	0.0385 (0.0090 to 0.1052)	0.0480 (0.0137 to 0.1165)	0.0579 (0.0124 to 0.1572)	0.0812 (0.0296 to 0.1670)	
16 Months	0.0385 (0.0090 to 0.1052)	0.0480 (0.0137 to 0.1165)	0.0579 (0.0124 to 0.1572)	0.0609 (0.0178 to 0.1433)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.1.14.4 Treatment emergent mild adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	13	14	10	13	
4 Months	7	7	6	9	
6 Months	4	5	4	5	
8 Months	4	3	3	4	
10 Months	3	3	2	4	
12 Months	2	2	2	4	
14 Months	2	2	2	4	
16 Months	1	1	0	1	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_auto_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.1.14.5 Treatment emergent severe adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	60 (68.2)	64 (79.0)	43 (70.5)	65 (91.5)	0.8528
Number (%) of patients censored	28 (31.8)	17 (21.0)	18 (29.5)	6 (8.5)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.7228 (0.2957 to 0.7885)	0.5257 (0.2957 to 0.6242)	0.5257 (0.2628 to 0.7228)	0.4928 (0.2957 to 0.5914)	
Median (95% CI)	2.1684 (1.1499 to 4.4353)	0.8214 (0.7228 to 1.9384)	1.1499 (0.7228 to 2.6283)	0.8542 (0.6571 to 1.2156)	
75% quantile (95% CI)	NC (6.0452 to NC)	5.6181 (2.2669 to NC)	NC (2.8255 to NC)	2.7926 (1.4127 to 4.4353)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0446		0.0332	
Hazard ratio (95% CI) vs Pd		1.4360 (1.0069 to 2.0481)		1.5232 (1.0312 to 2.2501)	
P-value		0.0457		0.0345	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.1.14.5 Treatment emergent severe adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6964 (0.4883 to 0.9932)		0.6565 (0.4444 to 0.9697)		
probability (95% CI)[b]					
2 Months	0.5227 (0.4138 to 0.6207)	0.3809 (0.2748 to 0.4861)	0.4082 (0.2829 to 0.5295)	0.2958 (0.1948 to 0.4036)	
4 Months	0.4205 (0.3166 to 0.5206)	0.2765 (0.1827 to 0.3783)	0.3231 (0.2087 to 0.4429)	0.1831 (0.1036 to 0.2805)	
6 Months	0.3490 (0.2508 to 0.4487)	0.2328 (0.1453 to 0.3326)	0.3061 (0.1944 to 0.4251)	0.1408 (0.0722 to 0.2317)	
8 Months	0.3240 (0.2282 to 0.4233)	0.1892 (0.1097 to 0.2853)	0.2891 (0.1802 to 0.4071)	0.1268 (0.0623 to 0.2150)	
10 Months	0.3240 (0.2282 to 0.4233)	0.1892 (0.1097 to 0.2853)	0.2891 (0.1802 to 0.4071)	0.1127 (0.0527 to 0.1981)	
12 Months	0.3240 (0.2282 to 0.4233)	0.1892 (0.1097 to 0.2853)	0.2891 (0.1802 to 0.4071)	0.0986 (0.0433 to 0.1808)	
14 Months	0.3240 (0.2282 to 0.4233)	0.1892 (0.1097 to 0.2853)	0.2891 (0.1802 to 0.4071)	0.0822 (0.0325 to 0.1616)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.1.14.5 Treatment emergent severe adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3024 (0.2057 to 0.4046)	0.1892 (0.1097 to 0.2853)	0.2891 (0.1802 to 0.4071)	0.0822 (0.0325 to 0.1616)	
Number of patients at risk[b]					
2 Months	46	30	24	21	
4 Months	37	20	19	13	
6 Months	29	16	18	10	
8 Months	25	13	15	9	
10 Months	25	12	15	8	
12 Months	22	9	12	7	
14 Months	15	7	5	4	
16 Months	10	2	2	1	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_auto_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.1.14.6 Treatment emergent severe adverse event including death by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	61 (69.3)	67 (82.7)	44 (72.1)	65 (91.5)	0.9758
Number (%) of patients censored	27 (30.7)	14 (17.3)	17 (27.9)	6 (8.5)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.7228 (0.2957 to 0.7885)	0.5257 (0.2957 to 0.5914)	0.5257 (0.2628 to 0.6242)	0.4928 (0.2957 to 0.5914)	
Median (95% CI)	2.1684 (1.1499 to 4.4353)	0.8214 (0.7228 to 1.9384)	1.1335 (0.6242 to 2.6283)	0.8542 (0.6571 to 1.2156)	
75% quantile (95% CI)	NC (5.5852 to NC)	5.6181 (2.0370 to NC)	NC (2.6283 to NC)	2.7926 (1.4127 to 4.4353)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0239		0.0447	
Hazard ratio (95% CI) vs Pd		1.4924 (1.0521 to 2.1170)		1.4833 (1.0069 to 2.1850)	
P-value		0.0248		0.0461	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.1.14.6 Treatment emergent severe adverse event including death by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6701 (0.4724 to 0.9505)		0.6742 (0.4577 to 0.9931)		
probability (95% CI)[b]					
2 Months	0.5227 (0.4138 to 0.6207)	0.3625 (0.2589 to 0.4667)	0.4000 (0.2766 to 0.5203)	0.2958 (0.1948 to 0.4036)	
4 Months	0.4205 (0.3166 to 0.5206)	0.2609 (0.1703 to 0.3606)	0.3167 (0.2042 to 0.4350)	0.1831 (0.1036 to 0.2805)	
6 Months	0.3387 (0.2419 to 0.4379)	0.2197 (0.1357 to 0.3166)	0.3000 (0.1902 to 0.4175)	0.1408 (0.0722 to 0.2317)	
8 Months	0.3144 (0.2202 to 0.4129)	0.1785 (0.1026 to 0.2714)	0.2833 (0.1764 to 0.3999)	0.1268 (0.0623 to 0.2150)	
10 Months	0.3144 (0.2202 to 0.4129)	0.1648 (0.0920 to 0.2559)	0.2833 (0.1764 to 0.3999)	0.1127 (0.0527 to 0.1981)	
12 Months	0.3144 (0.2202 to 0.4129)	0.1648 (0.0920 to 0.2559)	0.2833 (0.1764 to 0.3999)	0.0986 (0.0433 to 0.1808)	
14 Months	0.3144 (0.2202 to 0.4129)	0.1648 (0.0920 to 0.2559)	0.2833 (0.1764 to 0.3999)	0.0822 (0.0325 to 0.1616)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.1.14.6 Treatment emergent severe adverse event including death by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.2935 (0.1986 to 0.3946)	0.1648 (0.0920 to 0.2559)	0.2833 (0.1764 to 0.3999)	0.0822 (0.0325 to 0.1616)	
Number of patients at risk[b]					
2 Months	46	29	24	21	
4 Months	37	20	19	13	
6 Months	29	16	18	10	
8 Months	25	13	15	9	
10 Months	25	12	15	8	
12 Months	22	9	12	7	
14 Months	15	7	5	4	
16 Months	10	2	2	1	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.1.15.1 Treatment emergent adverse event by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	2 (100.0)	144 (98.0)	149 (99.3)	0.6703
Number (%) of patients censored	0 (0.0)	0 (0.0)	3 (2.0)	1 (0.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.2628 (0.2628 to 0.8214)	0.1643 (0.1643 to 0.1971)	0.1314 (0.1314 to 0.1643)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.5421 (0.2628 to 0.8214)	0.1807 (0.1643 to 0.1971)	0.3285 (0.2628 to 0.4928)	0.1971 (0.1643 to 0.2628)	
75% quantile (95% CI)	0.8214 (0.2628 to 0.8214)	0.1971 (0.1643 to 0.1971)	0.8871 (0.7228 to 1.4127)	0.5585 (0.4271 to 0.7556)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0896		0.0047	
Hazard ratio (95% CI) vs Pd		NC (NC to NC)		1.3986 (1.1073 to 1.7665)	
P-value		0.9985		0.0049	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_allt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.1.15.1 Treatment emergent adverse event by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.7150 (0.5661 to 0.9031)		
probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.1127 (0.0674 to 0.1708)	0.0608 (0.0299 to 0.1072)	
4 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0493 (0.0218 to 0.0937)	0.0203 (0.0055 to 0.0537)	
6 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0411 (0.0164 to 0.0838)	0.0135 (0.0027 to 0.0439)	
8 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0329 (0.0115 to 0.0735)	0.0068 (0.0006 to 0.0340)	
10 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0246 (0.0071 to 0.0628)	0.0068 (0.0006 to 0.0340)	
12 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0164 (0.0034 to 0.0516)	0.0068 (0.0006 to 0.0340)	
14 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0164 (0.0034 to 0.0516)	0.0068 (0.0006 to 0.0340)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_allt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.1.15.1 Treatment emergent adverse event by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0164 (0.0034 to 0.0516)	0.0068 (0.0006 to 0.0340)	
Number of patients at risk[b]					
2 Months	0	0	16	9	
4 Months	0	0	7	3	
6 Months	0	0	5	2	
8 Months	0	0	4	1	
10 Months	0	0	3	1	
12 Months	0	0	2	0	
14 Months	0	0	2	0	
16 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.1.15.2 Treatment emergent serious adverse event by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	79 (53.7)	93 (62.0)	0.6273
Number (%) of patients censored	1 (50.0)	1 (50.0)	68 (46.3)	57 (38.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.2628 (0.2628 to NC)	8.8049 (8.8049 to NC)	1.3799 (0.7556 to 1.9384)	0.7885 (0.4600 to 1.4127)	
Median (95% CI)	NC (0.2628 to NC)	NC (8.8049 to NC)	6.5708 (3.7782 to NC)	5.9795 (3.3183 to 9.9548)	
75% quantile (95% CI)	NC (0.2628 to NC)	NC (8.8049 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.8084		0.2334	
Hazard ratio (95% CI) vs Pd		0.7071 (0.0424 to 11.7865)		1.2000 (0.8884 to 1.6209)	
P-value		0.8092		0.2347	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.1.15.2 Treatment emergent serious adverse event by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.6803 (0.5983 to 0.7490)	0.6443 (0.5618 to 0.7153)	
4 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.5841 (0.4999 to 0.6590)	0.5561 (0.4726 to 0.6317)	
6 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.5132 (0.4292 to 0.5910)	0.4942 (0.4113 to 0.5716)	
8 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.4835 (0.3997 to 0.5621)	0.4663 (0.3841 to 0.5443)	
10 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.4835 (0.3997 to 0.5621)	0.4176 (0.3373 to 0.4958)	
12 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.4755 (0.3918 to 0.5545)	0.3745 (0.2963 to 0.4525)	
14 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.4572 (0.3733 to 0.5372)	0.3745 (0.2963 to 0.4525)	
16 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.4397 (0.3523 to 0.5235)	0.3745 (0.2963 to 0.4525)	
Number of patients at risk[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_allt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.1.15.2 Treatment emergent serious adverse event by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1	2	99	96	
4 Months	1	2	85	81	
6 Months	1	2	71	71	
8 Months	1	2	62	67	
10 Months	1	1	61	60	
12 Months	1	1	52	49	
14 Months	1	0	28	35	
16 Months	0	0	15	14	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.1.15.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	19 (12.9)	11 (7.3)	0.9998
Number (%) of patients censored	2 (100.0)	2 (100.0)	128 (87.1)	139 (92.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd				0.0831	
Hazard ratio (95% CI) vs Pd		NC (NC to NC)		0.5244 (0.2495 to 1.1021)	
P-value				0.0885	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.1.15.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9108 (0.8513 to 0.9472)	0.9933 (0.9533 to 0.9991)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9038 (0.8429 to 0.9419)	0.9728 (0.9292 to 0.9897)	
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8819 (0.8169 to 0.9249)	0.9515 (0.9010 to 0.9766)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8737 (0.8068 to 0.9186)	0.9436 (0.8902 to 0.9714)	
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8737 (0.8068 to 0.9186)	0.9352 (0.8790 to 0.9659)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8737 (0.8068 to 0.9186)	0.9265 (0.8672 to 0.9599)	
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8614 (0.7897 to 0.9100)	0.9265 (0.8672 to 0.9599)	
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8614 (0.7897 to 0.9100)	0.8966 (0.7968 to 0.9489)	
Number of patients at risk[b]					
2 Months	2	2	131	146	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.1.15.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	2	2	125	137	
6 Months	2	2	111	124	
8 Months	2	2	101	118	
10 Months	1	2	98	111	
12 Months	1	1	84	99	
14 Months	1	0	51	68	
16 Months	0	0	24	28	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.1.15.4 Treatment emergent mild adverse event by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	2 (100.0)	135 (91.8)	139 (92.7)	0.5398
Number (%) of patients censored	0 (0.0)	0 (0.0)	12 (8.2)	11 (7.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.3285 (0.3285 to 0.8214)	0.1643 (0.1643 to 0.1971)	0.1643 (0.1314 to 0.2628)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.5749 (0.3285 to 0.8214)	0.1807 (0.1643 to 0.1971)	0.4928 (0.3285 to 0.7228)	0.2300 (0.1643 to 0.3285)	
75% quantile (95% CI)	0.8214 (0.3285 to 0.8214)	0.1971 (0.1643 to 0.1971)	1.4456 (0.9199 to 1.8727)	0.8214 (0.6571 to 2.0698)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0896		0.1656	
Hazard ratio (95% CI) vs Pd		NC (NC to NC)		1.1853 (0.9324 to 1.5066)	
P-value		0.9985		0.1650	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_allt_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.1.15.4 Treatment emergent mild adverse event by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.1765 (0.1184 to 0.2443)	0.1879 (0.1299 to 0.2543)	
4 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0998 (0.0565 to 0.1574)	0.1231 (0.0759 to 0.1825)	
6 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0831 (0.0440 to 0.1381)	0.0904 (0.0498 to 0.1458)	
8 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0728 (0.0359 to 0.1269)	0.0633 (0.0297 to 0.1147)	
10 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0624 (0.0283 to 0.1153)	0.0633 (0.0297 to 0.1147)	
12 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0499 (0.0194 to 0.1023)	0.0633 (0.0297 to 0.1147)	
14 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0499 (0.0194 to 0.1023)	0.0633 (0.0297 to 0.1147)	
16 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0499 (0.0194 to 0.1023)	0.0527 (0.0222 to 0.1030)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_allt_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.1.15.4 Treatment emergent mild adverse event by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	0	0	23	27	
4 Months	0	0	13	16	
6 Months	0	0	8	10	
8 Months	0	0	7	7	
10 Months	0	0	5	7	
12 Months	0	0	4	6	
14 Months	0	0	4	6	
16 Months	0	0	1	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_allt_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.1.15.5 Treatment emergent severe adverse event by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	2 (100.0)	102 (69.4)	127 (84.7)	0.9425
Number (%) of patients censored	1 (50.0)	0 (0.0)	45 (30.6)	23 (15.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.2628 (0.2628 to NC)	2.0370 (2.0370 to 3.6468)	0.5585 (0.3943 to 0.7556)	0.5257 (0.3614 to 0.5585)	
Median (95% CI)	NC (0.2628 to NC)	2.8419 (2.0370 to 3.6468)	1.6756 (0.9856 to 2.8255)	0.8542 (0.7556 to 1.0185)	
75% quantile (95% CI)	NC (0.2628 to NC)	3.6468 (2.0370 to 3.6468)	NC (6.0452 to NC)	3.7782 (2.1355 to 6.9651)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.6949		0.0022	
Hazard ratio (95% CI) vs Pd		1.6179 (0.1430 to 18.3118)		1.5026 (1.1552 to 1.9545)	
P-value		0.6975		0.0024	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.1.15.5 Treatment emergent severe adverse event by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.6655 (0.5116 to 0.8656)		
probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.4765 (0.3934 to 0.5550)	0.3316 (0.2572 to 0.4077)	
4 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3799 (0.3012 to 0.4580)	0.2354 (0.1704 to 0.3066)	
6 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3299 (0.2546 to 0.4070)	0.1917 (0.1322 to 0.2595)	
8 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3076 (0.2339 to 0.3840)	0.1622 (0.1072 to 0.2272)	
10 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3076 (0.2339 to 0.3840)	0.1548 (0.1011 to 0.2190)	
12 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3076 (0.2339 to 0.3840)	0.1467 (0.0942 to 0.2101)	
14 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3076 (0.2339 to 0.3840)	0.1354 (0.0840 to 0.1990)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_allt_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.1.15.5 Treatment emergent severe adverse event by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2905 (0.2147 to 0.3703)	0.1354 (0.0840 to 0.1990)	
Number of patients at risk[b]					
2 Months	1	2	69	49	
4 Months	1	0	55	33	
6 Months	1	0	46	26	
8 Months	1	0	39	22	
10 Months	1	0	39	20	
12 Months	1	0	33	16	
14 Months	1	0	19	11	
16 Months	0	0	12	3	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.1.15.6 Treatment emergent severe adverse event including death by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	2 (100.0)	104 (70.7)	130 (86.7)	0.9385
Number (%) of patients censored	1 (50.0)	0 (0.0)	43 (29.3)	20 (13.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.2628 (0.2628 to NC)	2.0370 (2.0370 to 3.6468)	0.5585 (0.3285 to 0.7556)	0.5257 (0.3285 to 0.5585)	
Median (95% CI)	NC (0.2628 to NC)	2.8419 (2.0370 to 3.6468)	1.6263 (0.9856 to 2.8255)	0.8542 (0.7556 to 1.0185)	
75% quantile (95% CI)	NC (0.2628 to NC)	3.6468 (2.0370 to 3.6468)	NC (5.5852 to NC)	3.3183 (1.9713 to 6.1766)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.6949		0.0016	
Hazard ratio (95% CI) vs Pd		1.6179 (0.1430 to 18.3118)		1.5151 (1.1680 to 1.9653)	
P-value		0.6975		0.0018	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.1.15.6 Treatment emergent severe adverse event including death by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.6600 (0.5088 to 0.8562)		
probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.4726 (0.3898 to 0.5508)	0.3221 (0.2487 to 0.3976)	
4 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3767 (0.2985 to 0.4546)	0.2273 (0.1637 to 0.2974)	
6 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3209 (0.2467 to 0.3973)	0.1851 (0.1271 to 0.2517)	
8 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2991 (0.2267 to 0.3748)	0.1566 (0.1031 to 0.2202)	
10 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2991 (0.2267 to 0.3748)	0.1424 (0.0914 to 0.2043)	
12 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2991 (0.2267 to 0.3748)	0.1349 (0.0852 to 0.1959)	
14 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2991 (0.2267 to 0.3748)	0.1245 (0.0761 to 0.1854)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_allt_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.1.15.6 Treatment emergent severe adverse event including death by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2825 (0.2082 to 0.3613)	0.1245 (0.0761 to 0.1854)	
Number of patients at risk[b]					
2 Months	1	2	69	48	
4 Months	1	0	55	33	
6 Months	1	0	46	26	
8 Months	1	0	39	22	
10 Months	1	0	39	20	
12 Months	1	0	33	16	
14 Months	1	0	19	11	
16 Months	0	0	12	3	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_allt_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.1 Treatment emergent adverse event by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	96 (98.0)	102 (99.0)	39 (97.5)	32 (100.0)	0.0208
Number (%) of patients censored	2 (2.0)	1 (1.0)	1 (2.5)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0986 to 0.1314)	0.1314 (0.0657 to 0.1643)	0.1643 (0.0986 to 0.2957)	0.0657 (0.0329 to 0.1314)	
Median (95% CI)	0.2957 (0.1971 to 0.3943)	0.2300 (0.1643 to 0.3285)	0.3614 (0.2957 to 0.7228)	0.1643 (0.0986 to 0.1971)	
75% quantile (95% CI)	0.8214 (0.5585 to 1.1170)	0.5914 (0.4600 to 0.7885)	0.8871 (0.4928 to 3.1540)	0.2957 (0.1643 to 0.5914)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.3160		0.0005	
Hazard ratio (95% CI) vs Pd		1.1556 (0.8709 to 1.5333)		2.4013 (1.4409 to 4.0017)	
P-value		0.3162		0.0008	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_semm_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.1 Treatment emergent adverse event by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.4164 (0.2499 to 0.6940)		
probability (95% CI)[b]					
2 Months	0.0842 (0.0394 to 0.1507)	0.0784 (0.0367 to 0.1408)	0.1795 (0.0790 to 0.3128)	0.0323 (0.0024 to 0.1411)	
4 Months	0.0421 (0.0137 to 0.0963)	0.0294 (0.0079 to 0.0765)	0.0513 (0.0093 to 0.1517)	0.0323 (0.0024 to 0.1411)	
6 Months	0.0316 (0.0085 to 0.0818)	0.0196 (0.0038 to 0.0624)	0.0513 (0.0093 to 0.1517)	0.0323 (0.0024 to 0.1411)	
8 Months	0.0316 (0.0085 to 0.0818)	0.0098 (0.0009 to 0.0481)	0.0513 (0.0093 to 0.1517)	0.0323 (0.0024 to 0.1411)	
10 Months	0.0211 (0.0041 to 0.0668)	0.0098 (0.0009 to 0.0481)	0.0513 (0.0093 to 0.1517)	0.0323 (0.0024 to 0.1411)	
12 Months	0.0211 (0.0041 to 0.0668)	0.0098 (0.0009 to 0.0481)	0.0513 (0.0093 to 0.1517)	0.0323 (0.0024 to 0.1411)	
14 Months	0.0211 (0.0041 to 0.0668)	0.0098 (0.0009 to 0.0481)	0.0513 (0.0093 to 0.1517)	0.0323 (0.0024 to 0.1411)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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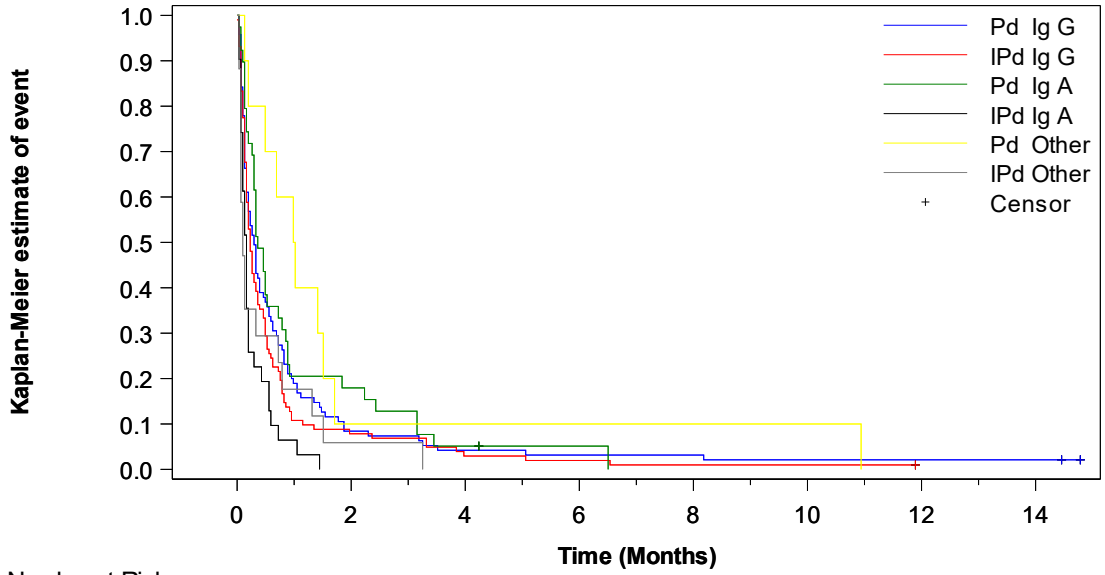
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.1 Treatment emergent adverse event by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0211 (0.0041 to 0.0668)	0.0098 (0.0009 to 0.0481)	0.0513 (0.0093 to 0.1517)	0.0323 (0.0024 to 0.1411)	
Number of patients at risk[b]					
2 Months	8	8	7	0	
4 Months	4	3	2	0	
6 Months	3	2	1	0	
8 Months	3	1	0	0	
10 Months	2	1	0	0	
12 Months	2	0	0	0	
14 Months	2	0	0	0	
16 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_semm_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event by treatment group according to MM type at SE - Safety population



Number at Risk

Pd Ig G	95	8	4	3	3	2	2	2
IPd Ig G	102	8	3	2	1	1	0	0
Pd Ig A	39	7	2	1	0	0	0	0
IPd Ig A	31	0	0	0	0	0	0	0
Pd Other	10	1	1	1	1	1	0	0
IPd Other	17	1	0	0	0	0	0	0

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.3 Treatment emergent serious adverse event by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	54 (55.1)	62 (60.2)	19 (47.5)	21 (65.6)	0.6761
Number (%) of patients censored	44 (44.9)	41 (39.8)	21 (52.5)	11 (34.4)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.3142 (0.5585 to 2.2669)	0.8871 (0.4600 to 1.9713)	1.5934 (0.4928 to 3.7782)	0.9692 (0.1314 to 2.7598)	
Median (95% CI)	6.0452 (2.9569 to NC)	6.3080 (3.9754 to 11.3018)	NC (3.0883 to NC)	6.9158 (1.4127 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.5934 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.7043		0.2158	
Hazard ratio (95% CI) vs Pd		1.0734 (0.7442 to 1.5482)		1.4765 (0.7935 to 2.7472)	
P-value		0.7047		0.2187	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_semm_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.3 Treatment emergent serious adverse event by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.6837 (0.5817 to 0.7658)	0.6667 (0.5662 to 0.7490)	0.7000 (0.5326 to 0.8171)	0.6875 (0.4971 to 0.8180)	
4 Months	0.5816 (0.4777 to 0.6720)	0.5973 (0.4954 to 0.6851)	0.5963 (0.4276 to 0.7300)	0.5313 (0.3471 to 0.6852)	
6 Months	0.5084 (0.4053 to 0.6024)	0.5176 (0.4165 to 0.6096)	0.5421 (0.3749 to 0.6824)	0.5000 (0.3190 to 0.6567)	
8 Months	0.4752 (0.3729 to 0.5705)	0.4878 (0.3875 to 0.5806)	0.5421 (0.3749 to 0.6824)	0.5000 (0.3190 to 0.6567)	
10 Months	0.4752 (0.3729 to 0.5705)	0.4380 (0.3401 to 0.5316)	0.5421 (0.3749 to 0.6824)	0.4063 (0.2383 to 0.5679)	
12 Months	0.4636 (0.3616 to 0.5594)	0.3973 (0.3018 to 0.4910)	0.5421 (0.3749 to 0.6824)	0.3385 (0.1824 to 0.5019)	
14 Months	0.4503 (0.3483 to 0.5469)	0.3973 (0.3018 to 0.4910)	0.5082 (0.3402 to 0.6539)	0.3385 (0.1824 to 0.5019)	
16 Months	0.4266 (0.3205 to 0.5285)	0.3973 (0.3018 to 0.4910)	0.5082 (0.3402 to 0.6539)	0.3385 (0.1824 to 0.5019)	
Number of patients at risk[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_semm_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.3 Treatment emergent serious adverse event by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	67	68	27	22	
4 Months	57	60	23	17	
6 Months	47	52	20	16	
8 Months	41	49	18	16	
10 Months	41	44	18	13	
12 Months	35	36	16	10	
14 Months	20	26	7	7	
16 Months	10	11	4	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_semm_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (14.3)	9 (8.7)	5 (12.5)	1 (3.1)	0.7340
Number (%) of patients censored	84 (85.7)	94 (91.3)	35 (87.5)	31 (96.9)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (12.8789 to NC)	NC (15.9671 to NC)	NC (2.3326 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.1797		0.1451	
Hazard ratio (95% CI) vs Pd		0.5679 (0.2458 to 1.3123)		0.2315 (0.0270 to 1.9831)	
P-value		0.1855		0.1818	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_semm_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9074 (0.8295 to 0.9507)	0.9902 (0.9324 to 0.9986)	0.9000 (0.7551 to 0.9612)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9074 (0.8295 to 0.9507)	0.9706 (0.9116 to 0.9904)	0.8750 (0.7254 to 0.9460)	1.0000 (1.0000 to 1.0000)	
6 Months	0.8752 (0.7906 to 0.9272)	0.9399 (0.8711 to 0.9726)	0.8750 (0.7254 to 0.9460)	1.0000 (1.0000 to 1.0000)	
8 Months	0.8629 (0.7753 to 0.9181)	0.9286 (0.8559 to 0.9654)	0.8750 (0.7254 to 0.9460)	1.0000 (1.0000 to 1.0000)	
10 Months	0.8629 (0.7753 to 0.9181)	0.9166 (0.8396 to 0.9575)	0.8750 (0.7254 to 0.9460)	1.0000 (1.0000 to 1.0000)	
12 Months	0.8629 (0.7753 to 0.9181)	0.9166 (0.8396 to 0.9575)	0.8750 (0.7254 to 0.9460)	0.9615 (0.7569 to 0.9945)	
14 Months	0.8445 (0.7488 to 0.9060)	0.9166 (0.8396 to 0.9575)	0.8750 (0.7254 to 0.9460)	0.9615 (0.7569 to 0.9945)	
16 Months	0.8445 (0.7488 to 0.9060)	0.8683 (0.7151 to 0.9423)	0.8750 (0.7254 to 0.9460)	0.9615 (0.7569 to 0.9945)	
Number of patients at risk[b]					
2 Months	87	101	36	31	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_semm_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	85	95	33	30	
6 Months	73	87	32	29	
8 Months	67	81	28	29	
10 Months	65	75	27	28	
12 Months	56	66	23	25	
14 Months	34	45	12	16	
16 Months	16	17	6	6	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_semm_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.5 Treatment emergent mild adverse event by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	89 (90.8)	95 (92.2)	37 (92.5)	31 (96.9)	0.0378
Number (%) of patients censored	9 (9.2)	8 (7.8)	3 (7.5)	1 (3.1)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0986 to 0.2300)	0.1314 (0.0657 to 0.1643)	0.1643 (0.0986 to 0.3285)	0.0986 (0.0329 to 0.1643)	
Median (95% CI)	0.3943 (0.2957 to 0.6242)	0.2628 (0.1971 to 0.4928)	0.4928 (0.3285 to 0.9199)	0.1643 (0.0986 to 0.2957)	
75% quantile (95% CI)	0.9856 (0.8214 to 1.6756)	1.0513 (0.7556 to 3.3183)	2.0370 (0.8871 to 3.1540)	0.5585 (0.1971 to 1.0513)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.9624		0.0102	
Hazard ratio (95% CI) vs Pd		1.0071 (0.7517 to 1.3492)		1.9041 (1.1562 to 3.1357)	
P-value		0.9624		0.0114	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.5 Treatment emergent mild adverse event by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.5252 (0.3189 to 0.8649)		
probability (95% CI)[b]					
2 Months	0.1253 (0.0673 to 0.2023)	0.2233 (0.1486 to 0.3076)	0.2564 (0.1332 to 0.3989)	0.0645 (0.0115 to 0.1862)	
4 Months	0.0912 (0.0430 to 0.1615)	0.1444 (0.0846 to 0.2196)	0.1140 (0.0371 to 0.2389)	0.0645 (0.0115 to 0.1862)	
6 Months	0.0798 (0.0354 to 0.1475)	0.1013 (0.0518 to 0.1702)	0.0760 (0.0163 to 0.1993)	0.0645 (0.0115 to 0.1862)	
8 Months	0.0798 (0.0354 to 0.1475)	0.0788 (0.0359 to 0.1435)	0.0380 (0.0032 to 0.1550)	0.0645 (0.0115 to 0.1862)	
10 Months	0.0638 (0.0242 to 0.1306)	0.0788 (0.0359 to 0.1435)	0.0380 (0.0032 to 0.1550)	0.0645 (0.0115 to 0.1862)	
12 Months	0.0638 (0.0242 to 0.1306)	0.0788 (0.0359 to 0.1435)	0.0380 (0.0032 to 0.1550)	0.0645 (0.0115 to 0.1862)	
14 Months	0.0638 (0.0242 to 0.1306)	0.0788 (0.0359 to 0.1435)	0.0380 (0.0032 to 0.1550)	0.0645 (0.0115 to 0.1862)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.5 Treatment emergent mild adverse event by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0638 (0.0242 to 0.1306)	0.0656 (0.0269 to 0.1286)	0.0380 (0.0032 to 0.1550)	0.0645 (0.0115 to 0.1862)	
Number of patients at risk[b]					
2 Months	11	23	9	1	
4 Months	8	14	4	1	
6 Months	5	9	2	1	
8 Months	5	7	1	0	
10 Months	3	7	1	0	
12 Months	3	6	1	0	
14 Months	3	6	1	0	
16 Months	0	2	1	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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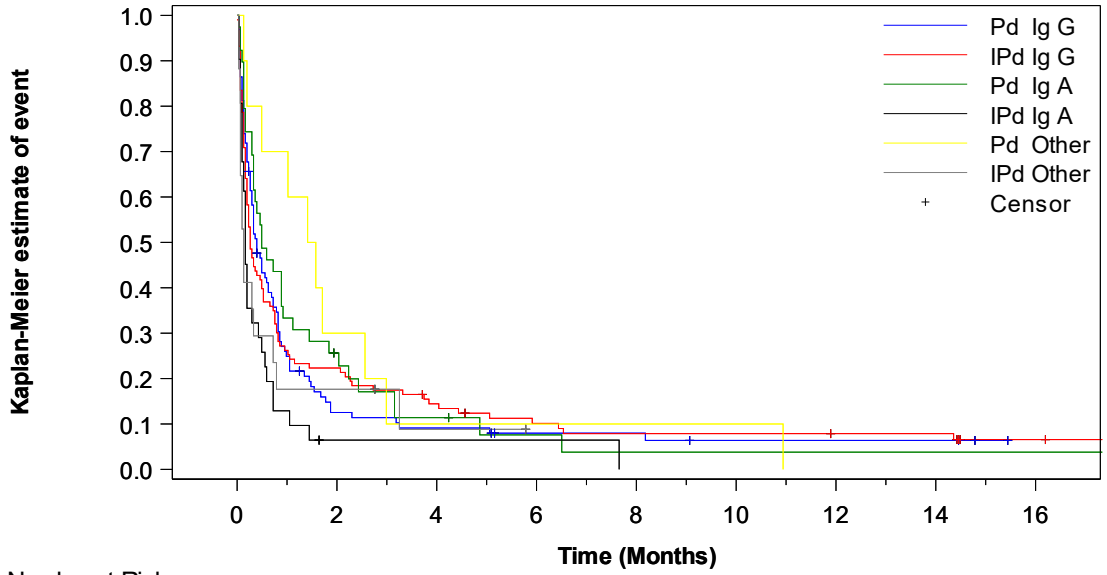
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.6 Kaplan-Meier cumulative incidence curve of treatment emergent mild adverse event by treatment group according to MM type at SE - Safety population



Number at Risk

Pd Ig G	96	11	8	5	5	3	3	3	0
IPd Ig G	103	23	14	9	7	7	6	6	2
Pd Ig A	39	9	4	2	1	1	1	1	1
IPd Ig A	31	1	1	1	0	0	0	0	0
Pd Other	10	3	1	1	1	1	0	0	0
IPd Other	17	3	1	0	0	0	0	0	0

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.7 Treatment emergent severe adverse event by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	71 (72.4)	86 (83.5)	23 (57.5)	29 (90.6)	0.3226
Number (%) of patients censored	27 (27.6)	17 (16.5)	17 (42.5)	3 (9.4)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.5257 (0.2628 to 0.7228)	0.5257 (0.3614 to 0.6242)	0.5914 (0.4600 to 0.8542)	0.5092 (0.1314 to 0.5914)	
Median (95% CI)	1.9384 (0.7885 to 2.9569)	0.8542 (0.7556 to 1.3470)	1.5441 (0.7885 to NC)	0.8542 (0.5257 to 1.8398)	
75% quantile (95% CI)	NC (4.6653 to NC)	4.2053 (2.1027 to 8.3450)	NC (NC to NC)	2.5133 (0.8542 to 10.9076)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0710		0.0084	
Hazard ratio (95% CI) vs Pd		1.3387 (0.9742 to 1.8397)		2.0649 (1.1907 to 3.5808)	
P-value		0.0721		0.0098	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.7 Treatment emergent severe adverse event by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.4843 (0.2793 to 0.8398)		
probability (95% CI)[b]					
2 Months	0.4845 (0.3822 to 0.5794)	0.3571 (0.2651 to 0.4500)	0.4886 (0.3258 to 0.6329)	0.2813 (0.1404 to 0.4406)	
4 Months	0.3711 (0.2760 to 0.4662)	0.2569 (0.1762 to 0.3451)	0.4371 (0.2801 to 0.5839)	0.1875 (0.0761 to 0.3369)	
6 Months	0.3184 (0.2283 to 0.4119)	0.2041 (0.1313 to 0.2883)	0.4098 (0.2560 to 0.5577)	0.1563 (0.0570 to 0.3003)	
8 Months	0.2865 (0.2002 to 0.3786)	0.1719 (0.1049 to 0.2528)	0.4098 (0.2560 to 0.5577)	0.1250 (0.0395 to 0.2623)	
10 Months	0.2865 (0.2002 to 0.3786)	0.1611 (0.0963 to 0.2407)	0.4098 (0.2560 to 0.5577)	0.1250 (0.0395 to 0.2623)	
12 Months	0.2865 (0.2002 to 0.3786)	0.1611 (0.0963 to 0.2407)	0.4098 (0.2560 to 0.5577)	0.0938 (0.0240 to 0.2228)	
14 Months	0.2865 (0.2002 to 0.3786)	0.1432 (0.0801 to 0.2241)	0.4098 (0.2560 to 0.5577)	0.0938 (0.0240 to 0.2228)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_semm_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.7 Treatment emergent severe adverse event by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.2661 (0.1789 to 0.3611)	0.1432 (0.0801 to 0.2241)	0.4098 (0.2560 to 0.5577)	0.0938 (0.0240 to 0.2228)	
Number of patients at risk[b]					
2 Months	47	36	19	9	
4 Months	36	25	17	6	
6 Months	30	19	15	5	
8 Months	26	16	12	4	
10 Months	26	14	12	4	
12 Months	23	11	10	3	
14 Months	15	8	4	2	
16 Months	9	3	2	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.8 Treatment emergent severe adverse event including death by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	72 (73.5)	89 (86.4)	24 (60.0)	29 (90.6)	0.4141
Number (%) of patients censored	26 (26.5)	14 (13.6)	16 (40.0)	3 (9.4)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.5257 (0.2628 to 0.7228)	0.5257 (0.3614 to 0.6242)	0.5749 (0.3614 to 0.8542)	0.5092 (0.1314 to 0.5914)	
Median (95% CI)	1.9384 (0.7885 to 2.9569)	0.8542 (0.7556 to 1.3142)	1.5441 (0.7885 to NC)	0.8542 (0.5257 to 1.8398)	
75% quantile (95% CI)	NC (4.6653 to NC)	3.9754 (2.0370 to 7.4251)	NC (4.3368 to NC)	2.5133 (0.8542 to 10.9076)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0444		0.0126	
Hazard ratio (95% CI) vs Pd		1.3783 (1.0066 to 1.8872)		1.9731 (1.1452 to 3.3995)	
P-value		0.0454		0.0143	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.8 Treatment emergent severe adverse event including death by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.7255 (0.5299 to 0.9935)		0.5068 (0.2942 to 0.8732)		
probability (95% CI)[b]					
2 Months	0.4845 (0.3822 to 0.5794)	0.3431 (0.2529 to 0.4351)	0.4750 (0.3156 to 0.6184)	0.2813 (0.1404 to 0.4406)	
4 Months	0.3711 (0.2760 to 0.4662)	0.2451 (0.1667 to 0.3317)	0.4250 (0.2715 to 0.5704)	0.1875 (0.0761 to 0.3369)	
6 Months	0.3093 (0.2205 to 0.4022)	0.1947 (0.1244 to 0.2769)	0.3984 (0.2481 to 0.5447)	0.1563 (0.0570 to 0.3003)	
8 Months	0.2784 (0.1934 to 0.3696)	0.1640 (0.0995 to 0.2426)	0.3984 (0.2481 to 0.5447)	0.1250 (0.0395 to 0.2623)	
10 Months	0.2784 (0.1934 to 0.3696)	0.1435 (0.0834 to 0.2193)	0.3984 (0.2481 to 0.5447)	0.1250 (0.0395 to 0.2623)	
12 Months	0.2784 (0.1934 to 0.3696)	0.1435 (0.0834 to 0.2193)	0.3984 (0.2481 to 0.5447)	0.0938 (0.0240 to 0.2228)	
14 Months	0.2784 (0.1934 to 0.3696)	0.1276 (0.0696 to 0.2038)	0.3984 (0.2481 to 0.5447)	0.0938 (0.0240 to 0.2228)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_semm_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.16 Subgroup analyses by MM type at SE
16.2.7.1.1.16.8 Treatment emergent severe adverse event including death by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.2585 (0.1729 to 0.3523)	0.1276 (0.0696 to 0.2038)	0.3984 (0.2481 to 0.5447)	0.0938 (0.0240 to 0.2228)	
Number of patients at risk[b]					
2 Months	47	35	19	9	
4 Months	36	25	17	6	
6 Months	30	19	15	5	
8 Months	26	16	12	4	
10 Months	26	14	12	4	
12 Months	23	11	10	3	
14 Months	15	8	4	2	
16 Months	9	3	2	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_semm_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.1 Treatment emergent adverse event by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	95 (97.9)	100 (99.0)	50 (98.0)	50 (100.0)	0.0072
Number (%) of patients censored	2 (2.1)	1 (1.0)	1 (2.0)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0657 to 0.1314)	0.1314 (0.0657 to 0.1643)	0.1971 (0.1314 to 0.3285)	0.0657 (0.0657 to 0.0986)	
Median (95% CI)	0.2957 (0.1971 to 0.3943)	0.2300 (0.1643 to 0.3285)	0.4928 (0.3285 to 0.7885)	0.1314 (0.0986 to 0.1643)	
75% quantile (95% CI)	0.8214 (0.5585 to 1.0513)	0.6078 (0.4600 to 0.7885)	1.0185 (0.7885 to 2.4312)	0.3285 (0.1643 to 0.7228)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.3791		<.0001	
Hazard ratio (95% CI) vs Pd		1.1363 (0.8547 to 1.5106)		2.2504 (1.4825 to 3.4161)	
P-value		0.3793		0.0001	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_dghc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.1 Treatment emergent adverse event by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.4444 (0.2927 to 0.6745)		
probability (95% CI)[b]					
2 Months	0.0851 (0.0398 to 0.1522)	0.0800 (0.0374 to 0.1435)	0.1633 (0.0764 to 0.2787)	0.0204 (0.0017 to 0.0940)	
4 Months	0.0426 (0.0139 to 0.0973)	0.0300 (0.0081 to 0.0779)	0.0612 (0.0160 to 0.1516)	0.0204 (0.0017 to 0.0940)	
6 Months	0.0319 (0.0086 to 0.0826)	0.0200 (0.0039 to 0.0636)	0.0612 (0.0160 to 0.1516)	0.0204 (0.0017 to 0.0940)	
8 Months	0.0319 (0.0086 to 0.0826)	0.0100 (0.0009 to 0.0490)	0.0306 (0.0031 to 0.1224)	0.0204 (0.0017 to 0.0940)	
10 Months	0.0213 (0.0041 to 0.0674)	0.0100 (0.0009 to 0.0490)	0.0306 (0.0031 to 0.1224)	0.0204 (0.0017 to 0.0940)	
12 Months	0.0213 (0.0041 to 0.0674)	0.0100 (0.0009 to 0.0490)	0.0306 (0.0031 to 0.1224)	0.0204 (0.0017 to 0.0940)	
14 Months	0.0213 (0.0041 to 0.0674)	0.0100 (0.0009 to 0.0490)	0.0306 (0.0031 to 0.1224)	0.0204 (0.0017 to 0.0940)	

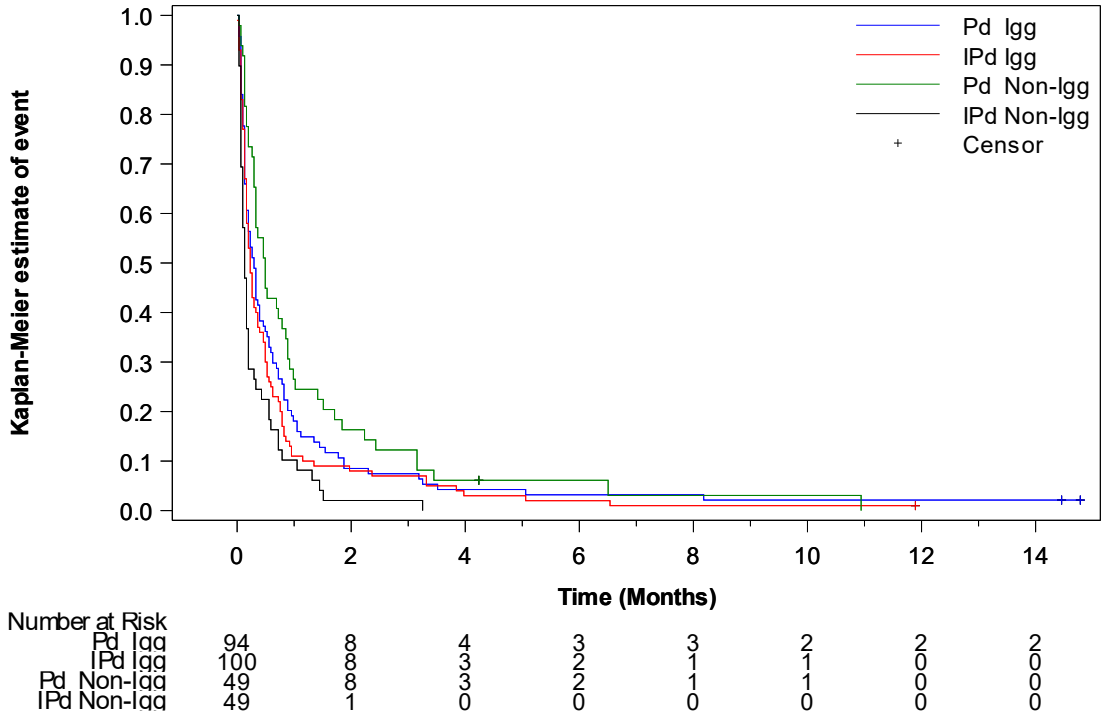
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_dghc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.1 Treatment emergent adverse event by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0213 (0.0041 to 0.0674)	0.0100 (0.0009 to 0.0490)	0.0306 (0.0031 to 0.1224)	0.0204 (0.0017 to 0.0940)	
Number of patients at risk[b]					
2 Months	8	8	8	1	
4 Months	4	3	3	0	
6 Months	3	2	2	0	
8 Months	3	1	1	0	
10 Months	2	1	1	0	
12 Months	2	0	0	0	
14 Months	2	0	0	0	
16 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_dghc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event by treatment group according to MM type at initial diagnosis - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.3 Treatment emergent serious adverse event by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	53 (54.6)	60 (59.4)	26 (51.0)	33 (66.0)	0.3472
Number (%) of patients censored	44 (45.4)	41 (40.6)	25 (49.0)	17 (34.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.3142 (0.5585 to 2.2669)	0.8378 (0.4600 to 1.9713)	1.5113 (0.5257 to 3.0883)	0.6571 (0.2628 to 1.5770)	
Median (95% CI)	6.0452 (2.9569 to NC)	6.2752 (3.7782 to NC)	12.1889 (2.2669 to NC)	3.3840 (1.4127 to 10.9076)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.5462 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.6995		0.1492	
Hazard ratio (95% CI) vs Pd		1.0757 (0.7423 to 1.5589)		1.4567 (0.8711 to 2.4360)	
P-value		0.6999		0.1516	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_dghc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.3 Treatment emergent serious adverse event by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.6804 (0.5777 to 0.7632)	0.6600 (0.5583 to 0.7437)	0.6667 (0.5198 to 0.7778)	0.6200 (0.4711 to 0.7381)	
4 Months	0.5773 (0.4728 to 0.6684)	0.5892 (0.4862 to 0.6784)	0.5859 (0.4383 to 0.7071)	0.4992 (0.3546 to 0.6278)	
6 Months	0.5033 (0.3998 to 0.5979)	0.5079 (0.4060 to 0.6011)	0.5231 (0.3771 to 0.6501)	0.4775 (0.3341 to 0.6075)	
8 Months	0.4811 (0.3782 to 0.5766)	0.4775 (0.3766 to 0.5714)	0.5013 (0.3561 to 0.6301)	0.4558 (0.3138 to 0.5870)	
10 Months	0.4811 (0.3782 to 0.5766)	0.4267 (0.3284 to 0.5212)	0.5013 (0.3561 to 0.6301)	0.3907 (0.2550 to 0.5239)	
12 Months	0.4694 (0.3667 to 0.5654)	0.4059 (0.3089 to 0.5005)	0.5013 (0.3561 to 0.6301)	0.3217 (0.1950 to 0.4554)	
14 Months	0.4560 (0.3533 to 0.5528)	0.4059 (0.3089 to 0.5005)	0.4734 (0.3276 to 0.6060)	0.3217 (0.1950 to 0.4554)	
16 Months	0.4320 (0.3250 to 0.5343)	0.4059 (0.3089 to 0.5005)	0.4734 (0.3276 to 0.6060)	0.3217 (0.1950 to 0.4554)	
Number of patients at risk[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_dghc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.3 Treatment emergent serious adverse event by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	66	66	33	31	
4 Months	56	58	29	24	
6 Months	46	50	25	22	
8 Months	41	47	22	21	
10 Months	41	42	21	18	
12 Months	35	36	18	14	
14 Months	20	26	9	9	
16 Months	10	11	5	3	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (14.4)	9 (8.9)	5 (9.8)	2 (4.0)	0.6552
Number (%) of patients censored	83 (85.6)	92 (91.1)	46 (90.2)	48 (96.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (12.8789 to NC)	NC (15.9671 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.1846		0.2283	
Hazard ratio (95% CI) vs Pd		0.5714 (0.2473 to 1.3205)		0.3791 (0.0735 to 1.9548)	
P-value		0.1904		0.2465	

probability (95% CI)[b]

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_dghc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9064 (0.8278 to 0.9502)	0.9900 (0.9311 to 0.9986)	0.9208 (0.8024 to 0.9695)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9064 (0.8278 to 0.9502)	0.9700 (0.9099 to 0.9902)	0.9003 (0.7768 to 0.9573)	0.9792 (0.8612 to 0.9970)	
6 Months	0.8739 (0.7886 to 0.9264)	0.9387 (0.8686 to 0.9720)	0.9003 (0.7768 to 0.9573)	0.9792 (0.8612 to 0.9970)	
8 Months	0.8614 (0.7730 to 0.9172)	0.9271 (0.8530 to 0.9646)	0.9003 (0.7768 to 0.9573)	0.9792 (0.8612 to 0.9970)	
10 Months	0.8614 (0.7730 to 0.9172)	0.9148 (0.8363 to 0.9566)	0.9003 (0.7768 to 0.9573)	0.9792 (0.8612 to 0.9970)	
12 Months	0.8614 (0.7730 to 0.9172)	0.9148 (0.8363 to 0.9566)	0.9003 (0.7768 to 0.9573)	0.9527 (0.8220 to 0.9881)	
14 Months	0.8427 (0.7459 to 0.9049)	0.9148 (0.8363 to 0.9566)	0.9003 (0.7768 to 0.9573)	0.9527 (0.8220 to 0.9881)	
16 Months	0.8427 (0.7459 to 0.9049)	0.8666 (0.7135 to 0.9411)	0.9003 (0.7768 to 0.9573)	0.9527 (0.8220 to 0.9881)	
Number of patients at risk[b]					
2 Months	86	99	46	48	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_dghc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	84	93	42	45	
6 Months	72	85	40	40	
8 Months	66	79	36	40	
10 Months	64	73	34	39	
12 Months	55	64	29	35	
14 Months	33	44	18	24	
16 Months	15	17	8	11	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_dghc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.5 Treatment emergent mild adverse event by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	88 (90.7)	93 (92.1)	48 (94.1)	47 (94.0)	0.0107
Number (%) of patients censored	9 (9.3)	8 (7.9)	3 (5.9)	3 (6.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0986 to 0.2300)	0.1314 (0.0657 to 0.1643)	0.2957 (0.1314 to 0.3943)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.3943 (0.2957 to 0.6242)	0.2628 (0.1971 to 0.4928)	0.7228 (0.3614 to 1.1170)	0.1643 (0.0986 to 0.1971)	
75% quantile (95% CI)	0.9856 (0.7885 to 1.6756)	1.0513 (0.7556 to 3.3183)	2.0370 (1.1170 to 3.1540)	0.5585 (0.1971 to 1.0513)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.9583		0.0033	
Hazard ratio (95% CI) vs Pd		0.9922 (0.7388 to 1.3324)		1.8526 (1.2200 to 2.8133)	
P-value		0.9583		0.0038	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_dghc_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.5 Treatment emergent mild adverse event by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.5398 (0.3555 to 0.8197)		
probability (95% CI)[b]					
2 Months	0.1271 (0.0683 to 0.2048)	0.2277 (0.1517 to 0.3133)	0.2653 (0.1518 to 0.3930)	0.1020 (0.0375 to 0.2047)	
4 Months	0.0924 (0.0437 to 0.1636)	0.1473 (0.0863 to 0.2237)	0.1105 (0.0412 to 0.2186)	0.0680 (0.0161 to 0.1738)	
6 Months	0.0809 (0.0360 to 0.1494)	0.1033 (0.0528 to 0.1734)	0.0829 (0.0245 to 0.1880)	0.0680 (0.0161 to 0.1738)	
8 Months	0.0809 (0.0360 to 0.1494)	0.0803 (0.0366 to 0.1462)	0.0553 (0.0111 to 0.1550)	0.0680 (0.0161 to 0.1738)	
10 Months	0.0647 (0.0246 to 0.1323)	0.0803 (0.0366 to 0.1462)	0.0553 (0.0111 to 0.1550)	0.0680 (0.0161 to 0.1738)	
12 Months	0.0647 (0.0246 to 0.1323)	0.0803 (0.0366 to 0.1462)	0.0276 (0.0023 to 0.1196)	0.0680 (0.0161 to 0.1738)	
14 Months	0.0647 (0.0246 to 0.1323)	0.0803 (0.0366 to 0.1462)	0.0276 (0.0023 to 0.1196)	0.0680 (0.0161 to 0.1738)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.5 Treatment emergent mild adverse event by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0647 (0.0246 to 0.1323)	0.0669 (0.0274 to 0.1310)	0.0276 (0.0023 to 0.1196)	0.0680 (0.0161 to 0.1738)	
Number of patients at risk[b]					
2 Months	11	23	12	4	
4 Months	8	14	5	2	
6 Months	5	9	3	1	
8 Months	5	7	2	0	
10 Months	3	7	2	0	
12 Months	3	6	1	0	
14 Months	3	6	1	0	
16 Months	0	2	1	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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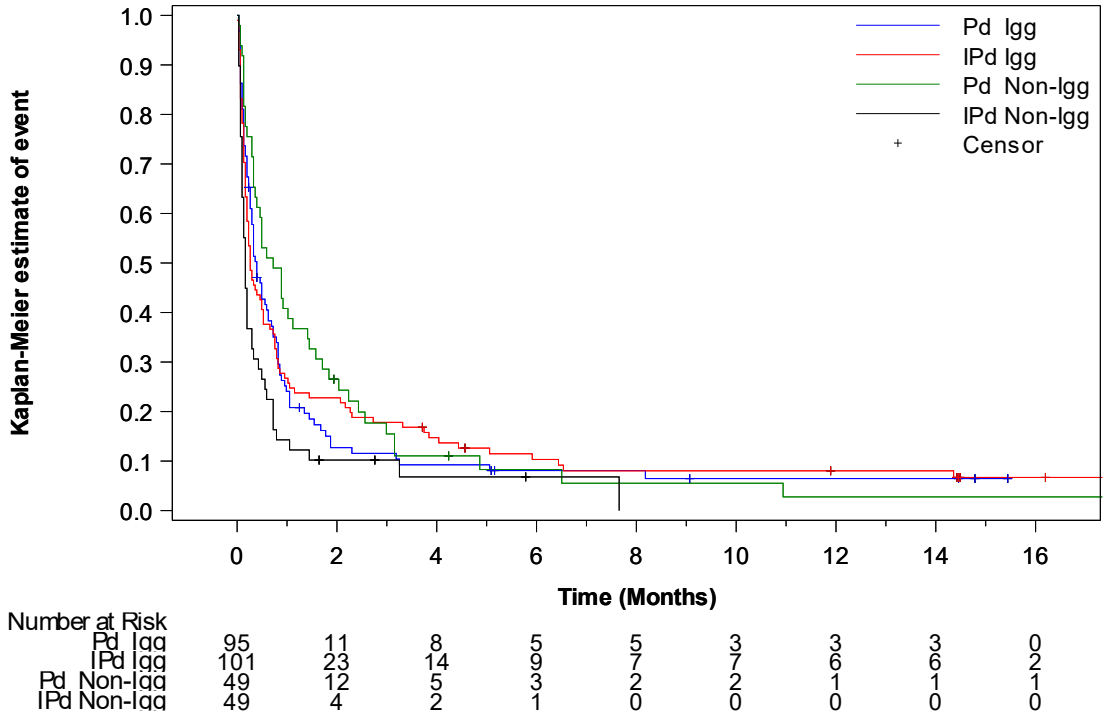
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.6 Kaplan-Meier cumulative incidence curve of treatment emergent mild adverse event by treatment group according to MM type at initial diagnosis - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.7 Treatment emergent severe adverse event by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	70 (72.2)	84 (83.2)	32 (62.7)	44 (88.0)	0.2048
Number (%) of patients censored	27 (27.8)	17 (16.8)	19 (37.3)	6 (12.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.5257 (0.2628 to 0.7228)	0.5257 (0.3614 to 0.6242)	0.7556 (0.4928 to 0.9199)	0.5257 (0.2628 to 0.5585)	
Median (95% CI)	1.9384 (0.7885 to 2.9569)	0.8542 (0.7556 to 1.3470)	1.5441 (0.8542 to 5.5852)	0.8542 (0.5585 to 1.4127)	
75% quantile (95% CI)	NC (4.6653 to NC)	4.4353 (2.3655 to 8.3450)	NC (4.3368 to NC)	2.7926 (1.3142 to 7.4908)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0886		0.0063	
Hazard ratio (95% CI) vs Pd		1.3201 (0.9580 to 1.8190)		1.8749 (1.1856 to 2.9649)	
P-value		0.0896		0.0072	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.7 Treatment emergent severe adverse event by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.5334 (0.3373 to 0.8434)		
probability (95% CI)[b]					
2 Months	0.4792 (0.3765 to 0.5746)	0.3644 (0.2708 to 0.4584)	0.4608 (0.3195 to 0.5909)	0.3000 (0.1806 to 0.4287)	
4 Months	0.3646 (0.2696 to 0.4599)	0.2621 (0.1799 to 0.3516)	0.4007 (0.2658 to 0.5319)	0.1760 (0.0851 to 0.2938)	
6 Months	0.3112 (0.2215 to 0.4050)	0.2082 (0.1340 to 0.2938)	0.3585 (0.2288 to 0.4900)	0.1540 (0.0697 to 0.2688)	
8 Months	0.2898 (0.2026 to 0.3825)	0.1754 (0.1071 to 0.2576)	0.3585 (0.2288 to 0.4900)	0.1320 (0.0550 to 0.2431)	
10 Months	0.2898 (0.2026 to 0.3825)	0.1644 (0.0983 to 0.2453)	0.3585 (0.2288 to 0.4900)	0.1320 (0.0550 to 0.2431)	
12 Months	0.2898 (0.2026 to 0.3825)	0.1644 (0.0983 to 0.2453)	0.3585 (0.2288 to 0.4900)	0.1100 (0.0413 to 0.2167)	
14 Months	0.2898 (0.2026 to 0.3825)	0.1461 (0.0817 to 0.2284)	0.3585 (0.2288 to 0.4900)	0.1100 (0.0413 to 0.2167)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_dghc_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.7 Treatment emergent severe adverse event by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.2691 (0.1810 to 0.3648)	0.1461 (0.0817 to 0.2284)	0.3585 (0.2288 to 0.4900)	0.1100 (0.0413 to 0.2167)	
Number of patients at risk[b]					
2 Months	46	36	23	15	
4 Months	35	25	20	8	
6 Months	29	19	17	7	
8 Months	26	16	14	6	
10 Months	26	14	14	6	
12 Months	23	11	11	5	
14 Months	15	8	5	3	
16 Months	9	3	3	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_dghc_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.8 Treatment emergent severe adverse event including death by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	71 (73.2)	87 (86.1)	33 (64.7)	44 (88.0)	0.2813
Number (%) of patients censored	26 (26.8)	14 (13.9)	18 (35.3)	6 (12.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.5257 (0.2628 to 0.7228)	0.5092 (0.3614 to 0.6242)	0.6899 (0.4600 to 0.8542)	0.5257 (0.2628 to 0.5585)	
Median (95% CI)	1.9384 (0.7885 to 2.9569)	0.8378 (0.7556 to 1.3470)	1.5441 (0.8214 to 5.5852)	0.8542 (0.5585 to 1.4127)	
75% quantile (95% CI)	NC (4.6653 to NC)	4.0903 (2.0370 to 7.4251)	NC (4.3368 to NC)	2.7926 (1.3142 to 7.4908)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0563		0.0094	
Hazard ratio (95% CI) vs Pd		1.3599 (0.9906 to 1.8669)		1.8107 (1.1496 to 2.8518)	
P-value		0.0573		0.0104	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.8 Treatment emergent severe adverse event including death by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.5523 (0.3507 to 0.8698)		
probability (95% CI)[b]					
2 Months	0.4792 (0.3765 to 0.5746)	0.3500 (0.2582 to 0.4431)	0.4510 (0.3120 to 0.5802)	0.3000 (0.1806 to 0.4287)	
4 Months	0.3646 (0.2696 to 0.4599)	0.2500 (0.1702 to 0.3378)	0.3922 (0.2596 to 0.5221)	0.1760 (0.0851 to 0.2938)	
6 Months	0.3021 (0.2137 to 0.3951)	0.1986 (0.1269 to 0.2820)	0.3509 (0.2236 to 0.4809)	0.1540 (0.0697 to 0.2688)	
8 Months	0.2813 (0.1955 to 0.3731)	0.1673 (0.1015 to 0.2472)	0.3509 (0.2236 to 0.4809)	0.1320 (0.0550 to 0.2431)	
10 Months	0.2813 (0.1955 to 0.3731)	0.1464 (0.0851 to 0.2235)	0.3509 (0.2236 to 0.4809)	0.1320 (0.0550 to 0.2431)	
12 Months	0.2813 (0.1955 to 0.3731)	0.1464 (0.0851 to 0.2235)	0.3509 (0.2236 to 0.4809)	0.1100 (0.0413 to 0.2167)	
14 Months	0.2813 (0.1955 to 0.3731)	0.1301 (0.0710 to 0.2076)	0.3509 (0.2236 to 0.4809)	0.1100 (0.0413 to 0.2167)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_dghc_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.1.17.8 Treatment emergent severe adverse event including death by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.2612 (0.1748 to 0.3557)	0.1301 (0.0710 to 0.2076)	0.3509 (0.2236 to 0.4809)	0.1100 (0.0413 to 0.2167)	
Number of patients at risk[b]					
2 Months	46	35	23	15	
4 Months	35	25	20	8	
6 Months	29	19	17	7	
8 Months	26	16	14	6	
10 Months	26	14	14	6	
12 Months	23	11	11	5	
14 Months	15	8	5	3	
16 Months	9	3	3	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_dghc_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.1.18.1 Treatment emergent adverse event by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (90.0)	14 (100.0)	137 (98.6)	137 (99.3)	0.7002
Number (%) of patients censored	1 (10.0)	0 (0.0)	2 (1.4)	1 (0.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.0986 (0.0329 to 0.4928)	0.0986 (0.0657 to 0.1643)	0.1314 (0.1314 to 0.1643)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.4107 (0.0329 to 2.2341)	0.1643 (0.0657 to 0.5257)	0.3285 (0.2628 to 0.4600)	0.1971 (0.1643 to 0.2628)	
75% quantile (95% CI)	2.2341 (0.3285 to NC)	0.5257 (0.1314 to 6.5380)	0.8871 (0.7228 to 1.1170)	0.5585 (0.3614 to 0.7885)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.5490		0.0063	
Hazard ratio (95% CI) vs Pd		1.3072 (0.5430 to 3.1470)		1.3976 (1.0981 to 1.7789)	
P-value		0.5501		0.0065	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_mri_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.1.18.1 Treatment emergent adverse event by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.7155 (0.5621 to 0.9107)		
probability (95% CI)[b]					
2 Months	0.3000 (0.0711 to 0.5779)	0.0769 (0.0048 to 0.2920)	0.0970 (0.0544 to 0.1542)	0.0584 (0.0273 to 0.1063)	
4 Months	0.1000 (0.0057 to 0.3581)	0.0769 (0.0048 to 0.2920)	0.0448 (0.0184 to 0.0894)	0.0146 (0.0029 to 0.0472)	
6 Months	0.1000 (0.0057 to 0.3581)	0.0769 (0.0048 to 0.2920)	0.0373 (0.0140 to 0.0795)	0.0073 (0.0007 to 0.0366)	
8 Months	0.1000 (0.0057 to 0.3581)	0.0769 (0.0048 to 0.2920)	0.0299 (0.0098 to 0.0694)	0.0073 (0.0007 to 0.0366)	
10 Months	0.1000 (0.0057 to 0.3581)	0.0769 (0.0048 to 0.2920)	0.0224 (0.0061 to 0.0590)	0.0073 (0.0007 to 0.0366)	
12 Months	0.1000 (0.0057 to 0.3581)	0.0769 (0.0048 to 0.2920)	0.0149 (0.0029 to 0.0482)	0.0073 (0.0007 to 0.0366)	
14 Months	0.1000 (0.0057 to 0.3581)	0.0769 (0.0048 to 0.2920)	0.0149 (0.0029 to 0.0482)	0.0073 (0.0007 to 0.0366)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.1.18.1 Treatment emergent adverse event by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.1000 (0.0057 to 0.3581)	0.0769 (0.0048 to 0.2920)	0.0149 (0.0029 to 0.0482)	0.0073 (0.0007 to 0.0366)	
Number of patients at risk[b]					
2 Months	3	1	13	8	
4 Months	1	1	6	2	
6 Months	0	1	5	1	
8 Months	0	0	4	1	
10 Months	0	0	3	1	
12 Months	0	0	2	0	
14 Months	0	0	2	0	
16 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.1.18.2 Treatment emergent serious adverse event by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (60.0)	8 (57.1)	74 (53.2)	86 (62.3)	0.3517
Number (%) of patients censored	4 (40.0)	6 (42.9)	65 (46.8)	52 (37.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.0842 (0.0329 to 4.4682)	0.5585 (0.1314 to 8.8049)	1.4784 (0.7228 to 2.2669)	0.8214 (0.4928 to 1.5113)	
Median (95% CI)	3.0062 (0.0329 to NC)	9.9713 (0.4600 to NC)	6.8994 (4.0739 to NC)	5.8152 (2.7926 to 9.8234)	
75% quantile (95% CI)	NC (1.5441 to NC)	NC (8.8049 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.5149		0.1861	
Hazard ratio (95% CI) vs Pd		0.6956 (0.2320 to 2.0853)		1.2335 (0.9032 to 1.6846)	
P-value		0.5169		0.1869	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.1.18.2 Treatment emergent serious adverse event by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.5000 (0.1836 to 0.7532)	0.6429 (0.3433 to 0.8331)	0.6906 (0.6066 to 0.7603)	0.6496 (0.5635 to 0.7230)	
4 Months	0.5000 (0.1836 to 0.7532)	0.6429 (0.3433 to 0.8331)	0.5889 (0.5022 to 0.6655)	0.5537 (0.4664 to 0.6324)	
6 Months	0.3750 (0.0995 to 0.6591)	0.6429 (0.3433 to 0.8331)	0.5220 (0.4354 to 0.6015)	0.4861 (0.3998 to 0.5669)	
8 Months	0.3750 (0.0995 to 0.6591)	0.5714 (0.2840 to 0.7797)	0.4911 (0.4049 to 0.5716)	0.4633 (0.3776 to 0.5446)	
10 Months	0.3750 (0.0995 to 0.6591)	0.5000 (0.2286 to 0.7221)	0.4911 (0.4049 to 0.5716)	0.4101 (0.3267 to 0.4916)	
12 Months	0.3750 (0.0995 to 0.6591)	0.4286 (0.1773 to 0.6604)	0.4831 (0.3970 to 0.5638)	0.3708 (0.2895 to 0.4521)	
14 Months	0.3750 (0.0995 to 0.6591)	0.4286 (0.1773 to 0.6604)	0.4645 (0.3782 to 0.5462)	0.3708 (0.2895 to 0.4521)	
16 Months	0.3750 (0.0995 to 0.6591)	0.4286 (0.1773 to 0.6604)	0.4466 (0.3570 to 0.5322)	0.3708 (0.2895 to 0.4521)	
Number of patients at risk[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_mri_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.1.18.2 Treatment emergent serious adverse event by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	5	9	95	89	
4 Months	5	9	81	74	
6 Months	3	9	69	64	
8 Months	1	8	62	61	
10 Months	1	7	61	54	
12 Months	1	6	52	44	
14 Months	1	5	28	30	
16 Months	0	3	15	11	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.1.18.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (10.0)	0 (0.0)	18 (12.9)	11 (8.0)	0.9882
Number (%) of patients censored	9 (90.0)	14 (100.0)	121 (87.1)	127 (92.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (4.4682 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (4.4682 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.1410		0.1474	
Hazard ratio (95% CI) vs Pd		NC (NC to NC)		0.5783 (0.2731 to 1.2246)	
P-value		0.9985		0.1525	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.1.18.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9060 (0.8436 to 0.9443)	0.9927 (0.9493 to 0.9990)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8986 (0.8348 to 0.9387)	0.9704 (0.9231 to 0.9888)	
6 Months	0.8333 (0.2731 to 0.9747)	1.0000 (1.0000 to 1.0000)	0.8836 (0.8170 to 0.9270)	0.9473 (0.8926 to 0.9745)	
8 Months	0.8333 (0.2731 to 0.9747)	1.0000 (1.0000 to 1.0000)	0.8752 (0.8068 to 0.9206)	0.9389 (0.8813 to 0.9690)	
10 Months	0.8333 (0.2731 to 0.9747)	1.0000 (1.0000 to 1.0000)	0.8752 (0.8068 to 0.9206)	0.9299 (0.8694 to 0.9630)	
12 Months	0.8333 (0.2731 to 0.9747)	1.0000 (1.0000 to 1.0000)	0.8752 (0.8068 to 0.9206)	0.9205 (0.8569 to 0.9566)	
14 Months	0.8333 (0.2731 to 0.9747)	1.0000 (1.0000 to 1.0000)	0.8627 (0.7894 to 0.9119)	0.9205 (0.8569 to 0.9566)	
16 Months	0.8333 (0.2731 to 0.9747)	1.0000 (1.0000 to 1.0000)	0.8627 (0.7894 to 0.9119)	0.8851 (0.7706 to 0.9445)	
Number of patients at risk[b]					
2 Months	9	14	124	134	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.1.18.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	7	13	120	126	
6 Months	5	11	108	115	
8 Months	2	10	101	110	
10 Months	2	10	97	103	
12 Months	2	8	83	92	
14 Months	2	7	50	61	
16 Months	0	5	24	23	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.1.18.4 Treatment emergent mild adverse event by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (80.0)	12 (85.7)	129 (92.8)	129 (93.5)	0.5765
Number (%) of patients censored	2 (20.0)	2 (14.3)	10 (7.2)	9 (6.5)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0657 to 0.4928)	0.1314 (0.0657 to 0.1971)	0.1643 (0.1314 to 0.2628)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.4928 (0.0657 to 3.2526)	0.1971 (0.0657 to 6.5380)	0.4928 (0.3285 to 0.7228)	0.2300 (0.1643 to 0.3285)	
75% quantile (95% CI)	2.2341 (0.4928 to NC)	6.5380 (0.1643 to NC)	1.3470 (0.8871 to 1.8398)	0.7885 (0.5585 to 1.1499)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.7466		0.0901	
Hazard ratio (95% CI) vs Pd		0.8539 (0.3273 to 2.2278)		1.2373 (0.9668 to 1.5835)	
P-value		0.7468		0.0907	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.1.18.4 Treatment emergent mild adverse event by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.3600 (0.0899 to 0.6484)	0.3846 (0.1405 to 0.6280)	0.1620 (0.1051 to 0.2298)	0.1667 (0.1101 to 0.2334)	
4 Months	0.1200 (0.0066 to 0.4079)	0.3077 (0.0950 to 0.5543)	0.0972 (0.0538 to 0.1559)	0.1031 (0.0587 to 0.1620)	
6 Months	0.1200 (0.0066 to 0.4079)	0.3077 (0.0950 to 0.5543)	0.0810 (0.0419 to 0.1366)	0.0677 (0.0322 to 0.1211)	
8 Months	0.1200 (0.0066 to 0.4079)	0.2051 (0.0385 to 0.4629)	0.0709 (0.0343 to 0.1253)	0.0483 (0.0192 to 0.0981)	
10 Months	0.1200 (0.0066 to 0.4079)	0.2051 (0.0385 to 0.4629)	0.0608 (0.0271 to 0.1137)	0.0483 (0.0192 to 0.0981)	
12 Months	0.1200 (0.0066 to 0.4079)	0.2051 (0.0385 to 0.4629)	0.0486 (0.0186 to 0.1007)	0.0483 (0.0192 to 0.0981)	
14 Months	0.1200 (0.0066 to 0.4079)	0.2051 (0.0385 to 0.4629)	0.0486 (0.0186 to 0.1007)	0.0483 (0.0192 to 0.0981)	
16 Months	0.1200 (0.0066 to 0.4079)	0.1026 (0.0067 to 0.3553)	0.0486 (0.0186 to 0.1007)	0.0483 (0.0192 to 0.0981)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.1.18.4 Treatment emergent mild adverse event by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	3	5	20	22	
4 Months	1	4	12	12	
6 Months	0	3	8	7	
8 Months	0	2	7	5	
10 Months	0	2	5	5	
12 Months	0	2	4	4	
14 Months	0	2	4	4	
16 Months	0	1	1	1	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.1.18.5 Treatment emergent severe adverse event by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (60.0)	12 (85.7)	97 (69.8)	117 (84.8)	0.6975
Number (%) of patients censored	4 (40.0)	2 (14.3)	42 (30.2)	21 (15.2)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.7556 (0.0329 to 1.5441)	0.4600 (0.0986 to 0.6242)	0.5585 (0.3285 to 0.7556)	0.5257 (0.3614 to 0.5914)	
Median (95% CI)	1.4127 (0.0329 to NC)	0.7392 (0.1643 to 2.0370)	1.9384 (0.9856 to 2.9569)	0.8542 (0.7556 to 1.2156)	
75% quantile (95% CI)	NC (1.2813 to NC)	2.0370 (0.6242 to NC)	NC (6.0452 to NC)	3.7782 (2.2669 to 6.1766)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.2869		0.0042	
Hazard ratio (95% CI) vs Pd		1.6963 (0.6342 to 4.5369)		1.4835 (1.1303 to 1.9470)	
P-value		0.2925		0.0045	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.1.18.5 Treatment emergent severe adverse event by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.6741 (0.5136 to 0.8847)		
probability (95% CI)[b]					
2 Months	0.4000 (0.1227 to 0.6702)	0.2857 (0.0883 to 0.5237)	0.4825 (0.3967 to 0.5630)	0.3462 (0.2674 to 0.4260)	
4 Months	0.4000 (0.1227 to 0.6702)	0.2143 (0.0521 to 0.4479)	0.3802 (0.2993 to 0.4606)	0.2336 (0.1661 to 0.3079)	
6 Months	0.4000 (0.1227 to 0.6702)	0.2143 (0.0521 to 0.4479)	0.3290 (0.2519 to 0.4080)	0.1857 (0.1247 to 0.2562)	
8 Months	0.4000 (0.1227 to 0.6702)	0.2143 (0.0521 to 0.4479)	0.3065 (0.2314 to 0.3847)	0.1534 (0.0978 to 0.2206)	
10 Months	0.4000 (0.1227 to 0.6702)	0.2143 (0.0521 to 0.4479)	0.3065 (0.2314 to 0.3847)	0.1453 (0.0912 to 0.2115)	
12 Months	0.4000 (0.1227 to 0.6702)	0.2143 (0.0521 to 0.4479)	0.3065 (0.2314 to 0.3847)	0.1363 (0.0837 to 0.2016)	
14 Months	0.4000 (0.1227 to 0.6702)	0.1071 (0.0082 to 0.3540)	0.3065 (0.2314 to 0.3847)	0.1363 (0.0837 to 0.2016)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_mri_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.1.18.5 Treatment emergent severe adverse event by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.4000 (0.1227 to 0.6702)	0.1071 (0.0082 to 0.3540)	0.2895 (0.2125 to 0.3708)	0.1363 (0.0837 to 0.2016)	
Number of patients at risk[b]					
2 Months	4	4	66	47	
4 Months	4	3	52	30	
6 Months	2	3	45	23	
8 Months	1	3	39	19	
10 Months	1	3	39	17	
12 Months	1	3	33	13	
14 Months	1	1	19	10	
16 Months	0	0	12	3	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_mri_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.1.18.6 Treatment emergent severe adverse event including death by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (70.0)	12 (85.7)	98 (70.5)	120 (87.0)	0.9622
Number (%) of patients censored	3 (30.0)	2 (14.3)	41 (29.5)	18 (13.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.7556 (0.0329 to 1.5441)	0.4600 (0.0986 to 0.6242)	0.5257 (0.3285 to 0.7556)	0.5257 (0.3614 to 0.5585)	
Median (95% CI)	1.4127 (0.0329 to NC)	0.7392 (0.1643 to 2.0370)	1.8070 (0.9856 to 2.9569)	0.8542 (0.7556 to 1.1499)	
75% quantile (95% CI)	NC (1.2813 to NC)	2.0370 (0.6242 to NC)	NC (5.5852 to NC)	3.6468 (2.1355 to 5.9795)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.4209		0.0025	
Hazard ratio (95% CI) vs Pd		1.4653 (0.5747 to 3.7360)		1.5120 (1.1547 to 1.9799)	
P-value		0.4237		0.0027	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.1.18.6 Treatment emergent severe adverse event including death by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.6614 (0.5051 to 0.8661)		
probability (95% CI)[b]					
2 Months	0.4000 (0.1227 to 0.6702)	0.2857 (0.0883 to 0.5237)	0.4783 (0.3929 to 0.5586)	0.3358 (0.2582 to 0.4150)	
4 Months	0.4000 (0.1227 to 0.6702)	0.2143 (0.0521 to 0.4479)	0.3768 (0.2964 to 0.4569)	0.2251 (0.1591 to 0.2982)	
6 Months	0.2667 (0.0476 to 0.5634)	0.2143 (0.0521 to 0.4479)	0.3261 (0.2496 to 0.4047)	0.1789 (0.1196 to 0.2480)	
8 Months	0.2667 (0.0476 to 0.5634)	0.2143 (0.0521 to 0.4479)	0.3038 (0.2292 to 0.3816)	0.1478 (0.0938 to 0.2134)	
10 Months	0.2667 (0.0476 to 0.5634)	0.2143 (0.0521 to 0.4479)	0.3038 (0.2292 to 0.3816)	0.1323 (0.0813 to 0.1958)	
12 Months	0.2667 (0.0476 to 0.5634)	0.2143 (0.0521 to 0.4479)	0.3038 (0.2292 to 0.3816)	0.1240 (0.0747 to 0.1864)	
14 Months	0.2667 (0.0476 to 0.5634)	0.1071 (0.0082 to 0.3540)	0.3038 (0.2292 to 0.3816)	0.1240 (0.0747 to 0.1864)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.1.18.6 Treatment emergent severe adverse event including death by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.2667 (0.0476 to 0.5634)	0.1071 (0.0082 to 0.3540)	0.2870 (0.2105 to 0.3677)	0.1240 (0.0747 to 0.1864)	
Number of patients at risk[b]					
2 Months	4	4	66	46	
4 Months	4	3	52	30	
6 Months	2	3	45	23	
8 Months	1	3	39	19	
10 Months	1	3	39	17	
12 Months	1	3	33	13	
14 Months	1	1	19	10	
16 Months	0	0	12	3	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.1.19.1 Treatment emergent adverse event by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	91 (96.8)	85 (98.8)	47 (100.0)	54 (100.0)	0.2184
Number (%) of patients censored	3 (3.2)	1 (1.2)	0 (0.0)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1478 (0.1314 to 0.1971)	0.0986 (0.0657 to 0.1314)	0.1314 (0.0657 to 0.1643)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.3285 (0.2957 to 0.5914)	0.1643 (0.1314 to 0.2300)	0.3285 (0.1643 to 0.5257)	0.1971 (0.1314 to 0.3614)	
75% quantile (95% CI)	1.0185 (0.7228 to 1.8727)	0.4928 (0.2957 to 0.7556)	0.8214 (0.5257 to 1.0185)	0.5914 (0.3614 to 0.8542)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0038		0.4133	
Hazard ratio (95% CI) vs Pd		1.5535 (1.1502 to 2.0983)		1.1819 (0.7916 to 1.7647)	
P-value		0.0041		0.4138	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_crcl_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.1.19.1 Treatment emergent adverse event by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6437 (0.4766 to 0.8694)				
probability (95% CI)[b]					
2 Months	0.1522 (0.0878 to 0.2329)	0.0706 (0.0288 to 0.1378)	0.0444 (0.0081 to 0.1333)	0.0556 (0.0146 to 0.1387)	
4 Months	0.0652 (0.0267 to 0.1279)	0.0353 (0.0094 to 0.0909)	0.0222 (0.0018 to 0.1015)	0.0185 (0.0015 to 0.0862)	
6 Months	0.0522 (0.0185 to 0.1124)	0.0235 (0.0045 to 0.0741)	0.0222 (0.0018 to 0.1015)	0.0185 (0.0015 to 0.0862)	
8 Months	0.0391 (0.0113 to 0.0962)	0.0118 (0.0010 to 0.0570)	0.0222 (0.0018 to 0.1015)	0.0185 (0.0015 to 0.0862)	
10 Months	0.0261 (0.0053 to 0.0791)	0.0118 (0.0010 to 0.0570)	0.0222 (0.0018 to 0.1015)	0.0185 (0.0015 to 0.0862)	
12 Months	0.0261 (0.0053 to 0.0791)	0.0118 (0.0010 to 0.0570)	0.0222 (0.0018 to 0.1015)	0.0185 (0.0015 to 0.0862)	
14 Months	0.0261 (0.0053 to 0.0791)	0.0118 (0.0010 to 0.0570)	0.0222 (0.0018 to 0.1015)	0.0185 (0.0015 to 0.0862)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.1.19.1 Treatment emergent adverse event by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0261 (0.0053 to 0.0791)	0.0118 (0.0010 to 0.0570)	0.0222 (0.0018 to 0.1015)	0.0185 (0.0015 to 0.0862)	
Number of patients at risk[b]					
2 Months	14	6	2	3	
4 Months	6	3	1	0	
6 Months	4	2	1	0	
8 Months	3	1	1	0	
10 Months	2	1	1	0	
12 Months	2	0	0	0	
14 Months	2	0	0	0	
16 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.1.19.2 Treatment emergent serious adverse event by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (51.1)	44 (51.2)	28 (59.6)	42 (77.8)	0.3124
Number (%) of patients censored	46 (48.9)	42 (48.8)	19 (40.4)	12 (22.2)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.7741 (1.0513 to 3.0883)	1.9713 (0.6571 to 3.7782)	0.5914 (0.2628 to 1.5770)	0.4928 (0.2628 to 1.2813)	
Median (95% CI)	12.1889 (4.3368 to NC)	11.1376 (5.1253 to NC)	4.3696 (1.5770 to NC)	3.3183 (1.2813 to 6.2752)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.0862 to NC)	10.9076 (6.2752 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.9722		0.2078	
Hazard ratio (95% CI) vs Pd		0.9927 (0.6577 to 1.4983)		1.3584 (0.8419 to 2.1918)	
P-value		0.9722		0.2095	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_crcl_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.1.19.2 Treatment emergent serious adverse event by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.7234 (0.6210 to 0.8024)	0.7412 (0.6341 to 0.8213)	0.6170 (0.4631 to 0.7387)	0.5556 (0.4139 to 0.6759)	
4 Months	0.6277 (0.5217 to 0.7165)	0.6586 (0.5474 to 0.7487)	0.5068 (0.3563 to 0.6392)	0.4603 (0.3238 to 0.5864)	
6 Months	0.5412 (0.4352 to 0.6357)	0.5987 (0.4864 to 0.6942)	0.4606 (0.3130 to 0.5960)	0.3836 (0.2547 to 0.5110)	
8 Months	0.5192 (0.4135 to 0.6147)	0.5743 (0.4619 to 0.6715)	0.4107 (0.2668 to 0.5491)	0.3452 (0.2215 to 0.4722)	
10 Months	0.5192 (0.4135 to 0.6147)	0.5254 (0.4136 to 0.6255)	0.4107 (0.2668 to 0.5491)	0.2685 (0.1580 to 0.3918)	
12 Months	0.5192 (0.4135 to 0.6147)	0.4873 (0.3764 to 0.5892)	0.3791 (0.2363 to 0.5209)	0.2110 (0.1133 to 0.3289)	
14 Months	0.4944 (0.3889 to 0.5914)	0.4873 (0.3764 to 0.5892)	0.3791 (0.2363 to 0.5209)	0.2110 (0.1133 to 0.3289)	
16 Months	0.4697 (0.3591 to 0.5727)	0.4873 (0.3764 to 0.5892)	0.3791 (0.2363 to 0.5209)	0.2110 (0.1133 to 0.3289)	
Number of patients at risk[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.1.19.2 Treatment emergent serious adverse event by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	68	63	28	30	
4 Months	59	55	23	24	
6 Months	50	49	19	20	
8 Months	46	47	14	18	
10 Months	46	43	13	14	
12 Months	42	35	10	11	
14 Months	22	24	6	8	
16 Months	11	12	3	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.1.19.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (11.7)	5 (5.8)	7 (14.9)	6 (11.1)	0.6177
Number (%) of patients censored	83 (88.3)	81 (94.2)	40 (85.1)	48 (88.9)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.1396 to NC)	NC (15.9671 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.1471		0.4466	
Hazard ratio (95% CI) vs Pd		0.4662 (0.1620 to 1.3419)		0.6565 (0.2204 to 1.9557)	
P-value		0.1571		0.4499	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.1.19.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9146 (0.8366 to 0.9564)	1.0000 (1.0000 to 1.0000)	0.9139 (0.7867 to 0.9668)	0.9815 (0.8757 to 0.9974)	
4 Months	0.9146 (0.8366 to 0.9564)	0.9882 (0.9194 to 0.9983)	0.8916 (0.7589 to 0.9534)	0.9444 (0.8376 to 0.9817)	
6 Months	0.8923 (0.8091 to 0.9406)	0.9521 (0.8773 to 0.9817)	0.8688 (0.7308 to 0.9389)	0.9444 (0.8376 to 0.9817)	
8 Months	0.8803 (0.7940 to 0.9319)	0.9392 (0.8600 to 0.9743)	0.8688 (0.7308 to 0.9389)	0.9444 (0.8376 to 0.9817)	
10 Months	0.8803 (0.7940 to 0.9319)	0.9392 (0.8600 to 0.9743)	0.8688 (0.7308 to 0.9389)	0.9208 (0.8012 to 0.9698)	
12 Months	0.8803 (0.7940 to 0.9319)	0.9392 (0.8600 to 0.9743)	0.8688 (0.7308 to 0.9389)	0.8953 (0.7638 to 0.9556)	
14 Months	0.8803 (0.7940 to 0.9319)	0.9392 (0.8600 to 0.9743)	0.8230 (0.6498 to 0.9158)	0.8953 (0.7638 to 0.9556)	
16 Months	0.8803 (0.7940 to 0.9319)	0.9392 (0.8600 to 0.9743)	0.8230 (0.6498 to 0.9158)	0.8057 (0.5362 to 0.9279)	
Number of patients at risk[b]					
2 Months	85	85	42	53	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_crcl_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.1.19.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	83	82	39	49	
6 Months	76	76	33	45	
8 Months	70	73	29	42	
10 Months	67	70	28	38	
12 Months	60	61	23	34	
14 Months	35	41	15	23	
16 Months	15	19	7	8	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_crcl_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.1.19.4 Treatment emergent mild adverse event by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	87 (92.6)	80 (93.0)	44 (93.6)	50 (92.6)	0.3587
Number (%) of patients censored	7 (7.4)	6 (7.0)	3 (6.4)	4 (7.4)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1807 (0.1314 to 0.2957)	0.0986 (0.0657 to 0.1314)	0.1314 (0.0657 to 0.2628)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.4928 (0.3285 to 0.8214)	0.2136 (0.1643 to 0.3285)	0.4600 (0.2300 to 0.7228)	0.2300 (0.1314 to 0.4928)	
75% quantile (95% CI)	1.5441 (0.8871 to 2.9897)	0.7556 (0.4928 to 2.2669)	1.3470 (0.6242 to 2.0370)	0.9528 (0.4928 to 4.0411)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.1329		0.9206	
Hazard ratio (95% CI) vs Pd		1.2642 (0.9305 to 1.7177)		0.9791 (0.6463 to 1.4832)	
P-value		0.1338		0.9205	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.1.19.4 Treatment emergent mild adverse event by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.1922 (0.1188 to 0.2789)	0.1977 (0.1215 to 0.2875)	0.1381 (0.0562 to 0.2564)	0.1852 (0.0954 to 0.2981)	
4 Months	0.1130 (0.0582 to 0.1881)	0.1151 (0.0585 to 0.1928)	0.0552 (0.0106 to 0.1579)	0.1440 (0.0657 to 0.2519)	
6 Months	0.0879 (0.0403 to 0.1588)	0.1023 (0.0493 to 0.1778)	0.0552 (0.0106 to 0.1579)	0.0772 (0.0231 to 0.1751)	
8 Months	0.0754 (0.0319 to 0.1436)	0.0731 (0.0292 to 0.1443)	0.0552 (0.0106 to 0.1579)	0.0514 (0.0105 to 0.1446)	
10 Months	0.0628 (0.0241 to 0.1280)	0.0731 (0.0292 to 0.1443)	0.0552 (0.0106 to 0.1579)	0.0514 (0.0105 to 0.1446)	
12 Months	0.0628 (0.0241 to 0.1280)	0.0731 (0.0292 to 0.1443)	0.0552 (0.0106 to 0.1579)	0.0514 (0.0105 to 0.1446)	
14 Months	0.0628 (0.0241 to 0.1280)	0.0731 (0.0292 to 0.1443)	0.0552 (0.0106 to 0.1579)	0.0514 (0.0105 to 0.1446)	
16 Months	0.0628 (0.0241 to 0.1280)	0.0548 (0.0173 to 0.1250)	0.0552 (0.0106 to 0.1579)	0.0514 (0.0105 to 0.1446)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_crcl_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.1.19.4 Treatment emergent mild adverse event by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	17	17	5	10	
4 Months	10	9	2	7	
6 Months	7	7	1	3	
8 Months	6	5	1	2	
10 Months	4	5	1	2	
12 Months	4	4	0	2	
14 Months	4	4	0	2	
16 Months	1	2	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_crcl_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.1.19.5 Treatment emergent severe adverse event by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	61 (64.9)	74 (86.0)	37 (78.7)	48 (88.9)	0.2241
Number (%) of patients censored	33 (35.1)	12 (14.0)	10 (21.3)	6 (11.1)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.7556 (0.5257 to 0.9199)	0.5585 (0.4271 to 0.6571)	0.3943 (0.1643 to 0.5914)	0.3285 (0.2628 to 0.5257)	
Median (95% CI)	2.2669 (1.2813 to 4.9610)	0.8871 (0.7228 to 1.8398)	0.9856 (0.5257 to 2.0370)	0.7885 (0.5257 to 1.0185)	
75% quantile (95% CI)	NC (14.5544 to NC)	2.8912 (1.9713 to 6.9651)	4.6653 (1.5770 to NC)	3.9754 (1.0185 to 10.9076)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0010		0.3485	
Hazard ratio (95% CI) vs Pd		1.7683 (1.2553 to 2.4908)		1.2276 (0.7990 to 1.8862)	
P-value		0.0011		0.3493	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_crcl_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.1.19.5 Treatment emergent severe adverse event by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.5655 (0.4015 to 0.7966)				
probability (95% CI)[b]					
2 Months	0.5277 (0.4217 to 0.6230)	0.3412 (0.2428 to 0.4417)	0.3830 (0.2464 to 0.5181)	0.3148 (0.1970 to 0.4394)	
4 Months	0.4308 (0.3291 to 0.5283)	0.2100 (0.1307 to 0.3022)	0.2766 (0.1586 to 0.4078)	0.2407 (0.1372 to 0.3602)	
6 Months	0.3746 (0.2768 to 0.4722)	0.1729 (0.1010 to 0.2610)	0.2340 (0.1257 to 0.3616)	0.1852 (0.0954 to 0.2981)	
8 Months	0.3512 (0.2552 to 0.4485)	0.1359 (0.0728 to 0.2186)	0.2128 (0.1099 to 0.3380)	0.1667 (0.0821 to 0.2768)	
10 Months	0.3512 (0.2552 to 0.4485)	0.1359 (0.0728 to 0.2186)	0.2128 (0.1099 to 0.3380)	0.1481 (0.0693 to 0.2551)	
12 Months	0.3512 (0.2552 to 0.4485)	0.1359 (0.0728 to 0.2186)	0.2128 (0.1099 to 0.3380)	0.1270 (0.0546 to 0.2311)	
14 Months	0.3512 (0.2552 to 0.4485)	0.1359 (0.0728 to 0.2186)	0.2128 (0.1099 to 0.3380)	0.1016 (0.0372 to 0.2041)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_crcl_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.1.19.5 Treatment emergent severe adverse event by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3242 (0.2240 to 0.4283)	0.1359 (0.0728 to 0.2186)	0.2128 (0.1099 to 0.3380)	0.1016 (0.0372 to 0.2041)	
Number of patients at risk[b]					
2 Months	49	29	18	17	
4 Months	40	17	13	13	
6 Months	33	14	11	10	
8 Months	29	11	8	9	
10 Months	29	11	8	7	
12 Months	26	8	7	6	
14 Months	14	5	5	4	
16 Months	8	3	3	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_crcl_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.1.19.6 Treatment emergent severe adverse event including death by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	63 (67.0)	74 (86.0)	37 (78.7)	49 (90.7)	0.2917
Number (%) of patients censored	31 (33.0)	12 (14.0)	10 (21.3)	5 (9.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.7556 (0.5257 to 0.8871)	0.5585 (0.4271 to 0.6571)	0.2957 (0.1643 to 0.5914)	0.3285 (0.2628 to 0.5257)	
Median (95% CI)	2.1684 (1.2813 to 4.4682)	0.8871 (0.7228 to 1.8398)	0.9856 (0.5257 to 2.0370)	0.7885 (0.5257 to 1.0185)	
75% quantile (95% CI)	NC (7.6222 to NC)	2.8912 (1.9713 to 6.9651)	4.6653 (1.5770 to NC)	3.9754 (1.0185 to 9.1335)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0017		0.3094	
Hazard ratio (95% CI) vs Pd		1.7134 (1.2200 to 2.4065)		1.2477 (0.8136 to 1.9135)	
P-value		0.0019		0.3104	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_crcl_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.1.19.6 Treatment emergent severe adverse event including death by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.5836 (0.4155 to 0.8197)				
probability (95% CI)[b]					
2 Months	0.5213 (0.4160 to 0.6164)	0.3412 (0.2428 to 0.4417)	0.3830 (0.2464 to 0.5181)	0.3148 (0.1970 to 0.4394)	
4 Months	0.4255 (0.3247 to 0.5225)	0.2100 (0.1307 to 0.3022)	0.2766 (0.1586 to 0.4078)	0.2407 (0.1372 to 0.3602)	
6 Months	0.3601 (0.2642 to 0.4566)	0.1729 (0.1010 to 0.2610)	0.2340 (0.1257 to 0.3616)	0.1852 (0.0954 to 0.2981)	
8 Months	0.3376 (0.2438 to 0.4336)	0.1359 (0.0728 to 0.2186)	0.2128 (0.1099 to 0.3380)	0.1667 (0.0821 to 0.2768)	
10 Months	0.3376 (0.2438 to 0.4336)	0.1359 (0.0728 to 0.2186)	0.2128 (0.1099 to 0.3380)	0.1296 (0.0570 to 0.2330)	
12 Months	0.3376 (0.2438 to 0.4336)	0.1359 (0.0728 to 0.2186)	0.2128 (0.1099 to 0.3380)	0.1111 (0.0452 to 0.2104)	
14 Months	0.3376 (0.2438 to 0.4336)	0.1359 (0.0728 to 0.2186)	0.2128 (0.1099 to 0.3380)	0.0889 (0.0311 to 0.1849)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_crcl_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.1.19.6 Treatment emergent severe adverse event including death by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3116 (0.2142 to 0.4138)	0.1359 (0.0728 to 0.2186)	0.2128 (0.1099 to 0.3380)	0.0889 (0.0311 to 0.1849)	
Number of patients at risk[b]					
2 Months	49	29	18	17	
4 Months	40	17	13	13	
6 Months	33	14	11	10	
8 Months	29	11	8	9	
10 Months	29	11	8	7	
12 Months	26	8	7	6	
14 Months	14	5	5	4	
16 Months	8	3	3	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_crcl_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.1 Treatment emergent adverse event by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	2 (100.0)	144 (98.0)	149 (99.3)	0.3030
Number (%) of patients censored	0 (0.0)	0 (0.0)	3 (2.0)	1 (0.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.0657 (0.0657 to 0.1971)	0.0986 (0.0986 to 0.5257)	0.1314 (0.1314 to 0.1643)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.1314 (0.0657 to 0.1971)	0.3121 (0.0986 to 0.5257)	0.3285 (0.2957 to 0.4928)	0.1971 (0.1643 to 0.2300)	
75% quantile (95% CI)	0.1971 (0.0657 to 0.1971)	0.5257 (0.0986 to 0.5257)	0.8871 (0.7228 to 1.4127)	0.5585 (0.3943 to 0.7556)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.4328		0.0032	
Hazard ratio (95% CI) vs Pd		0.3904 (0.0343 to 4.4383)		1.4179 (1.1225 to 1.7910)	
P-value		0.4482		0.0034	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_prmab_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.1 Treatment emergent adverse event by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.7053 (0.5583 to 0.8908)		
probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.1127 (0.0674 to 0.1708)	0.0608 (0.0299 to 0.1072)	
4 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0493 (0.0218 to 0.0937)	0.0203 (0.0055 to 0.0537)	
6 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0411 (0.0164 to 0.0838)	0.0135 (0.0027 to 0.0439)	
8 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0329 (0.0115 to 0.0735)	0.0068 (0.0006 to 0.0340)	
10 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0246 (0.0071 to 0.0628)	0.0068 (0.0006 to 0.0340)	
12 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0164 (0.0034 to 0.0516)	0.0068 (0.0006 to 0.0340)	
14 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0164 (0.0034 to 0.0516)	0.0068 (0.0006 to 0.0340)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.1 Treatment emergent adverse event by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0164 (0.0034 to 0.0516)	0.0068 (0.0006 to 0.0340)	
Number of patients at risk[b]					
2 Months	0	0	16	9	
4 Months	0	0	7	3	
6 Months	0	0	5	2	
8 Months	0	0	4	1	
10 Months	0	0	3	1	
12 Months	0	0	2	0	
14 Months	0	0	2	0	
16 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.2 Treatment emergent serious adverse event by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (50.0)	1 (50.0)	79 (53.7)	93 (62.0)	0.5886
Number (%) of patients censored	1 (50.0)	1 (50.0)	68 (46.3)	57 (38.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.4271 (0.4271 to NC)	5.8152 (5.8152 to NC)	1.3799 (0.7556 to 1.9384)	0.7885 (0.4600 to 1.4127)	
Median (95% CI)	NC (0.4271 to NC)	NC (5.8152 to NC)	6.5708 (3.7782 to NC)	6.2752 (3.3183 to 9.9548)	
75% quantile (95% CI)	NC (0.4271 to NC)	NC (5.8152 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.8084		0.2331	
Hazard ratio (95% CI) vs Pd		0.7071 (0.0424 to 11.7865)		1.2001 (0.8885 to 1.6211)	
P-value		0.8092		0.2344	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.2 Treatment emergent serious adverse event by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.6803 (0.5983 to 0.7490)	0.6443 (0.5618 to 0.7153)	
4 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.5841 (0.4999 to 0.6590)	0.5561 (0.4726 to 0.6317)	
6 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.5132 (0.4292 to 0.5910)	0.5011 (0.4181 to 0.5784)	
8 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.4837 (0.4000 to 0.5623)	0.4733 (0.3909 to 0.5511)	
10 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.4837 (0.4000 to 0.5623)	0.4176 (0.3373 to 0.4958)	
12 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.4759 (0.3922 to 0.5548)	0.3745 (0.2963 to 0.4525)	
14 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.4579 (0.3741 to 0.5377)	0.3745 (0.2963 to 0.4525)	
16 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.4410 (0.3541 to 0.5243)	0.3745 (0.2963 to 0.4525)	
Number of patients at risk[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.2 Treatment emergent serious adverse event by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1	2	99	96	
4 Months	1	2	85	81	
6 Months	1	1	71	72	
8 Months	0	1	63	68	
10 Months	0	1	62	60	
12 Months	0	1	53	49	
14 Months	0	1	29	34	
16 Months	0	0	15	14	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	0 (0.0)	17 (11.6)	11 (7.3)	0.9888
Number (%) of patients censored	0 (0.0)	2 (100.0)	130 (88.4)	139 (92.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1643 (0.1643 to 0.4271)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	0.2957 (0.1643 to 0.4271)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	0.4271 (0.1643 to 0.4271)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0896		0.1704	
Hazard ratio (95% CI) vs Pd		NC (NC to NC)		0.5918 (0.2772 to 1.2636)	
P-value		0.9991		0.1753	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.9245 (0.8678 to 0.9575)	0.9933 (0.9533 to 0.9991)	
4 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.9174 (0.8591 to 0.9522)	0.9728 (0.9292 to 0.9897)	
6 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.8956 (0.8328 to 0.9358)	0.9515 (0.9010 to 0.9766)	
8 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.8874 (0.8226 to 0.9295)	0.9436 (0.8902 to 0.9714)	
10 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.8874 (0.8226 to 0.9295)	0.9352 (0.8790 to 0.9659)	
12 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.8874 (0.8226 to 0.9295)	0.9265 (0.8672 to 0.9599)	
14 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.8751 (0.8051 to 0.9212)	0.9265 (0.8672 to 0.9599)	
16 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.8751 (0.8051 to 0.9212)	0.8966 (0.7968 to 0.9489)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	0	2	133	146	
4 Months	0	2	127	137	
6 Months	0	2	113	124	
8 Months	0	2	103	118	
10 Months	0	2	99	111	
12 Months	0	2	85	98	
14 Months	0	2	52	66	
16 Months	0	0	24	28	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.4 Treatment emergent mild adverse event by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	2 (100.0)	135 (91.8)	139 (92.7)	0.3930
Number (%) of patients censored	0 (0.0)	0 (0.0)	12 (8.2)	11 (7.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.0657 (0.0657 to 0.1971)	0.0986 (0.0986 to 0.5257)	0.1643 (0.1314 to 0.2628)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.1314 (0.0657 to 0.1971)	0.3121 (0.0986 to 0.5257)	0.4928 (0.3285 to 0.7228)	0.2300 (0.1643 to 0.3285)	
75% quantile (95% CI)	0.1971 (0.0657 to 0.1971)	0.5257 (0.0986 to 0.5257)	1.4456 (0.9199 to 1.8727)	0.8214 (0.6571 to 2.0698)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.4328		0.1372	
Hazard ratio (95% CI) vs Pd		0.3904 (0.0343 to 4.4383)		1.1993 (0.9434 to 1.5247)	
P-value		0.4482		0.1377	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.4 Treatment emergent mild adverse event by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.1765 (0.1183 to 0.2442)	0.1879 (0.1299 to 0.2543)	
4 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0997 (0.0565 to 0.1573)	0.1231 (0.0759 to 0.1825)	
6 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0831 (0.0439 to 0.1380)	0.0904 (0.0498 to 0.1458)	
8 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0727 (0.0359 to 0.1268)	0.0633 (0.0297 to 0.1147)	
10 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0623 (0.0283 to 0.1152)	0.0633 (0.0297 to 0.1147)	
12 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0499 (0.0194 to 0.1023)	0.0633 (0.0297 to 0.1147)	
14 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0499 (0.0194 to 0.1023)	0.0633 (0.0297 to 0.1147)	
16 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.0499 (0.0194 to 0.1023)	0.0527 (0.0222 to 0.1030)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.4 Treatment emergent mild adverse event by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	0	0	23	27	
4 Months	0	0	13	16	
6 Months	0	0	8	10	
8 Months	0	0	7	7	
10 Months	0	0	5	7	
12 Months	0	0	4	6	
14 Months	0	0	4	6	
16 Months	0	0	1	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.5 Treatment emergent severe adverse event by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	1 (50.0)	101 (68.7)	128 (85.3)	0.0035
Number (%) of patients censored	0 (0.0)	1 (50.0)	46 (31.3)	22 (14.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1643 (0.1643 to 0.3285)	5.8152 (5.8152 to NC)	0.5914 (0.4600 to 0.7556)	0.5257 (0.3614 to 0.5585)	
Median (95% CI)	0.2464 (0.1643 to 0.3285)	NC (5.8152 to NC)	1.9384 (1.1170 to 2.9569)	0.8542 (0.7556 to 1.0185)	
75% quantile (95% CI)	0.3285 (0.1643 to 0.3285)	NC (5.8152 to NC)	NC (7.0308 to NC)	3.6468 (2.1027 to 6.1766)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0896		0.0008	
Hazard ratio (95% CI) vs Pd		NC (NC to NC)		1.5630 (1.2010 to 2.0341)	
P-value		0.9985		0.0009	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.5 Treatment emergent severe adverse event by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.6398 (0.4916 to 0.8327)		
probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.4834 (0.4000 to 0.5618)	0.3316 (0.2572 to 0.4077)	
4 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.3867 (0.3076 to 0.4650)	0.2215 (0.1582 to 0.2916)	
6 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3368 (0.2610 to 0.4142)	0.1850 (0.1265 to 0.2522)	
8 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3145 (0.2403 to 0.3913)	0.1554 (0.1016 to 0.2196)	
10 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3145 (0.2403 to 0.3913)	0.1480 (0.0955 to 0.2114)	
12 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3145 (0.2403 to 0.3913)	0.1398 (0.0886 to 0.2024)	
14 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3145 (0.2403 to 0.3913)	0.1281 (0.0780 to 0.1910)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.5 Treatment emergent severe adverse event by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2980 (0.2218 to 0.3778)	0.1281 (0.0780 to 0.1910)	
Number of patients at risk[b]					
2 Months	0	2	70	49	
4 Months	0	2	56	31	
6 Months	0	1	47	25	
8 Months	0	1	40	21	
10 Months	0	1	40	19	
12 Months	0	1	34	15	
14 Months	0	1	20	10	
16 Months	0	0	12	3	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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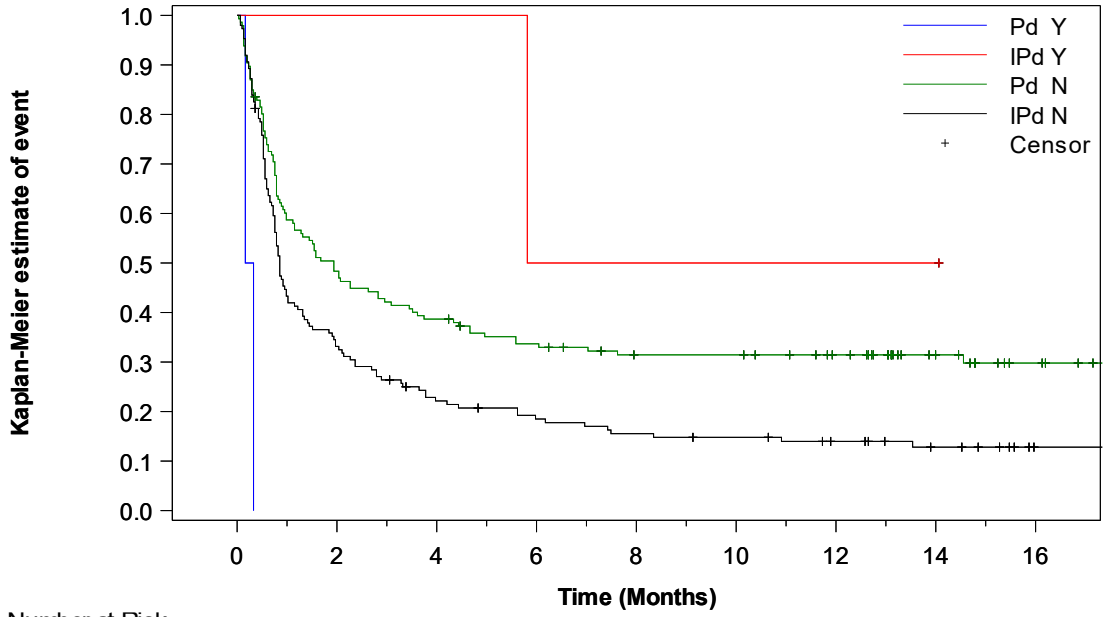
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.6 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event by treatment group according to previous therapy with anti-CD38 mAB - Safety population



Number at Risk

Pd Y	2	0	0	0	0	0	0	0	0
IPd Y	2	2	2	1	1	1	1	1	0
Pd N	146	70	56	47	40	40	34	20	12
IPd N	149	49	31	25	21	19	15	10	3

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.7 Treatment emergent severe adverse event including death by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (100.0)	1 (50.0)	103 (70.1)	131 (87.3)	0.0035
Number (%) of patients censored	0 (0.0)	1 (50.0)	44 (29.9)	19 (12.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1643 (0.1643 to 0.3285)	5.8152 (5.8152 to NC)	0.5585 (0.3614 to 0.7556)	0.5257 (0.3285 to 0.5585)	
Median (95% CI)	0.2464 (0.1643 to 0.3285)	NC (5.8152 to NC)	1.8070 (0.9856 to 2.9569)	0.8542 (0.7556 to 1.0185)	
75% quantile (95% CI)	0.3285 (0.1643 to 0.3285)	NC (5.8152 to NC)	NC (6.0452 to NC)	3.2854 (1.9713 to 5.9795)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0896		0.0006	
Hazard ratio (95% CI) vs Pd		NC (NC to NC)		1.5762 (1.2145 to 2.0457)	
P-value		0.9985		0.0006	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.7 Treatment emergent severe adverse event including death by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.6344 (0.4888 to 0.8234)		
probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.4795 (0.3965 to 0.5576)	0.3221 (0.2487 to 0.3976)	
4 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.3836 (0.3049 to 0.4615)	0.2137 (0.1518 to 0.2827)	
6 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3278 (0.2530 to 0.4044)	0.1785 (0.1215 to 0.2444)	
8 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3060 (0.2330 to 0.3820)	0.1499 (0.0976 to 0.2127)	
10 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3060 (0.2330 to 0.3820)	0.1356 (0.0859 to 0.1967)	
12 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3060 (0.2330 to 0.3820)	0.1281 (0.0798 to 0.1882)	
14 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3060 (0.2330 to 0.3820)	0.1174 (0.0704 to 0.1775)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.7 Treatment emergent severe adverse event including death by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2899 (0.2151 to 0.3687)	0.1174 (0.0704 to 0.1775)	
Number of patients at risk[b]					
2 Months	0	2	70	48	
4 Months	0	2	56	31	
6 Months	0	1	47	25	
8 Months	0	1	40	21	
10 Months	0	1	40	19	
12 Months	0	1	34	15	
14 Months	0	1	20	10	
16 Months	0	0	12	3	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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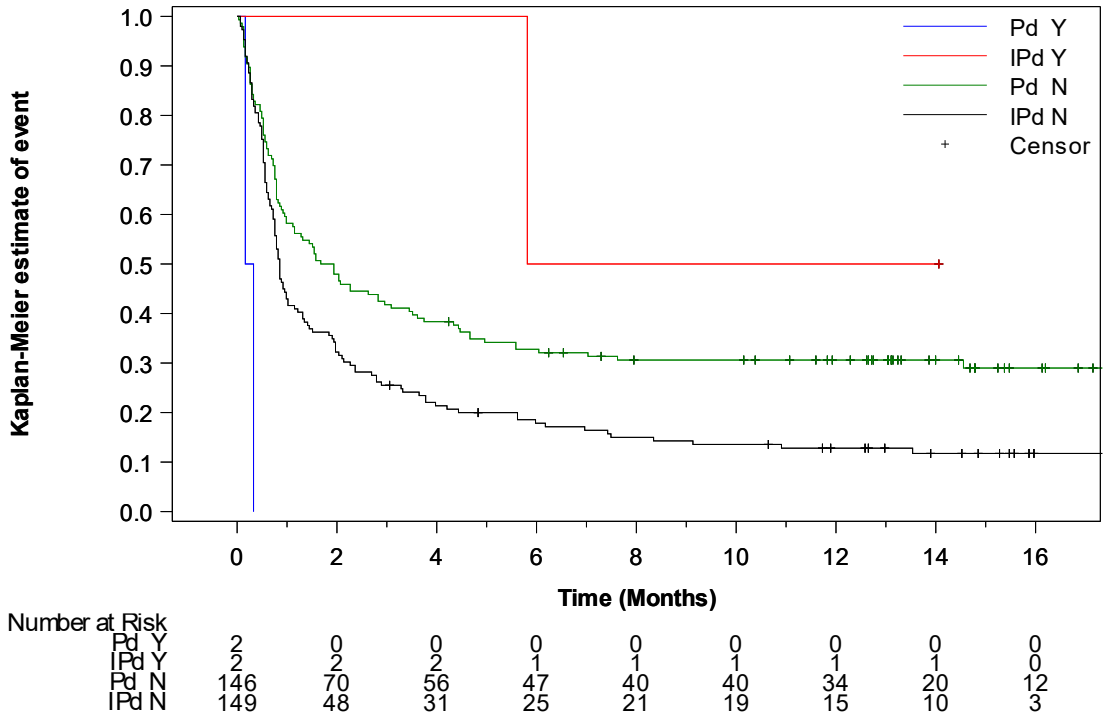
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.1.20.8 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death by treatment group according to previous therapy with anti-CD38 mAB - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.21 Subgroup analyses by refractory to PI status
16.2.7.1.1.21.1 Treatment emergent adverse event by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	109 (98.2)	116 (99.1)	37 (97.4)	35 (100.0)	0.1428
Number (%) of patients censored	2 (1.8)	1 (0.9)	1 (2.6)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0986 to 0.1643)	0.0986 (0.0657 to 0.1314)	0.1971 (0.0986 to 0.2628)	0.0657 (0.0329 to 0.0986)	
Median (95% CI)	0.3285 (0.2300 to 0.4600)	0.1971 (0.1643 to 0.2628)	0.3943 (0.1971 to 0.8871)	0.1643 (0.0986 to 0.2628)	
75% quantile (95% CI)	0.8214 (0.5585 to 1.1170)	0.6078 (0.4271 to 0.7885)	1.1663 (0.8214 to 2.4312)	0.4600 (0.1971 to 0.5585)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0711		0.0095	
Hazard ratio (95% CI) vs Pd		1.2758 (0.9787 to 1.6632)		1.8845 (1.1593 to 3.0636)	
P-value		0.0717		0.0106	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.21 Subgroup analyses by refractory to PI status
16.2.7.1.1.21.1 Treatment emergent adverse event by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.5306 (0.3264 to 0.8626)		
probability (95% CI)[b]					
2 Months	0.0926 (0.0474 to 0.1562)	0.0603 (0.0266 to 0.1137)	0.1667 (0.0676 to 0.3036)	0.0588 (0.0105 to 0.1716)	
4 Months	0.0463 (0.0173 to 0.0977)	0.0172 (0.0034 to 0.0553)	0.0556 (0.0100 to 0.1630)	0.0294 (0.0022 to 0.1301)	
6 Months	0.0347 (0.0105 to 0.0841)	0.0172 (0.0034 to 0.0553)	0.0556 (0.0100 to 0.1630)	0.0294 (0.0022 to 0.1301)	
8 Months	0.0347 (0.0105 to 0.0841)	0.0086 (0.0008 to 0.0427)	0.0278 (0.0021 to 0.1237)	0.0294 (0.0022 to 0.1301)	
10 Months	0.0231 (0.0049 to 0.0696)	0.0086 (0.0008 to 0.0427)	0.0278 (0.0021 to 0.1237)	0.0294 (0.0022 to 0.1301)	
12 Months	0.0116 (0.0011 to 0.0544)	0.0086 (0.0008 to 0.0427)	0.0278 (0.0021 to 0.1237)	0.0294 (0.0022 to 0.1301)	
14 Months	0.0116 (0.0011 to 0.0544)	0.0086 (0.0008 to 0.0427)	0.0278 (0.0021 to 0.1237)	0.0294 (0.0022 to 0.1301)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.21 Subgroup analyses by refractory to PI status
16.2.7.1.1.21.1 Treatment emergent adverse event by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0116 (0.0011 to 0.0544)	0.0086 (0.0008 to 0.0427)	0.0278 (0.0021 to 0.1237)	0.0294 (0.0022 to 0.1301)	
Number of patients at risk[b]					
2 Months	10	7	6	2	
4 Months	5	2	2	1	
6 Months	3	2	2	0	
8 Months	3	1	1	0	
10 Months	2	1	1	0	
12 Months	1	0	1	0	
14 Months	1	0	1	0	
16 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.21 Subgroup analyses by refractory to PI status
16.2.7.1.1.21.2 Treatment emergent serious adverse event by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	64 (57.7)	70 (59.8)	16 (42.1)	24 (68.6)	0.0914
Number (%) of patients censored	47 (42.3)	47 (40.2)	22 (57.9)	11 (31.4)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.2813 (0.5914 to 1.7741)	0.7885 (0.3614 to 1.5770)	2.2998 (0.1971 to 5.1910)	1.2813 (0.4600 to 1.9713)	
Median (95% CI)	5.5852 (2.9569 to 12.1889)	6.7351 (3.3183 to 11.1376)	NC (3.4497 to NC)	4.1725 (1.4127 to 9.9548)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.6078 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.8931		0.0423	
Hazard ratio (95% CI) vs Pd		1.0236 (0.7282 to 1.4388)		1.9103 (1.0119 to 3.6062)	
P-value		0.8931		0.0459	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_refr4_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.21 Subgroup analyses by refractory to PI status
16.2.7.1.1.21.2 Treatment emergent serious adverse event by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.5235 (0.2773 to 0.9882)		
probability (95% CI)[b]					
2 Months	0.6486 (0.5522 to 0.7294)	0.6638 (0.5700 to 0.7417)	0.7632 (0.5942 to 0.8690)	0.6000 (0.4200 to 0.7402)	
4 Months	0.5573 (0.4598 to 0.6440)	0.5772 (0.4820 to 0.6611)	0.6579 (0.4848 to 0.7849)	0.5113 (0.3362 to 0.6618)	
6 Months	0.4817 (0.3855 to 0.5715)	0.5157 (0.4211 to 0.6023)	0.6041 (0.4313 to 0.7393)	0.4511 (0.2821 to 0.6061)	
8 Months	0.4415 (0.3464 to 0.5324)	0.4890 (0.3950 to 0.5764)	0.6041 (0.4313 to 0.7393)	0.4211 (0.2560 to 0.5775)	
10 Months	0.4415 (0.3464 to 0.5324)	0.4446 (0.3523 to 0.5327)	0.6041 (0.4313 to 0.7393)	0.3308 (0.1817 to 0.4880)	
12 Months	0.4308 (0.3359 to 0.5220)	0.3984 (0.3084 to 0.4869)	0.6041 (0.4313 to 0.7393)	0.3008 (0.1583 to 0.4569)	
14 Months	0.4054 (0.3105 to 0.4981)	0.3984 (0.3084 to 0.4869)	0.6041 (0.4313 to 0.7393)	0.3008 (0.1583 to 0.4569)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.21 Subgroup analyses by refractory to PI status
16.2.7.1.1.21.2 Treatment emergent serious adverse event by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.4054 (0.3105 to 0.4981)	0.3984 (0.3084 to 0.4869)	0.5437 (0.3506 to 0.7017)	0.3008 (0.1583 to 0.4569)	
Number of patients at risk[b]					
2 Months	71	77	29	21	
4 Months	61	66	25	17	
6 Months	50	58	22	15	
8 Months	42	55	21	14	
10 Months	41	50	21	11	
12 Months	34	41	19	9	
14 Months	19	29	10	6	
16 Months	9	13	6	1	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesae_refr4_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.21 Subgroup analyses by refractory to PI status
16.2.7.1.1.21.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (12.6)	9 (7.7)	5 (13.2)	2 (5.7)	0.7617
Number (%) of patients censored	97 (87.4)	108 (92.3)	33 (86.8)	33 (94.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.3326 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.1635		0.2711	
Hazard ratio (95% CI) vs Pd		0.5558 (0.2404 to 1.2848)		0.4103 (0.0796 to 2.1147)	
P-value		0.1695		0.2869	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tedisc_refr4_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.21 Subgroup analyses by refractory to PI status
16.2.7.1.1.21.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9094 (0.8381 to 0.9502)	1.0000 (1.0000 to 1.0000)	0.9189 (0.7693 to 0.9731)	0.9714 (0.8140 to 0.9959)	
4 Months	0.9094 (0.8381 to 0.9502)	0.9826 (0.9323 to 0.9956)	0.8919 (0.7371 to 0.9580)	0.9420 (0.7873 to 0.9852)	
6 Months	0.8805 (0.8029 to 0.9288)	0.9553 (0.8959 to 0.9812)	0.8919 (0.7371 to 0.9580)	0.9420 (0.7873 to 0.9852)	
8 Months	0.8805 (0.8029 to 0.9288)	0.9452 (0.8818 to 0.9750)	0.8611 (0.6973 to 0.9399)	0.9420 (0.7873 to 0.9852)	
10 Months	0.8805 (0.8029 to 0.9288)	0.9343 (0.8667 to 0.9682)	0.8611 (0.6973 to 0.9399)	0.9420 (0.7873 to 0.9852)	
12 Months	0.8805 (0.8029 to 0.9288)	0.9230 (0.8513 to 0.9609)	0.8611 (0.6973 to 0.9399)	0.9420 (0.7873 to 0.9852)	
14 Months	0.8632 (0.7769 to 0.9179)	0.9230 (0.8513 to 0.9609)	0.8611 (0.6973 to 0.9399)	0.9420 (0.7873 to 0.9852)	
16 Months	0.8632 (0.7769 to 0.9179)	0.8875 (0.7675 to 0.9476)	0.8611 (0.6973 to 0.9399)	0.9420 (0.7873 to 0.9852)	
Number of patients at risk[b]					
2 Months	99	115	34	33	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.21 Subgroup analyses by refractory to PI status
16.2.7.1.1.21.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	95	108	32	31	
6 Months	83	97	30	29	
8 Months	77	92	26	28	
10 Months	73	85	26	28	
12 Months	61	76	24	24	
14 Months	38	53	14	15	
16 Months	16	24	8	4	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.21 Subgroup analyses by refractory to PI status
16.2.7.1.1.21.4 Treatment emergent mild adverse event by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	103 (92.8)	109 (93.2)	34 (89.5)	32 (91.4)	0.1238
Number (%) of patients censored	8 (7.2)	8 (6.8)	4 (10.5)	3 (8.6)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0986 to 0.2300)	0.1314 (0.0657 to 0.1314)	0.2628 (0.1314 to 0.3943)	0.0986 (0.0329 to 0.1643)	
Median (95% CI)	0.3943 (0.3285 to 0.5914)	0.2300 (0.1643 to 0.3614)	0.8871 (0.3285 to 1.3470)	0.1971 (0.0986 to 0.3943)	
75% quantile (95% CI)	1.0513 (0.8214 to 1.8398)	0.8214 (0.6571 to 2.0698)	2.0370 (0.9856 to 4.8624)	0.7228 (0.2628 to 3.8439)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.5955		0.0469	
Hazard ratio (95% CI) vs Pd		1.0767 (0.8195 to 1.4146)		1.6502 (1.0020 to 2.7179)	
P-value		0.5958		0.0491	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.21 Subgroup analyses by refractory to PI status
16.2.7.1.1.21.4 Treatment emergent mild adverse event by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.6060 (0.3679 to 0.9980)		
probability (95% CI)[b]					
2 Months	0.1467 (0.0870 to 0.2212)	0.1795 (0.1162 to 0.2539)	0.2548 (0.1274 to 0.4037)	0.2059 (0.0907 to 0.3532)	
4 Months	0.0838 (0.0400 to 0.1482)	0.1276 (0.0748 to 0.1951)	0.1416 (0.0519 to 0.2748)	0.0915 (0.0199 to 0.2325)	
6 Months	0.0719 (0.0316 to 0.1344)	0.0995 (0.0532 to 0.1627)	0.1133 (0.0360 to 0.2400)	0.0915 (0.0199 to 0.2325)	
8 Months	0.0719 (0.0316 to 0.1344)	0.0696 (0.0318 to 0.1275)	0.0755 (0.0159 to 0.1997)	0.0915 (0.0199 to 0.2325)	
10 Months	0.0575 (0.0217 to 0.1189)	0.0696 (0.0318 to 0.1275)	0.0755 (0.0159 to 0.1997)	0.0915 (0.0199 to 0.2325)	
12 Months	0.0383 (0.0095 to 0.1016)	0.0696 (0.0318 to 0.1275)	0.0755 (0.0159 to 0.1997)	0.0915 (0.0199 to 0.2325)	
14 Months	0.0383 (0.0095 to 0.1016)	0.0696 (0.0318 to 0.1275)	0.0755 (0.0159 to 0.1997)	0.0915 (0.0199 to 0.2325)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.21 Subgroup analyses by refractory to PI status
16.2.7.1.1.21.4 Treatment emergent mild adverse event by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0383 (0.0095 to 0.1016)	0.0580 (0.0238 to 0.1142)	0.0755 (0.0159 to 0.1997)	0.0915 (0.0199 to 0.2325)	
Number of patients at risk[b]					
2 Months	14	21	9	6	
4 Months	8	14	5	2	
6 Months	5	10	3	0	
8 Months	5	7	2	0	
10 Months	3	7	2	0	
12 Months	2	6	2	0	
14 Months	2	6	2	0	
16 Months	0	2	1	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.21 Subgroup analyses by refractory to PI status
16.2.7.1.1.21.5 Treatment emergent severe adverse event by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	78 (70.3)	101 (86.3)	25 (65.8)	28 (80.0)	0.6967
Number (%) of patients censored	33 (29.7)	16 (13.7)	13 (34.2)	7 (20.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.5585 (0.3285 to 0.7556)	0.5257 (0.2957 to 0.5914)	0.5257 (0.1971 to 1.4456)	0.5257 (0.2957 to 0.6899)	
Median (95% CI)	1.5441 (0.9199 to 2.2669)	0.8542 (0.7556 to 1.1499)	4.3368 (0.7885 to 14.5544)	0.7885 (0.5585 to 1.9713)	
75% quantile (95% CI)	NC (4.6653 to NC)	3.7782 (2.0370 to 6.1766)	NC (5.5852 to NC)	3.6468 (1.3142 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0126		0.0954	
Hazard ratio (95% CI) vs Pd		1.4560 (1.0819 to 1.9595)		1.5932 (0.9173 to 2.7672)	
P-value		0.0132		0.0982	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.21 Subgroup analyses by refractory to PI status
16.2.7.1.1.21.5 Treatment emergent severe adverse event by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6868 (0.5103 to 0.9243)				
probability (95% CI)[b]					
2 Months	0.4463 (0.3520 to 0.5362)	0.3399 (0.2550 to 0.4265)	0.5676 (0.3943 to 0.7084)	0.3429 (0.1934 to 0.4979)	
4 Months	0.3370 (0.2505 to 0.4254)	0.2339 (0.1611 to 0.3148)	0.5135 (0.3441 to 0.6595)	0.2250 (0.1041 to 0.3739)	
6 Months	0.3081 (0.2243 to 0.3957)	0.1784 (0.1141 to 0.2543)	0.4054 (0.2488 to 0.5565)	0.2250 (0.1041 to 0.3739)	
8 Months	0.2882 (0.2063 to 0.3751)	0.1502 (0.0913 to 0.2229)	0.3764 (0.2240 to 0.5284)	0.1929 (0.0817 to 0.3390)	
10 Months	0.2882 (0.2063 to 0.3751)	0.1408 (0.0838 to 0.2122)	0.3764 (0.2240 to 0.5284)	0.1929 (0.0817 to 0.3390)	
12 Months	0.2882 (0.2063 to 0.3751)	0.1300 (0.0751 to 0.2003)	0.3764 (0.2240 to 0.5284)	0.1929 (0.0817 to 0.3390)	
14 Months	0.2882 (0.2063 to 0.3751)	0.1155 (0.0627 to 0.1860)	0.3764 (0.2240 to 0.5284)	0.1929 (0.0817 to 0.3390)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_refr4_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.21 Subgroup analyses by refractory to PI status
16.2.7.1.1.21.5 Treatment emergent severe adverse event by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.2882 (0.2063 to 0.3751)	0.1155 (0.0627 to 0.1860)	0.3012 (0.1372 to 0.4842)	0.1929 (0.0817 to 0.3390)	
Number of patients at risk[b]					
2 Months	49	39	21	12	
4 Months	37	26	19	7	
6 Months	32	19	15	7	
8 Months	28	16	12	6	
10 Months	28	14	12	6	
12 Months	24	11	10	5	
14 Months	15	7	5	4	
16 Months	9	3	3	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_refr4_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.21 Subgroup analyses by refractory to PI status
16.2.7.1.1.21.6 Treatment emergent severe adverse event including death by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	80 (72.1)	103 (88.0)	25 (65.8)	29 (82.9)	0.5817
Number (%) of patients censored	31 (27.9)	14 (12.0)	13 (34.2)	6 (17.1)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.5585 (0.3285 to 0.7556)	0.5092 (0.2957 to 0.5914)	0.5257 (0.1971 to 1.4456)	0.5257 (0.2957 to 0.6899)	
Median (95% CI)	1.5441 (0.8871 to 2.2669)	0.8542 (0.7556 to 1.1499)	4.3368 (0.7885 to 14.5544)	0.7885 (0.5585 to 1.9713)	
75% quantile (95% CI)	NC (3.7454 to NC)	3.7782 (2.0370 to 6.1766)	NC (5.5852 to NC)	2.6940 (1.3142 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0123		0.0640	
Hazard ratio (95% CI) vs Pd		1.4521 (1.0826 to 1.9477)		1.6696 (0.9652 to 2.8879)	
P-value		0.0128		0.0667	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_refr4_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.21 Subgroup analyses by refractory to PI status
16.2.7.1.1.21.6 Treatment emergent severe adverse event including death by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6887 (0.5134 to 0.9237)				
probability (95% CI)[b]					
2 Months	0.4414 (0.3478 to 0.5310)	0.3362 (0.2520 to 0.4223)	0.5676 (0.3943 to 0.7084)	0.3143 (0.1709 to 0.4684)	
4 Months	0.3333 (0.2476 to 0.4212)	0.2314 (0.1592 to 0.3116)	0.5135 (0.3441 to 0.6595)	0.2000 (0.0881 to 0.3443)	
6 Months	0.2963 (0.2143 to 0.3827)	0.1764 (0.1128 to 0.2517)	0.4054 (0.2488 to 0.5565)	0.2000 (0.0881 to 0.3443)	
8 Months	0.2771 (0.1972 to 0.3627)	0.1486 (0.0902 to 0.2206)	0.3764 (0.2240 to 0.5284)	0.1714 (0.0696 to 0.3113)	
10 Months	0.2771 (0.1972 to 0.3627)	0.1300 (0.0757 to 0.1994)	0.3764 (0.2240 to 0.5284)	0.1714 (0.0696 to 0.3113)	
12 Months	0.2771 (0.1972 to 0.3627)	0.1200 (0.0678 to 0.1881)	0.3764 (0.2240 to 0.5284)	0.1714 (0.0696 to 0.3113)	
14 Months	0.2771 (0.1972 to 0.3627)	0.1067 (0.0568 to 0.1744)	0.3764 (0.2240 to 0.5284)	0.1714 (0.0696 to 0.3113)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.21 Subgroup analyses by refractory to PI status
16.2.7.1.1.21.6 Treatment emergent severe adverse event including death by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.2771 (0.1972 to 0.3627)	0.1067 (0.0568 to 0.1744)	0.3012 (0.1372 to 0.4842)	0.1714 (0.0696 to 0.3113)	
Number of patients at risk[b]					
2 Months	49	39	21	11	
4 Months	37	26	19	7	
6 Months	32	19	15	7	
8 Months	28	16	12	6	
10 Months	28	14	12	6	
12 Months	24	11	10	5	
14 Months	15	7	5	4	
16 Months	9	3	3	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.22 Subgroup analyses by refractory to IMID status
16.2.7.1.1.22.1 Treatment emergent adverse event by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	137 (97.9)	144 (99.3)	9 (100.0)	7 (100.0)	0.8011
Number (%) of patients censored	3 (2.1)	1 (0.7)	0 (0.0)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0986 to 0.1643)	0.0986 (0.0657 to 0.1314)	0.1971 (0.0329 to 0.3285)	0.1314 (0.0329 to 0.4928)	
Median (95% CI)	0.3285 (0.2628 to 0.4928)	0.1971 (0.1643 to 0.2300)	0.3285 (0.0329 to 1.7741)	0.4928 (0.0329 to 0.7228)	
75% quantile (95% CI)	0.8871 (0.6899 to 1.3470)	0.5257 (0.3614 to 0.7556)	0.9856 (0.2300 to 8.1807)	0.7228 (0.2628 to 0.7556)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0070		0.2382	
Hazard ratio (95% CI) vs Pd		1.3860 (1.0921 to 1.7589)		1.9910 (0.6208 to 6.3856)	
P-value		0.0073		0.2468	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_refr1_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.22 Subgroup analyses by refractory to IMID status
16.2.7.1.1.22.1 Treatment emergent adverse event by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.7215 (0.5685 to 0.9157)				
probability (95% CI)[b]					
2 Months	0.1111 (0.0652 to 0.1706)	0.0629 (0.0309 to 0.1108)	0.1111 (0.0061 to 0.3877)	0.1429 (0.0071 to 0.4649)	
4 Months	0.0444 (0.0183 to 0.0888)	0.0210 (0.0057 to 0.0555)	0.1111 (0.0061 to 0.3877)	0.1429 (0.0071 to 0.4649)	
6 Months	0.0356 (0.0127 to 0.0780)	0.0140 (0.0028 to 0.0454)	0.1111 (0.0061 to 0.3877)	0.1429 (0.0071 to 0.4649)	
8 Months	0.0267 (0.0078 to 0.0669)	0.0070 (0.0006 to 0.0351)	0.1111 (0.0061 to 0.3877)	0.1429 (0.0071 to 0.4649)	
10 Months	0.0267 (0.0078 to 0.0669)	0.0070 (0.0006 to 0.0351)	0.1111 (0.0061 to 0.3877)	0.1429 (0.0071 to 0.4649)	
12 Months	0.0178 (0.0037 to 0.0551)	0.0070 (0.0006 to 0.0351)	0.1111 (0.0061 to 0.3877)	0.1429 (0.0071 to 0.4649)	
14 Months	0.0178 (0.0037 to 0.0551)	0.0070 (0.0006 to 0.0351)	0.1111 (0.0061 to 0.3877)	0.1429 (0.0071 to 0.4649)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.22 Subgroup analyses by refractory to IMID status
16.2.7.1.1.22.1 Treatment emergent adverse event by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0178 (0.0037 to 0.0551)	0.0070 (0.0006 to 0.0351)	0.1111 (0.0061 to 0.3877)	0.1429 (0.0071 to 0.4649)	
Number of patients at risk[b]					
2 Months	15	9	1	0	
4 Months	6	3	1	0	
6 Months	4	2	1	0	
8 Months	3	1	1	0	
10 Months	3	1	0	0	
12 Months	2	0	0	0	
14 Months	2	0	0	0	
16 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.22 Subgroup analyses by refractory to IMID status
16.2.7.1.1.22.2 Treatment emergent serious adverse event by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	75 (53.6)	89 (61.4)	5 (55.6)	5 (71.4)	0.6609
Number (%) of patients censored	65 (46.4)	56 (38.6)	4 (44.4)	2 (28.6)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.3470 (0.7228 to 1.9384)	0.8049 (0.4928 to 1.4127)	3.6140 (0.1971 to 10.0862)	0.2628 (0.1314 to 4.3039)	
Median (95% CI)	6.5708 (3.5154 to NC)	6.2752 (3.3183 to 10.5462)	10.0862 (0.1971 to NC)	4.3039 (0.1314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.4209 to NC)	NC (2.3655 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.3130		0.4427	
Hazard ratio (95% CI) vs Pd		1.1713 (0.8607 to 1.5939)		1.6211 (0.4667 to 5.6307)	
P-value		0.3145		0.4470	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.22 Subgroup analyses by refractory to IMID status
16.2.7.1.1.22.2 Treatment emergent serious adverse event by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.6714 (0.5869 to 0.7424)	0.6458 (0.5618 to 0.7178)	0.7778 (0.3648 to 0.9393)	0.7143 (0.2582 to 0.9198)	
4 Months	0.5776 (0.4912 to 0.6545)	0.5615 (0.4764 to 0.6381)	0.6667 (0.2817 to 0.8783)	0.5714 (0.1719 to 0.8371)	
6 Months	0.5106 (0.4245 to 0.5902)	0.5045 (0.4199 to 0.5830)	0.5556 (0.2042 to 0.8045)	0.4286 (0.0978 to 0.7344)	
8 Months	0.4792 (0.3934 to 0.5598)	0.4756 (0.3917 to 0.5548)	0.5556 (0.2042 to 0.8045)	0.4286 (0.0978 to 0.7344)	
10 Months	0.4792 (0.3934 to 0.5598)	0.4252 (0.3431 to 0.5048)	0.5556 (0.2042 to 0.8045)	0.2857 (0.0411 to 0.6115)	
12 Months	0.4792 (0.3934 to 0.5598)	0.3806 (0.3006 to 0.4600)	0.4444 (0.1359 to 0.7193)	0.2857 (0.0411 to 0.6115)	
14 Months	0.4596 (0.3734 to 0.5414)	0.3806 (0.3006 to 0.4600)	0.4444 (0.1359 to 0.7193)	0.2857 (0.0411 to 0.6115)	
16 Months	0.4405 (0.3503 to 0.5268)	0.3806 (0.3006 to 0.4600)	0.4444 (0.1359 to 0.7193)	0.2857 (0.0411 to 0.6115)	
Number of patients at risk[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.22 Subgroup analyses by refractory to IMID status
16.2.7.1.1.22.2 Treatment emergent serious adverse event by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	93	93	7	5	
4 Months	80	79	6	4	
6 Months	67	70	5	3	
8 Months	58	66	5	3	
10 Months	57	59	5	2	
12 Months	49	48	4	2	
14 Months	26	34	3	1	
16 Months	13	14	2	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.22 Subgroup analyses by refractory to IMID status
16.2.7.1.1.22.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (13.6)	11 (7.6)	0 (0.0)	0 (0.0)	0.9997
Number (%) of patients censored	121 (86.4)	134 (92.4)	9 (100.0)	7 (100.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0719			
Hazard ratio (95% CI) vs Pd		0.5119 (0.2435 to 1.0759)		NC (NC to NC)	
P-value		0.0773			
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.22 Subgroup analyses by refractory to IMID status
16.2.7.1.1.22.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9063 (0.8441 to 0.9445)	0.9931 (0.9517 to 0.9990)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
4 Months	0.8989 (0.8352 to 0.9388)	0.9719 (0.9268 to 0.9894)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
6 Months	0.8759 (0.8079 to 0.9210)	0.9498 (0.8975 to 0.9758)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
8 Months	0.8671 (0.7972 to 0.9142)	0.9416 (0.8865 to 0.9704)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
10 Months	0.8671 (0.7972 to 0.9142)	0.9330 (0.8750 to 0.9647)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
12 Months	0.8671 (0.7972 to 0.9142)	0.9241 (0.8630 to 0.9586)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
14 Months	0.8540 (0.7788 to 0.9052)	0.9241 (0.8630 to 0.9586)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
16 Months	0.8540 (0.7788 to 0.9052)	0.8933 (0.7907 to 0.9472)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
Number of patients at risk[b]					
2 Months	124	141	9	7	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.22 Subgroup analyses by refractory to IMID status
16.2.7.1.1.22.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	118	132	9	7	
6 Months	104	119	9	7	
8 Months	94	115	9	5	
10 Months	90	108	9	5	
12 Months	77	95	8	5	
14 Months	47	65	5	3	
16 Months	22	28	2	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.22 Subgroup analyses by refractory to IMID status
16.2.7.1.1.22.4 Treatment emergent mild adverse event by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	128 (91.4)	134 (92.4)	9 (100.0)	7 (100.0)	0.9069
Number (%) of patients censored	12 (8.6)	11 (7.6)	0 (0.0)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1643 (0.1314 to 0.2628)	0.0986 (0.0657 to 0.1314)	0.2300 (0.0329 to 0.3285)	0.2628 (0.0329 to 0.5585)	
Median (95% CI)	0.4928 (0.3285 to 0.7228)	0.2136 (0.1643 to 0.2957)	0.3285 (0.0329 to 1.7741)	0.5585 (0.0329 to 0.7556)	
75% quantile (95% CI)	1.4456 (0.8871 to 1.8727)	0.8378 (0.5914 to 2.1684)	0.9856 (0.2628 to 8.1807)	0.7556 (0.4928 to 0.7556)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.1666		0.3541	
Hazard ratio (95% CI) vs Pd		1.1896 (0.9303 to 1.5211)		1.7178 (0.5398 to 5.4665)	
P-value		0.1663		0.3596	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_refr1_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.22 Subgroup analyses by refractory to IMID status
16.2.7.1.1.22.4 Treatment emergent mild adverse event by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.1783 (0.1185 to 0.2481)	0.1944 (0.1345 to 0.2627)	0.1111 (0.0061 to 0.3877)	0.2857 (0.0411 to 0.6115)	
4 Months	0.0973 (0.0537 to 0.1562)	0.1274 (0.0786 to 0.1885)	0.1111 (0.0061 to 0.3877)	0.2857 (0.0411 to 0.6115)	
6 Months	0.0796 (0.0405 to 0.1356)	0.0936 (0.0516 to 0.1506)	0.1111 (0.0061 to 0.3877)	0.2857 (0.0411 to 0.6115)	
8 Months	0.0682 (0.0319 to 0.1234)	0.0655 (0.0307 to 0.1185)	0.1111 (0.0061 to 0.3877)	0.2857 (0.0411 to 0.6115)	
10 Months	0.0682 (0.0319 to 0.1234)	0.0655 (0.0307 to 0.1185)	0.1111 (0.0061 to 0.3877)	0.2857 (0.0411 to 0.6115)	
12 Months	0.0546 (0.0217 to 0.1099)	0.0655 (0.0307 to 0.1185)	0.1111 (0.0061 to 0.3877)	0.2857 (0.0411 to 0.6115)	
14 Months	0.0546 (0.0217 to 0.1099)	0.0655 (0.0307 to 0.1185)	0.1111 (0.0061 to 0.3877)	0.2857 (0.0411 to 0.6115)	
16 Months	0.0546 (0.0217 to 0.1099)	0.0546 (0.0229 to 0.1064)	0.1111 (0.0061 to 0.3877)	0.2857 (0.0411 to 0.6115)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev12_refr1_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.22 Subgroup analyses by refractory to IMID status
16.2.7.1.1.22.4 Treatment emergent mild adverse event by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	22	27	1	0	
4 Months	12	16	1	0	
6 Months	7	10	1	0	
8 Months	6	7	1	0	
10 Months	5	7	0	0	
12 Months	4	6	0	0	
14 Months	4	6	0	0	
16 Months	1	2	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.22 Subgroup analyses by refractory to IMID status
16.2.7.1.1.22.5 Treatment emergent severe adverse event by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	96 (68.6)	123 (84.8)	7 (77.8)	6 (85.7)	0.9798
Number (%) of patients censored	44 (31.4)	22 (15.2)	2 (22.2)	1 (14.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.5585 (0.3285 to 0.7556)	0.5257 (0.3614 to 0.5585)	0.5914 (0.1971 to 0.9856)	0.2628 (0.1314 to 0.7228)	
Median (95% CI)	1.9384 (1.1170 to 2.9569)	0.8542 (0.7556 to 1.1499)	0.9856 (0.1971 to NC)	0.7228 (0.1314 to 2.3655)	
75% quantile (95% CI)	NC (7.0308 to NC)	3.7782 (2.1355 to 6.9651)	4.6653 (0.7556 to NC)	2.3655 (0.5585 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0025		0.4674	
Hazard ratio (95% CI) vs Pd		1.5103 (1.1536 to 1.9774)		1.5015 (0.4981 to 4.5266)	
P-value		0.0027		0.4703	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_refr1_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.22 Subgroup analyses by refractory to IMID status
16.2.7.1.1.22.5 Treatment emergent severe adverse event by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6621 (0.5057 to 0.8669)				
probability (95% CI)[b]					
2 Months	0.4790 (0.3937 to 0.5593)	0.3432 (0.2666 to 0.4210)	0.4444 (0.1359 to 0.7193)	0.2857 (0.0411 to 0.6115)	
4 Months	0.3847 (0.3037 to 0.4649)	0.2363 (0.1700 to 0.3088)	0.3333 (0.0783 to 0.6226)	0.1429 (0.0071 to 0.4649)	
6 Months	0.3397 (0.2618 to 0.4190)	0.1909 (0.1306 to 0.2601)	0.2222 (0.0337 to 0.5131)	0.1429 (0.0071 to 0.4649)	
8 Months	0.3161 (0.2399 to 0.3949)	0.1604 (0.1048 to 0.2265)	0.2222 (0.0337 to 0.5131)	0.1429 (0.0071 to 0.4649)	
10 Months	0.3161 (0.2399 to 0.3949)	0.1528 (0.0985 to 0.2180)	0.2222 (0.0337 to 0.5131)	0.1429 (0.0071 to 0.4649)	
12 Months	0.3161 (0.2399 to 0.3949)	0.1443 (0.0914 to 0.2087)	0.2222 (0.0337 to 0.5131)	0.1429 (0.0071 to 0.4649)	
14 Months	0.3161 (0.2399 to 0.3949)	0.1322 (0.0805 to 0.1970)	0.2222 (0.0337 to 0.5131)	0.1429 (0.0071 to 0.4649)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_refr1_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.22 Subgroup analyses by refractory to IMID status
16.2.7.1.1.22.5 Treatment emergent severe adverse event by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.2975 (0.2187 to 0.3803)	0.1322 (0.0805 to 0.1970)	0.2222 (0.0337 to 0.5131)	0.1429 (0.0071 to 0.4649)	
Number of patients at risk[b]					
2 Months	66	49	4	2	
4 Months	53	32	3	1	
6 Months	45	25	2	1	
8 Months	38	21	2	1	
10 Months	38	19	2	1	
12 Months	32	15	2	1	
14 Months	18	10	2	1	
16 Months	10	3	2	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.22 Subgroup analyses by refractory to IMID status
16.2.7.1.1.22.6 Treatment emergent severe adverse event including death by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	98 (70.0)	126 (86.9)	7 (77.8)	6 (85.7)	0.9702
Number (%) of patients censored	42 (30.0)	19 (13.1)	2 (22.2)	1 (14.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.5257 (0.3285 to 0.7556)	0.5257 (0.3614 to 0.5585)	0.5914 (0.1971 to 0.9856)	0.2628 (0.1314 to 0.7228)	
Median (95% CI)	1.6756 (0.9856 to 2.8255)	0.8542 (0.7556 to 1.1499)	0.9856 (0.1971 to NC)	0.7228 (0.1314 to 2.3655)	
75% quantile (95% CI)	NC (6.0452 to NC)	3.6468 (2.1027 to 6.1766)	4.6653 (0.7556 to NC)	2.3655 (0.5585 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0018		0.4674	
Hazard ratio (95% CI) vs Pd		1.5229 (1.1666 to 1.9880)		1.5015 (0.4981 to 4.5266)	
P-value		0.0020		0.4703	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.22 Subgroup analyses by refractory to IMID status
16.2.7.1.1.22.6 Treatment emergent severe adverse event including death by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6567 (0.5030 to 0.8572)				
probability (95% CI)[b]					
2 Months	0.4748 (0.3899 to 0.5549)	0.3333 (0.2578 to 0.4105)	0.4444 (0.1359 to 0.7193)	0.2857 (0.0411 to 0.6115)	
4 Months	0.3813 (0.3009 to 0.4611)	0.2281 (0.1633 to 0.2995)	0.3333 (0.0783 to 0.6226)	0.1429 (0.0071 to 0.4649)	
6 Months	0.3300 (0.2532 to 0.4086)	0.1843 (0.1255 to 0.2521)	0.2222 (0.0337 to 0.5131)	0.1429 (0.0071 to 0.4649)	
8 Months	0.3071 (0.2322 to 0.3850)	0.1548 (0.1008 to 0.2195)	0.2222 (0.0337 to 0.5131)	0.1429 (0.0071 to 0.4649)	
10 Months	0.3071 (0.2322 to 0.3850)	0.1401 (0.0887 to 0.2029)	0.2222 (0.0337 to 0.5131)	0.1429 (0.0071 to 0.4649)	
12 Months	0.3071 (0.2322 to 0.3850)	0.1323 (0.0824 to 0.1942)	0.2222 (0.0337 to 0.5131)	0.1429 (0.0071 to 0.4649)	
14 Months	0.3071 (0.2322 to 0.3850)	0.1213 (0.0727 to 0.1831)	0.2222 (0.0337 to 0.5131)	0.1429 (0.0071 to 0.4649)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.22 Subgroup analyses by refractory to IMID status
16.2.7.1.1.22.6 Treatment emergent severe adverse event including death by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.2890 (0.2117 to 0.3707)	0.1213 (0.0727 to 0.1831)	0.2222 (0.0337 to 0.5131)	0.1429 (0.0071 to 0.4649)	
Number of patients at risk[b]					
2 Months	66	48	4	2	
4 Months	53	32	3	1	
6 Months	45	25	2	1	
8 Months	38	21	2	1	
10 Months	38	19	2	1	
12 Months	32	15	2	1	
14 Months	18	10	2	1	
16 Months	10	3	2	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_refr1_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.1 Treatment emergent adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	85 (97.7)	91 (100.0)	61 (98.4)	60 (98.4)	0.0400
Number (%) of patients censored	2 (2.3)	0 (0.0)	1 (1.6)	1 (1.6)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0986 to 0.1971)	0.0657 (0.0657 to 0.0986)	0.1314 (0.0986 to 0.1643)	0.1314 (0.0986 to 0.1971)	
Median (95% CI)	0.3943 (0.2957 to 0.5914)	0.1643 (0.0986 to 0.1971)	0.2957 (0.1643 to 0.3614)	0.2957 (0.1971 to 0.4928)	
75% quantile (95% CI)	0.8871 (0.6899 to 1.4784)	0.3943 (0.2300 to 0.6242)	0.8871 (0.4600 to 1.5113)	0.7228 (0.4928 to 0.8542)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0004		0.6255	
Hazard ratio (95% CI) vs Pd		1.7327 (1.2751 to 2.3546)		1.0938 (0.7633 to 1.5674)	
P-value		0.0004		0.6252	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_llen_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.1 Treatment emergent adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.5771 (0.4247 to 0.7843)				
probability (95% CI)[b]					
2 Months	0.1084 (0.0533 to 0.1858)	0.0337 (0.0090 to 0.0870)	0.1148 (0.0504 to 0.2082)	0.0984 (0.0400 to 0.1880)	
4 Months	0.0361 (0.0097 to 0.0929)	0.0112 (0.0010 to 0.0546)	0.0656 (0.0211 to 0.1460)	0.0328 (0.0061 to 0.1009)	
6 Months	0.0361 (0.0097 to 0.0929)	0.0112 (0.0010 to 0.0546)	0.0437 (0.0095 to 0.1217)	0.0328 (0.0061 to 0.1009)	
8 Months	0.0241 (0.0046 to 0.0758)	0.0112 (0.0010 to 0.0546)	0.0437 (0.0095 to 0.1217)	0.0164 (0.0014 to 0.0772)	
10 Months	0.0241 (0.0046 to 0.0758)	0.0112 (0.0010 to 0.0546)	0.0219 (0.0020 to 0.0953)	0.0164 (0.0014 to 0.0772)	
12 Months	0.0241 (0.0046 to 0.0758)	0.0112 (0.0010 to 0.0546)	0.0219 (0.0020 to 0.0953)	0.0164 (0.0014 to 0.0772)	
14 Months	0.0241 (0.0046 to 0.0758)	0.0112 (0.0010 to 0.0546)	0.0219 (0.0020 to 0.0953)	0.0164 (0.0014 to 0.0772)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teae_llen_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.1 Treatment emergent adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0241 (0.0046 to 0.0758)	0.0112 (0.0010 to 0.0546)	0.0219 (0.0020 to 0.0953)	0.0164 (0.0014 to 0.0772)	
Number of patients at risk[b]					
2 Months	9	3	7	6	
4 Months	3	1	4	2	
6 Months	3	0	2	2	
8 Months	2	0	2	1	
10 Months	2	0	1	1	
12 Months	2	0	0	0	
14 Months	2	0	0	0	
16 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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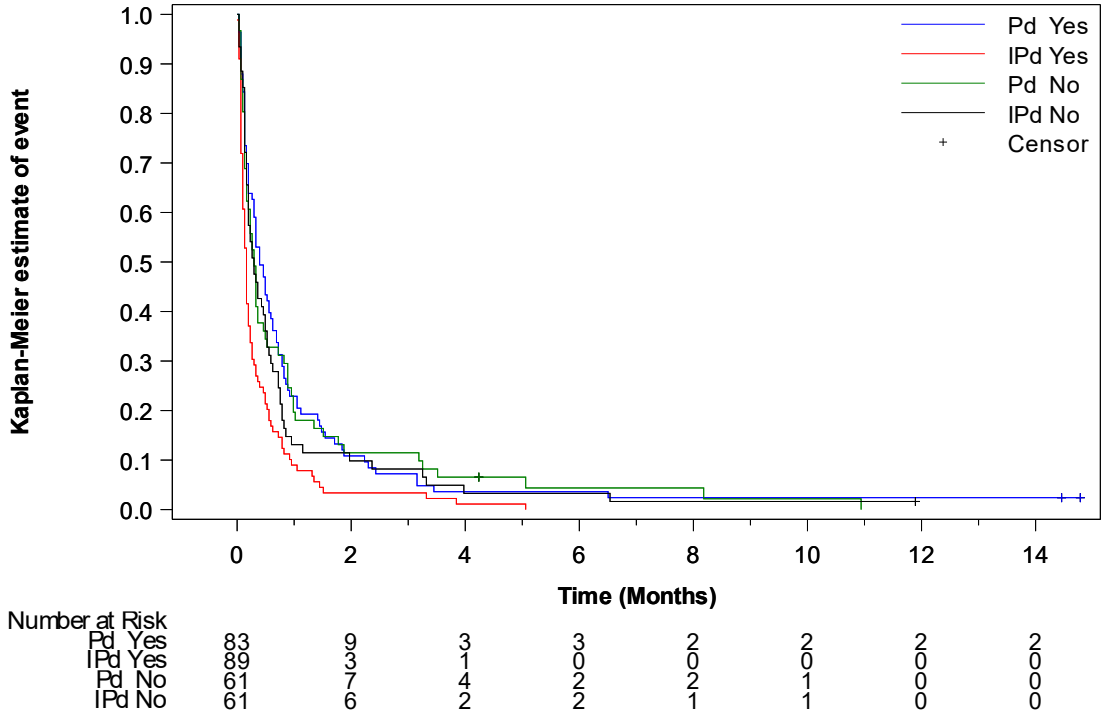
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.3 Treatment emergent serious adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (52.9)	57 (62.6)	34 (54.8)	37 (60.7)	0.6156
Number (%) of patients censored	41 (47.1)	34 (37.4)	28 (45.2)	24 (39.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.5770 (1.0185 to 2.6283)	1.1499 (0.4928 to 1.9713)	0.7228 (0.2957 to 1.9384)	0.7885 (0.3285 to 2.0041)	
Median (95% CI)	6.8994 (3.0883 to NC)	5.1253 (2.6940 to 10.9076)	5.4209 (1.9384 to NC)	8.8049 (2.3655 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.2263		0.7356	
Hazard ratio (95% CI) vs Pd		1.2715 (0.8608 to 1.8782)		1.0835 (0.6800 to 1.7263)	
P-value		0.2274		0.7358	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.3 Treatment emergent serious adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
2 Months	0.7126 (0.6051 to 0.7957)	0.6444 (0.5363 to 0.7336)	0.6290 (0.4965 to 0.7357)	0.6557 (0.5224 to 0.7601)	
4 Months	0.5958 (0.4847 to 0.6905)	0.5432 (0.4347 to 0.6395)	0.5645 (0.4325 to 0.6770)	0.5897 (0.4560 to 0.7010)	
6 Months	0.5237 (0.4131 to 0.6230)	0.4635 (0.3576 to 0.5626)	0.4980 (0.3682 to 0.6148)	0.5560 (0.4228 to 0.6702)	
8 Months	0.4860 (0.3762 to 0.5871)	0.4287 (0.3247 to 0.5284)	0.4802 (0.3511 to 0.5981)	0.5392 (0.4064 to 0.6546)	
10 Months	0.4860 (0.3762 to 0.5871)	0.4055 (0.3031 to 0.5054)	0.4802 (0.3511 to 0.5981)	0.4381 (0.3112 to 0.5579)	
12 Months	0.4860 (0.3762 to 0.5871)	0.3697 (0.2700 to 0.4695)	0.4617 (0.3333 to 0.5807)	0.3855 (0.2633 to 0.5062)	
14 Months	0.4712 (0.3614 to 0.5734)	0.3697 (0.2700 to 0.4695)	0.4386 (0.3099 to 0.5601)	0.3855 (0.2633 to 0.5062)	
16 Months	0.4398 (0.3219 to 0.5514)	0.3697 (0.2700 to 0.4695)	0.4386 (0.3099 to 0.5601)	0.3855 (0.2633 to 0.5062)	
Number of patients at risk[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.3 Treatment emergent serious adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	61	58	39	40	
4 Months	51	48	35	35	
6 Months	43	40	29	33	
8 Months	36	37	27	32	
10 Months	36	35	26	26	
12 Months	33	30	20	20	
14 Months	17	20	12	15	
16 Months	8	8	7	6	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (11.5)	5 (5.5)	9 (14.5)	6 (9.8)	0.6551
Number (%) of patients censored	77 (88.5)	86 (94.5)	53 (85.5)	55 (90.2)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.8789 to NC)	NC (15.9671 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.1322		0.3469	
Hazard ratio (95% CI) vs Pd		0.4481 (0.1531 to 1.3111)		0.6119 (0.2176 to 1.7206)	
P-value		0.1428		0.3517	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.8953 (0.8084 to 0.9441)	0.9889 (0.9237 to 0.9984)	0.9352 (0.8365 to 0.9752)	1.0000 (1.0000 to 1.0000)	
4 Months	0.8953 (0.8084 to 0.9441)	0.9775 (0.9131 to 0.9943)	0.9185 (0.8152 to 0.9653)	0.9667 (0.8732 to 0.9916)	
6 Months	0.8953 (0.8084 to 0.9441)	0.9656 (0.8971 to 0.9888)	0.8671 (0.7516 to 0.9313)	0.9327 (0.8306 to 0.9742)	
8 Months	0.8815 (0.7906 to 0.9345)	0.9522 (0.8772 to 0.9818)	0.8671 (0.7516 to 0.9313)	0.9327 (0.8306 to 0.9742)	
10 Months	0.8815 (0.7906 to 0.9345)	0.9522 (0.8772 to 0.9818)	0.8671 (0.7516 to 0.9313)	0.9129 (0.8027 to 0.9629)	
12 Months	0.8815 (0.7906 to 0.9345)	0.9375 (0.8555 to 0.9737)	0.8671 (0.7516 to 0.9313)	0.9129 (0.8027 to 0.9629)	
14 Months	0.8815 (0.7906 to 0.9345)	0.9375 (0.8555 to 0.9737)	0.8362 (0.7020 to 0.9135)	0.9129 (0.8027 to 0.9629)	
16 Months	0.8815 (0.7906 to 0.9345)	0.9375 (0.8555 to 0.9737)	0.8362 (0.7020 to 0.9135)	0.8477 (0.6369 to 0.9413)	
Number of patients at risk[b]					
2 Months	76	88	57	60	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	73	82	54	57	
6 Months	67	74	46	52	
8 Months	60	71	43	49	
10 Months	60	68	39	45	
12 Months	52	62	33	38	
14 Months	32	41	20	27	
16 Months	14	16	10	12	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.5 Treatment emergent mild adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	78 (89.7)	84 (92.3)	59 (95.2)	57 (93.4)	0.0407
Number (%) of patients censored	9 (10.3)	7 (7.7)	3 (4.8)	4 (6.6)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1807 (0.1314 to 0.2957)	0.0986 (0.0657 to 0.0986)	0.1643 (0.0986 to 0.2628)	0.1643 (0.1314 to 0.1971)	
Median (95% CI)	0.5585 (0.3285 to 0.8214)	0.1643 (0.1314 to 0.2300)	0.3614 (0.2628 to 0.8214)	0.4271 (0.2300 to 0.7228)	
75% quantile (95% CI)	1.6756 (1.0513 to 2.4312)	0.7228 (0.2957 to 2.1684)	0.9856 (0.8214 to 1.8727)	1.0513 (0.7228 to 3.3183)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0211		0.5545	
Hazard ratio (95% CI) vs Pd		1.4441 (1.0549 to 1.9768)		0.8944 (0.6179 to 1.2948)	
P-value		0.0218		0.5544	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.5 Treatment emergent mild adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6925 (0.5059 to 0.9480)				
probability (95% CI)[b]					
2 Months	0.2027 (0.1235 to 0.2959)	0.1667 (0.0984 to 0.2504)	0.1344 (0.0629 to 0.2332)	0.2131 (0.1210 to 0.3225)	
4 Months	0.1081 (0.0515 to 0.1886)	0.1019 (0.0486 to 0.1780)	0.0840 (0.0310 to 0.1711)	0.1475 (0.0726 to 0.2475)	
6 Months	0.0946 (0.0423 to 0.1723)	0.0849 (0.0361 to 0.1601)	0.0630 (0.0186 to 0.1470)	0.0984 (0.0400 to 0.1880)	
8 Months	0.0757 (0.0289 to 0.1527)	0.0424 (0.0095 to 0.1171)	0.0630 (0.0186 to 0.1470)	0.0820 (0.0302 to 0.1673)	
10 Months	0.0757 (0.0289 to 0.1527)	0.0424 (0.0095 to 0.1171)	0.0420 (0.0086 to 0.1212)	0.0820 (0.0302 to 0.1673)	
12 Months	0.0757 (0.0289 to 0.1527)	0.0424 (0.0095 to 0.1171)	0.0420 (0.0086 to 0.1212)	0.0820 (0.0302 to 0.1673)	
14 Months	0.0757 (0.0289 to 0.1527)	0.0424 (0.0095 to 0.1171)	0.0420 (0.0086 to 0.1212)	0.0820 (0.0302 to 0.1673)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.5 Treatment emergent mild adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.0757 (0.0289 to 0.1527)	0.0424 (0.0095 to 0.1171)	0.0420 (0.0086 to 0.1212)	0.0615 (0.0181 to 0.1437)	
Number of patients at risk[b]					
2 Months	15	14	8	13	
4 Months	8	7	5	9	
6 Months	5	4	3	6	
8 Months	4	2	3	5	
10 Months	4	2	1	5	
12 Months	4	2	0	4	
14 Months	4	2	0	4	
16 Months	1	0	0	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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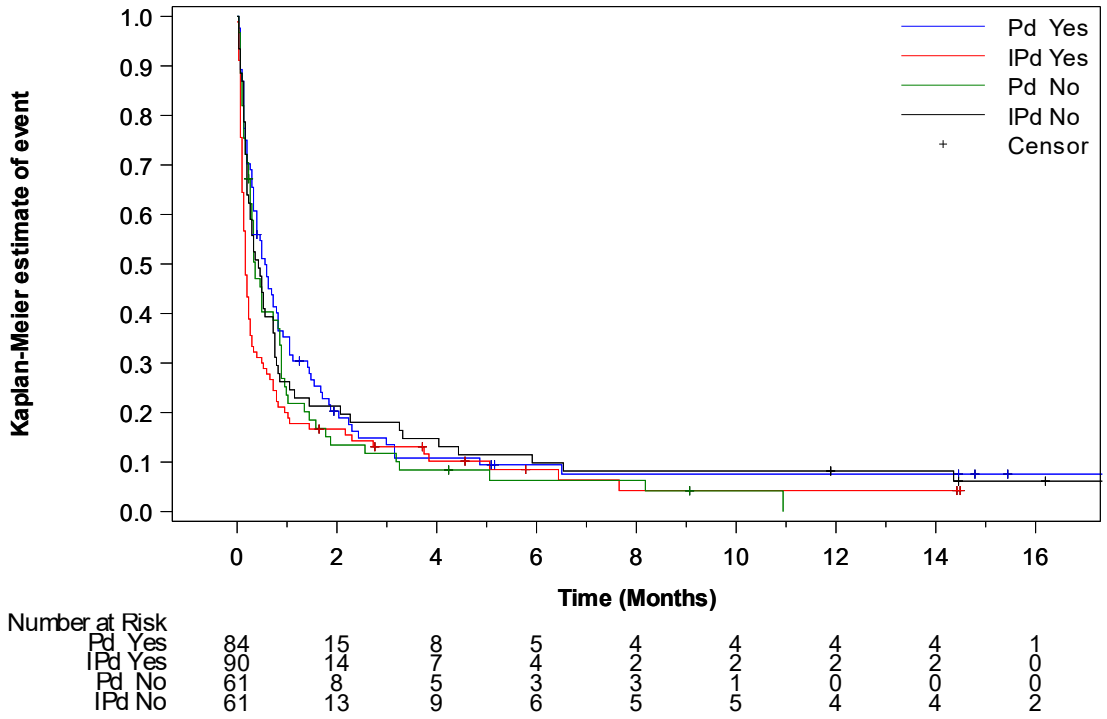
16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.6 Kaplan-Meier cumulative incidence curve of treatment emergent mild adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population



Number at Risk

Pd Yes	84	15	8	5	4	4	4	4	1
IPd Yes	90	14	7	4	2	2	2	2	0
Pd No	61	8	5	3	3	1	0	0	0
IPd No	61	13	9	6	5	5	4	4	2

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.7 Treatment emergent severe adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	61 (70.1)	79 (86.8)	42 (67.7)	50 (82.0)	0.6629
Number (%) of patients censored	26 (29.9)	12 (13.2)	20 (32.3)	11 (18.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.6242 (0.4600 to 0.7885)	0.5257 (0.3285 to 0.5914)	0.5257 (0.2628 to 0.7556)	0.5257 (0.2628 to 0.6242)	
Median (95% CI)	1.6263 (0.8542 to 3.4497)	0.8542 (0.6899 to 1.3470)	1.9384 (0.7885 to 3.6140)	0.8542 (0.7228 to 1.4456)	
75% quantile (95% CI)	NC (6.0452 to NC)	3.3183 (1.9713 to 6.1766)	NC (3.7454 to NC)	3.9754 (1.9384 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0060		0.1160	
Hazard ratio (95% CI) vs Pd		1.6010 (1.1408 to 2.2469)		1.3890 (0.9204 to 2.0960)	
P-value		0.0065		0.1176	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.7 Treatment emergent severe adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6246 (0.4451 to 0.8766)				
probability (95% CI)[b]					
2 Months	0.4884 (0.3794 to 0.5886)	0.3379 (0.2420 to 0.4361)	0.4612 (0.3333 to 0.5798)	0.3443 (0.2287 to 0.4627)	
4 Months	0.3953 (0.2923 to 0.4965)	0.2242 (0.1440 to 0.3155)	0.3624 (0.2443 to 0.4814)	0.2430 (0.1439 to 0.3562)	
6 Months	0.3488 (0.2502 to 0.4491)	0.1749 (0.1035 to 0.2617)	0.3088 (0.1974 to 0.4270)	0.2083 (0.1165 to 0.3183)	
8 Months	0.3135 (0.2189 to 0.4125)	0.1374 (0.0745 to 0.2195)	0.3088 (0.1974 to 0.4270)	0.1909 (0.1032 to 0.2990)	
10 Months	0.3135 (0.2189 to 0.4125)	0.1374 (0.0745 to 0.2195)	0.3088 (0.1974 to 0.4270)	0.1736 (0.0903 to 0.2794)	
12 Months	0.3135 (0.2189 to 0.4125)	0.1237 (0.0640 to 0.2041)	0.3088 (0.1974 to 0.4270)	0.1736 (0.0903 to 0.2794)	
14 Months	0.3135 (0.2189 to 0.4125)	0.1031 (0.0470 to 0.1848)	0.3088 (0.1974 to 0.4270)	0.1736 (0.0903 to 0.2794)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev34_llen_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.7 Treatment emergent severe adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.2787 (0.1769 to 0.3897)	0.1031 (0.0470 to 0.1848)	0.3088 (0.1974 to 0.4270)	0.1736 (0.0903 to 0.2794)	
Number of patients at risk[b]					
2 Months	42	30	28	21	
4 Months	34	19	22	14	
6 Months	30	14	17	12	
8 Months	25	11	15	11	
10 Months	25	11	15	9	
12 Months	21	8	13	8	
14 Months	10	5	10	6	
16 Months	5	1	7	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.8 Treatment emergent severe adverse event including death by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	61 (70.1)	81 (89.0)	44 (71.0)	51 (83.6)	0.5115
Number (%) of patients censored	26 (29.9)	10 (11.0)	18 (29.0)	10 (16.4)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.6242 (0.4600 to 0.7885)	0.4928 (0.3285 to 0.5585)	0.4928 (0.2628 to 0.7556)	0.5257 (0.2628 to 0.6242)	
Median (95% CI)	1.6263 (0.8542 to 3.4497)	0.8542 (0.6899 to 1.3142)	1.7413 (0.7556 to 3.6140)	0.8542 (0.7228 to 1.4456)	
75% quantile (95% CI)	NC (6.0452 to NC)	2.8912 (1.9055 to 5.9795)	NC (3.7454 to NC)	3.9754 (1.9384 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd		0.0034		0.1377	
Hazard ratio (95% CI) vs Pd		1.6473 (1.1759 to 2.3078)		1.3570 (0.9055 to 2.0336)	
P-value		0.0037		0.1392	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_llen_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.8 Treatment emergent severe adverse event including death by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.6070 (0.4333 to 0.8504)				
probability (95% CI)[b]					
2 Months	0.4884 (0.3794 to 0.5886)	0.3222 (0.2287 to 0.4193)	0.4516 (0.3255 to 0.5695)	0.3443 (0.2287 to 0.4627)	
4 Months	0.3953 (0.2923 to 0.4965)	0.2111 (0.1339 to 0.3002)	0.3548 (0.2387 to 0.4727)	0.2430 (0.1439 to 0.3562)	
6 Months	0.3488 (0.2502 to 0.4491)	0.1647 (0.0965 to 0.2488)	0.2873 (0.1806 to 0.4029)	0.2083 (0.1165 to 0.3183)	
8 Months	0.3135 (0.2189 to 0.4125)	0.1294 (0.0696 to 0.2084)	0.2873 (0.1806 to 0.4029)	0.1909 (0.1032 to 0.2990)	
10 Months	0.3135 (0.2189 to 0.4125)	0.1294 (0.0696 to 0.2084)	0.2873 (0.1806 to 0.4029)	0.1562 (0.0777 to 0.2595)	
12 Months	0.3135 (0.2189 to 0.4125)	0.1165 (0.0598 to 0.1937)	0.2873 (0.1806 to 0.4029)	0.1562 (0.0777 to 0.2595)	
14 Months	0.3135 (0.2189 to 0.4125)	0.0971 (0.0440 to 0.1753)	0.2873 (0.1806 to 0.4029)	0.1562 (0.0777 to 0.2595)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_tesev345_llen_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.1 Display of adverse events
16.2.7.1.1.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.1.23.8 Treatment emergent severe adverse event including death by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.2787 (0.1769 to 0.3897)	0.0971 (0.0440 to 0.1753)	0.2873 (0.1806 to 0.4029)	0.1562 (0.0777 to 0.2595)	
Number of patients at risk[b]					
2 Months	42	29	28	21	
4 Months	34	19	22	14	
6 Months	30	14	17	12	
8 Months	25	11	15	11	
10 Months	25	11	15	9	
12 Months	21	8	13	8	
14 Months	10	5	10	6	
16 Months	5	1	7	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Blood and lymphatic system disorders (days)		
Number (%) of events	65 (43.6)	89 (58.6)
Number (%) of patients censored	84 (56.4)	63 (41.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	0.95 (0.756 to 1.938)	0.66 (0.559 to 0.789)
Median (95% CI)	NC (4.665 to NC)	2.37 (0.920 to 9.331)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0070
Hazard ratio (95% CI) vs Pd	-	1.548 (1.124 to 2.132)
P-value	-	0.0075
Hazard ratio inverted (95% CI) vs IPd	0.646 (0.469 to 0.890)	-
Events probability (95% CI)[b]		
2 Months	0.678 (0.596 to 0.748)	0.517 (0.434 to 0.593)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.607 (0.523 to 0.681)	0.455 (0.374 to 0.533)
6 Months	0.562 (0.476 to 0.639)	0.441 (0.361 to 0.519)
8 Months	0.553 (0.467 to 0.631)	0.433 (0.352 to 0.510)
10 Months	0.544 (0.458 to 0.623)	0.414 (0.333 to 0.493)
12 Months	0.544 (0.458 to 0.623)	0.405 (0.324 to 0.484)
14 Months	0.544 (0.458 to 0.623)	0.392 (0.310 to 0.473)
16 Months	0.544 (0.458 to 0.623)	0.392 (0.310 to 0.473)
Number of patients at risk[b]		
2 Months	98	77
4 Months	84	64
6 Months	72	52
8 Months	64	49
10 Months	61	45
12 Months	53	40
14 Months	33	27
16 Months	19	9
Cardiac disorders (days)		
Number (%) of events	6 (4.0)	22 (14.5)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	143 (96.0)	130 (85.5)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0028
Hazard ratio (95% CI) vs Pd	-	3.626 (1.470 to 8.944)
P-value	-	0.0052
Hazard ratio inverted (95% CI) vs IPd	0.276 (0.112 to 0.680)	-
Events probability (95% CI)[b]		
2 Months	0.993 (0.952 to 0.999)	0.927 (0.872 to 0.959)
4 Months	0.993 (0.952 to 0.999)	0.907 (0.848 to 0.944)
6 Months	0.978 (0.933 to 0.993)	0.892 (0.830 to 0.933)
8 Months	0.969 (0.919 to 0.988)	0.877 (0.811 to 0.921)
10 Months	0.959 (0.904 to 0.983)	0.843 (0.771 to 0.894)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	0.959 (0.904 to 0.983)	0.843 (0.771 to 0.894)
14 Months	0.948 (0.885 to 0.976)	0.843 (0.771 to 0.894)
16 Months	0.948 (0.885 to 0.976)	0.843 (0.771 to 0.894)
Number of patients at risk[b]		
2 Months	142	138
4 Months	134	129
6 Months	115	116
8 Months	103	109
10 Months	98	98
12 Months	83	87
14 Months	51	60
16 Months	25	22
Eye disorders (days)		
Number (%) of events	15 (10.1)	13 (8.6)
Number (%) of patients censored	134 (89.9)	139 (91.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.4884
Hazard ratio (95% CI) vs Pd	-	0.770 (0.366 to 1.618)
P-value	-	0.4896
Events probability (95% CI)[b]		
2 Months	0.973 (0.929 to 0.990)	0.987 (0.948 to 0.997)
4 Months	0.907 (0.846 to 0.945)	0.980 (0.939 to 0.994)
6 Months	0.891 (0.826 to 0.933)	0.980 (0.939 to 0.994)
8 Months	0.891 (0.826 to 0.933)	0.940 (0.883 to 0.970)
10 Months	0.891 (0.826 to 0.933)	0.915 (0.851 to 0.952)
12 Months	0.891 (0.826 to 0.933)	0.897 (0.828 to 0.939)
14 Months	0.891 (0.826 to 0.933)	0.897 (0.828 to 0.939)
16 Months	0.891 (0.826 to 0.933)	0.897 (0.828 to 0.939)
Number of patients at risk[b]		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	139	147
4 Months	122	138
6 Months	104	125
8 Months	94	115
10 Months	91	105
12 Months	77	91
14 Months	47	63
16 Months	24	29
Gastrointestinal disorders (days)		
Number (%) of events	74 (49.7)	81 (53.3)
Number (%) of patients censored	75 (50.3)	71 (46.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	0.82 (0.559 to 1.971)	0.69 (0.460 to 1.183)
Median (95% CI)	7.46 (3.844 to NC)	7.20 (3.220 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.6267

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	1.082 (0.788 to 1.484)
P-value	-	0.6271
Events probability (95% CI)[b]		
2 Months	0.677 (0.594 to 0.746)	0.643 (0.561 to 0.713)
4 Months	0.573 (0.487 to 0.649)	0.553 (0.470 to 0.629)
6 Months	0.521 (0.434 to 0.601)	0.546 (0.462 to 0.622)
8 Months	0.492 (0.404 to 0.574)	0.499 (0.415 to 0.577)
10 Months	0.482 (0.394 to 0.565)	0.483 (0.399 to 0.562)
12 Months	0.471 (0.382 to 0.555)	0.457 (0.373 to 0.537)
14 Months	0.471 (0.382 to 0.555)	0.447 (0.362 to 0.527)
16 Months	0.446 (0.350 to 0.538)	0.420 (0.327 to 0.511)
Number of patients at risk[b]		
2 Months	95	95
4 Months	75	78
6 Months	58	71
8 Months	48	63
10 Months	46	55

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	41	46
14 Months	26	30
16 Months	13	12
General disorders and administration site conditions (days)		
Number (%) of events	89 (59.7)	82 (53.9)
Number (%) of patients censored	60 (40.3)	70 (46.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	0.82 (0.394 to 1.380)	1.56 (0.821 to 2.333)
Median (95% CI)	4.37 (2.990 to 8.345)	8.51 (4.402 to 16.000)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1251
Hazard ratio (95% CI) vs Pd	-	0.790 (0.585 to 1.068)
P-value	-	0.1259
Events probability (95% CI)[b]		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	0.624 (0.540 to 0.697)	0.724 (0.645 to 0.788)
4 Months	0.517 (0.432 to 0.595)	0.604 (0.521 to 0.677)
6 Months	0.471 (0.387 to 0.551)	0.549 (0.466 to 0.625)
8 Months	0.424 (0.341 to 0.504)	0.505 (0.422 to 0.583)
10 Months	0.398 (0.315 to 0.479)	0.465 (0.382 to 0.544)
12 Months	0.378 (0.296 to 0.460)	0.465 (0.382 to 0.544)
14 Months	0.365 (0.282 to 0.448)	0.465 (0.382 to 0.544)
16 Months	0.365 (0.282 to 0.448)	0.400 (0.302 to 0.496)
Number of patients at risk[b]		
2 Months	90	109
4 Months	71	90
6 Months	60	76
8 Months	51	68
10 Months	44	57
12 Months	37	49
14 Months	22	36
16 Months	12	18
Infections and infestations (days)		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of events	96 (64.4)	123 (80.9)
Number (%) of patients censored	53 (35.6)	29 (19.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	1.28 (0.854 to 1.511)	0.66 (0.493 to 0.789)
Median (95% CI)	2.40 (1.906 to 4.961)	2.23 (1.446 to 3.088)
75% quantile (95% CI)	NC (9.331 to NC)	5.91 (4.172 to 11.269)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0098
Hazard ratio (95% CI) vs Pd	-	1.421 (1.087 to 1.857)
P-value	-	0.0102
Hazard ratio inverted (95% CI) vs IPd	0.704 (0.538 to 0.920)	-
Events probability (95% CI)[b]		
2 Months	0.561 (0.476 to 0.637)	0.533 (0.450 to 0.609)
4 Months	0.423 (0.342 to 0.503)	0.342 (0.267 to 0.419)
6 Months	0.400 (0.319 to 0.480)	0.250 (0.183 to 0.323)
8 Months	0.348 (0.269 to 0.429)	0.204 (0.143 to 0.274)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
10 Months	0.321 (0.243 to 0.401)	0.188 (0.128 to 0.257)
12 Months	0.321 (0.243 to 0.401)	0.171 (0.113 to 0.239)
14 Months	0.308 (0.230 to 0.390)	0.161 (0.105 to 0.229)
16 Months	0.308 (0.230 to 0.390)	0.161 (0.105 to 0.229)
Number of patients at risk[b]		
2 Months	80	79
4 Months	57	49
6 Months	49	33
8 Months	39	27
10 Months	35	23
12 Months	28	19
14 Months	17	13
16 Months	9	8
Injury, poisoning and procedural complications (days)		
Number (%) of events	17 (11.4)	72 (47.4)
Number (%) of patients censored	132 (88.6)	80 (52.6)
Kaplan-Meier estimates of Events in months		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
25% quantile (95% CI)	NC (NC to NC)	0.13 (0.099 to 0.164)
Median (95% CI)	NC (NC to NC)	14.72 (5.224 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	<.0001
Hazard ratio (95% CI) vs Pd	-	5.771 (3.353 to 9.932)
P-value	-	<.0001
Hazard ratio inverted (95% CI) vs IPd	0.173 (0.101 to 0.298)	-
Events probability (95% CI)[b]		
2 Months	0.958 (0.910 to 0.981)	0.605 (0.523 to 0.678)
4 Months	0.937 (0.881 to 0.966)	0.591 (0.509 to 0.665)
6 Months	0.929 (0.872 to 0.961)	0.577 (0.494 to 0.651)
8 Months	0.894 (0.827 to 0.936)	0.546 (0.462 to 0.622)
10 Months	0.875 (0.803 to 0.922)	0.537 (0.453 to 0.614)
12 Months	0.875 (0.803 to 0.922)	0.528 (0.444 to 0.606)
14 Months	0.875 (0.803 to 0.922)	0.528 (0.444 to 0.606)
16 Months	0.875 (0.803 to 0.922)	0.465 (0.354 to 0.569)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[b]		
2 Months	135	91
4 Months	127	85
6 Months	111	75
8 Months	96	67
10 Months	91	61
12 Months	76	52
14 Months	46	30
16 Months	22	10
Investigations (days)		
Number (%) of events	10 (6.7)	17 (11.2)
Number (%) of patients censored	139 (93.3)	135 (88.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1542
Hazard ratio (95% CI) vs Pd	-	1.785 (0.796 to 4.004)
P-value	-	0.1600
Events probability (95% CI)[b]		
2 Months	0.972 (0.928 to 0.989)	0.947 (0.897 to 0.973)
4 Months	0.958 (0.909 to 0.981)	0.913 (0.855 to 0.949)
6 Months	0.942 (0.886 to 0.970)	0.906 (0.846 to 0.943)
8 Months	0.942 (0.886 to 0.970)	0.906 (0.846 to 0.943)
10 Months	0.942 (0.886 to 0.970)	0.898 (0.836 to 0.937)
12 Months	0.942 (0.886 to 0.970)	0.889 (0.824 to 0.931)
14 Months	0.929 (0.866 to 0.963)	0.879 (0.811 to 0.923)
16 Months	0.929 (0.866 to 0.963)	0.879 (0.811 to 0.923)
Number of patients at risk[b]		
2 Months	137	142
4 Months	127	129
6 Months	109	116

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	98	112
10 Months	95	104
12 Months	81	92
14 Months	49	64
16 Months	23	29
Metabolism and nutrition disorders (days)		
Number (%) of events	20 (13.4)	28 (18.4)
Number (%) of patients censored	129 (86.6)	124 (81.6)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (9.593 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2826
Hazard ratio (95% CI) vs Pd	-	1.368 (0.771 to 2.428)
P-value	-	0.2845

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CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[b]		
2 Months	0.911 (0.852 to 0.947)	0.901 (0.841 to 0.939)
4 Months	0.882 (0.817 to 0.925)	0.840 (0.770 to 0.890)
6 Months	0.859 (0.790 to 0.907)	0.832 (0.762 to 0.883)
8 Months	0.859 (0.790 to 0.907)	0.832 (0.762 to 0.883)
10 Months	0.859 (0.790 to 0.907)	0.816 (0.742 to 0.870)
12 Months	0.859 (0.790 to 0.907)	0.816 (0.742 to 0.870)
14 Months	0.859 (0.790 to 0.907)	0.806 (0.731 to 0.862)
16 Months	0.859 (0.790 to 0.907)	0.806 (0.731 to 0.862)
Number of patients at risk[b]		
2 Months	130	135
4 Months	121	120
6 Months	103	109
8 Months	94	105
10 Months	91	97
12 Months	77	87
14 Months	49	58
16 Months	24	25

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Musculoskeletal and connective tissue disorders (days)		
Number (%) of events	74 (49.7)	85 (55.9)
Number (%) of patients censored	75 (50.3)	67 (44.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	2.20 (0.986 to 3.154)	2.04 (1.216 to 2.891)
Median (95% CI)	9.13 (4.862 to NC)	8.71 (6.341 to 13.634)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.8903
Hazard ratio (95% CI) vs Pd	-	1.022 (0.747 to 1.399)
P-value	-	0.8904
Events probability (95% CI)[b]		
2 Months	0.752 (0.674 to 0.815)	0.755 (0.679 to 0.816)
4 Months	0.642 (0.557 to 0.715)	0.613 (0.530 to 0.686)
6 Months	0.542 (0.453 to 0.622)	0.591 (0.508 to 0.665)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.504 (0.415 to 0.587)	0.507 (0.422 to 0.585)
10 Months	0.483 (0.392 to 0.567)	0.460 (0.376 to 0.540)
12 Months	0.447 (0.355 to 0.534)	0.428 (0.344 to 0.508)
14 Months	0.434 (0.341 to 0.522)	0.416 (0.332 to 0.498)
16 Months	0.434 (0.341 to 0.522)	0.372 (0.278 to 0.466)
Number of patients at risk[b]		
2 Months	107	113
4 Months	85	88
6 Months	60	78
8 Months	48	66
10 Months	44	58
12 Months	34	49
14 Months	19	34
16 Months	8	13
Nervous system disorders (days)		
Number (%) of events	42 (28.2)	62 (40.8)
Number (%) of patients censored	107 (71.8)	90 (59.2)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	5.39 (3.450 to NC)	2.83 (1.906 to 5.848)
Median (95% CI)	NC (NC to NC)	NC (9.396 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0349
Hazard ratio (95% CI) vs Pd	-	1.529 (1.028 to 2.276)
P-value	-	0.0363
Hazard ratio inverted (95% CI) vs IPd	0.654 (0.439 to 0.973)	-
Events probability (95% CI)[b]		
2 Months	0.841 (0.770 to 0.891)	0.808 (0.736 to 0.862)
4 Months	0.795 (0.719 to 0.853)	0.726 (0.647 to 0.790)
6 Months	0.738 (0.655 to 0.804)	0.666 (0.583 to 0.736)
8 Months	0.720 (0.635 to 0.788)	0.618 (0.532 to 0.692)
10 Months	0.710 (0.624 to 0.780)	0.584 (0.496 to 0.661)
12 Months	0.700 (0.612 to 0.771)	0.566 (0.478 to 0.644)
14 Months	0.700 (0.612 to 0.771)	0.555 (0.466 to 0.635)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	0.700 (0.612 to 0.771)	0.555 (0.466 to 0.635)
Number of patients at risk[b]		
2 Months	118	120
4 Months	105	103
6 Months	86	85
8 Months	77	75
10 Months	72	66
12 Months	62	57
14 Months	35	39
16 Months	16	18
Psychiatric disorders (days)		
Number (%) of events	29 (19.5)	26 (17.1)
Number (%) of patients censored	120 (80.5)	126 (82.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (5.618 to NC)	NC (9.791 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.4831
Hazard ratio (95% CI) vs Pd	-	0.827 (0.487 to 1.405)
P-value	-	0.4834
Events probability (95% CI)[b]		
2 Months	0.891 (0.828 to 0.932)	0.908 (0.849 to 0.944)
4 Months	0.855 (0.786 to 0.903)	0.873 (0.808 to 0.917)
6 Months	0.821 (0.746 to 0.876)	0.829 (0.758 to 0.881)
8 Months	0.803 (0.725 to 0.861)	0.829 (0.758 to 0.881)
10 Months	0.803 (0.725 to 0.861)	0.821 (0.747 to 0.874)
12 Months	0.792 (0.712 to 0.853)	0.821 (0.747 to 0.874)
14 Months	0.781 (0.698 to 0.843)	0.821 (0.747 to 0.874)
16 Months	0.781 (0.698 to 0.843)	0.821 (0.747 to 0.874)
Number of patients at risk[b]		
2 Months	126	135
4 Months	114	124

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	95	108
8 Months	85	103
10 Months	82	95
12 Months	68	86
14 Months	41	60
16 Months	19	24
Renal and urinary disorders (days)		
Number (%) of events	23 (15.4)	18 (11.8)
Number (%) of patients censored	126 (84.6)	134 (88.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (16.263 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2934
Hazard ratio (95% CI) vs Pd	-	0.719 (0.388 to 1.333)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
P-value	-	0.2955
Events probability (95% CI)[b]		
2 Months	0.883 (0.819 to 0.926)	0.927 (0.872 to 0.959)
4 Months	0.869 (0.802 to 0.914)	0.907 (0.848 to 0.944)
6 Months	0.861 (0.793 to 0.908)	0.900 (0.839 to 0.938)
8 Months	0.835 (0.761 to 0.887)	0.892 (0.830 to 0.933)
10 Months	0.835 (0.761 to 0.887)	0.884 (0.820 to 0.926)
12 Months	0.835 (0.761 to 0.887)	0.884 (0.820 to 0.926)
14 Months	0.835 (0.761 to 0.887)	0.884 (0.820 to 0.926)
16 Months	0.835 (0.761 to 0.887)	0.884 (0.820 to 0.926)
Number of patients at risk[b]		
2 Months	126	139
4 Months	119	130
6 Months	105	118
8 Months	92	113
10 Months	89	106
12 Months	78	95
14 Months	48	64

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	23	28
Reproductive system and breast disorders (days)		
Number (%) of events	4 (2.7)	10 (6.6)
Number (%) of patients censored	145 (97.3)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1562
Hazard ratio (95% CI) vs Pd	-	2.262 (0.709 to 7.214)
P-value	-	0.1678
Events probability (95% CI)[b]		
2 Months	0.986 (0.946 to 0.997)	0.993 (0.954 to 0.999)
4 Months	0.986 (0.946 to 0.997)	0.980 (0.939 to 0.993)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	0.978 (0.933 to 0.993)	0.973 (0.929 to 0.990)
8 Months	0.969 (0.919 to 0.988)	0.965 (0.917 to 0.985)
10 Months	0.969 (0.919 to 0.988)	0.948 (0.893 to 0.975)
12 Months	0.969 (0.919 to 0.988)	0.939 (0.881 to 0.969)
14 Months	0.969 (0.919 to 0.988)	0.929 (0.867 to 0.963)
16 Months	0.969 (0.919 to 0.988)	0.905 (0.815 to 0.952)
Number of patients at risk[b]		
2 Months	140	148
4 Months	132	138
6 Months	114	125
8 Months	103	119
10 Months	99	111
12 Months	85	98
14 Months	52	67
16 Months	25	26
Respiratory, thoracic and mediastinal disorders (days)		
Number (%) of events	48 (32.2)	62 (40.8)
Number (%) of patients censored	101 (67.8)	90 (59.2)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	5.62 (1.676 to 10.086)	3.75 (1.840 to 4.567)
Median (95% CI)	NC (NC to NC)	NC (9.232 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2074
Hazard ratio (95% CI) vs Pd	-	1.274 (0.874 to 1.857)
P-value	-	0.2085
Events probability (95% CI)[b]		
2 Months	0.794 (0.719 to 0.851)	0.794 (0.721 to 0.851)
4 Months	0.758 (0.679 to 0.820)	0.732 (0.653 to 0.796)
6 Months	0.734 (0.652 to 0.799)	0.659 (0.576 to 0.730)
8 Months	0.716 (0.633 to 0.784)	0.618 (0.532 to 0.693)
10 Months	0.680 (0.594 to 0.752)	0.574 (0.486 to 0.652)
12 Months	0.671 (0.584 to 0.744)	0.555 (0.467 to 0.635)
14 Months	0.638 (0.546 to 0.715)	0.555 (0.467 to 0.635)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	0.638 (0.546 to 0.715)	0.555 (0.467 to 0.635)
Number of patients at risk[b]		
2 Months	113	118
4 Months	101	103
6 Months	87	83
8 Months	81	74
10 Months	74	63
12 Months	62	54
14 Months	36	41
16 Months	17	19
Skin and subcutaneous tissue disorders (days)		
Number (%) of events	36 (24.2)	39 (25.7)
Number (%) of patients censored	113 (75.8)	113 (74.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	9.20 (3.220 to NC)	9.23 (2.825 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.9731
Hazard ratio (95% CI) vs Pd	-	1.008 (0.641 to 1.586)
P-value	-	0.9731
Events probability (95% CI)[b]		
2 Months	0.851 (0.782 to 0.899)	0.848 (0.780 to 0.896)
4 Months	0.806 (0.732 to 0.862)	0.807 (0.735 to 0.862)
6 Months	0.780 (0.701 to 0.840)	0.800 (0.727 to 0.856)
8 Months	0.753 (0.670 to 0.817)	0.784 (0.708 to 0.842)
10 Months	0.743 (0.659 to 0.809)	0.741 (0.659 to 0.805)
12 Months	0.743 (0.659 to 0.809)	0.731 (0.649 to 0.798)
14 Months	0.729 (0.643 to 0.799)	0.731 (0.649 to 0.798)
16 Months	0.729 (0.643 to 0.799)	0.715 (0.627 to 0.786)
Number of patients at risk[b]		
2 Months	120	126
4 Months	107	114

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	87	101
8 Months	76	94
10 Months	72	82
12 Months	62	73
14 Months	38	49
16 Months	17	25
Vascular disorders (days)		
Number (%) of events	17 (11.4)	23 (15.1)
Number (%) of patients censored	132 (88.6)	129 (84.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.4238
Hazard ratio (95% CI) vs Pd	-	1.291 (0.689 to 2.416)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
P-value	-	0.4250
Events probability (95% CI)[b]		
2 Months	0.959 (0.911 to 0.981)	0.947 (0.897 to 0.973)
4 Months	0.930 (0.874 to 0.962)	0.892 (0.829 to 0.932)
6 Months	0.899 (0.835 to 0.939)	0.878 (0.813 to 0.921)
8 Months	0.872 (0.802 to 0.919)	0.870 (0.803 to 0.915)
10 Months	0.872 (0.802 to 0.919)	0.861 (0.793 to 0.908)
12 Months	0.872 (0.802 to 0.919)	0.843 (0.770 to 0.894)
14 Months	0.872 (0.802 to 0.919)	0.833 (0.758 to 0.886)
16 Months	0.872 (0.802 to 0.919)	0.833 (0.758 to 0.886)
Number of patients at risk[b]		
2 Months	136	141
4 Months	126	125
6 Months	106	111
8 Months	92	105
10 Months	88	97
12 Months	76	85
14 Months	46	57

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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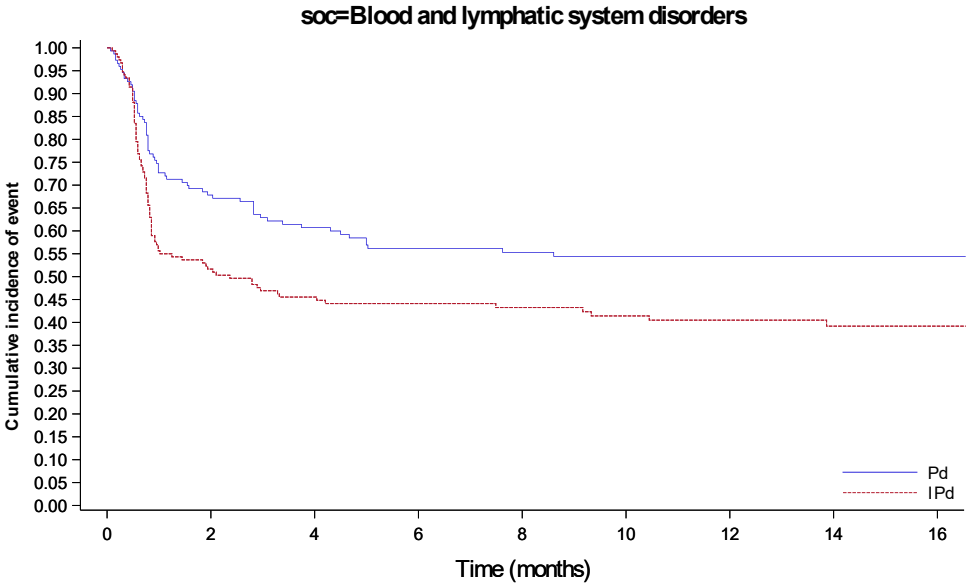
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	24	24

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16FEB2021 22:47)

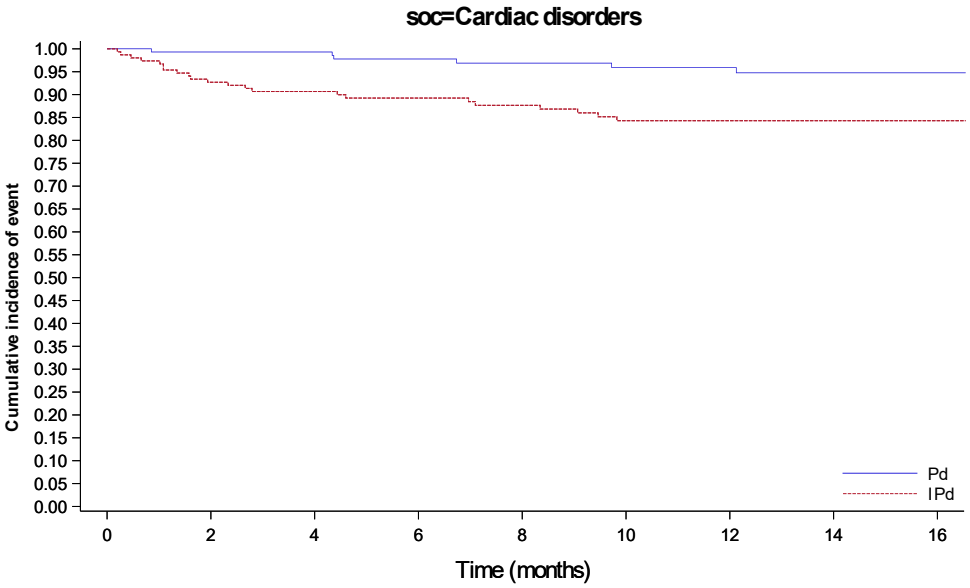
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	98	84	72	64	61	53	33	19
IPd	152	77	64	52	49	45	40	27	9

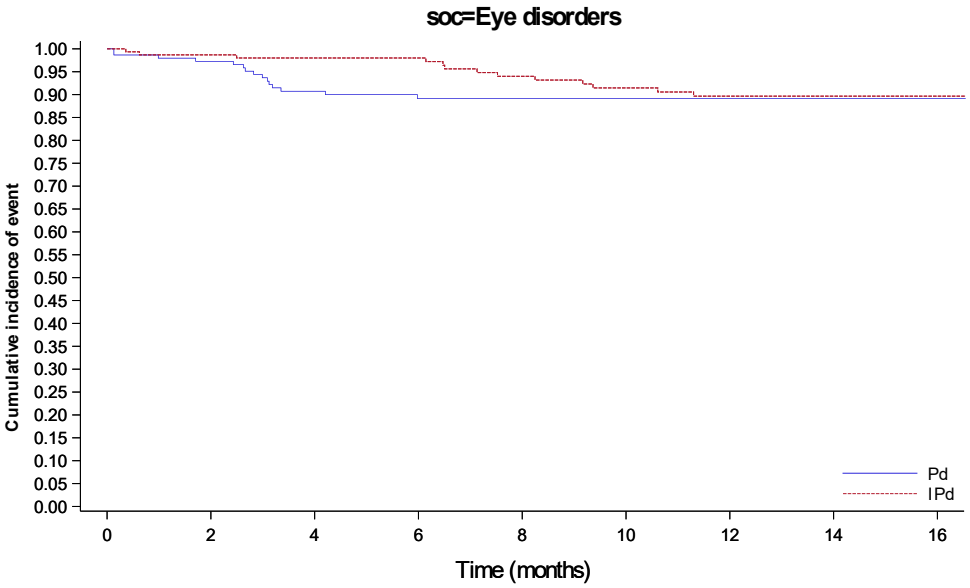
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	142	134	115	103	98	83	51	25
IPd	152	138	129	116	109	98	87	60	22

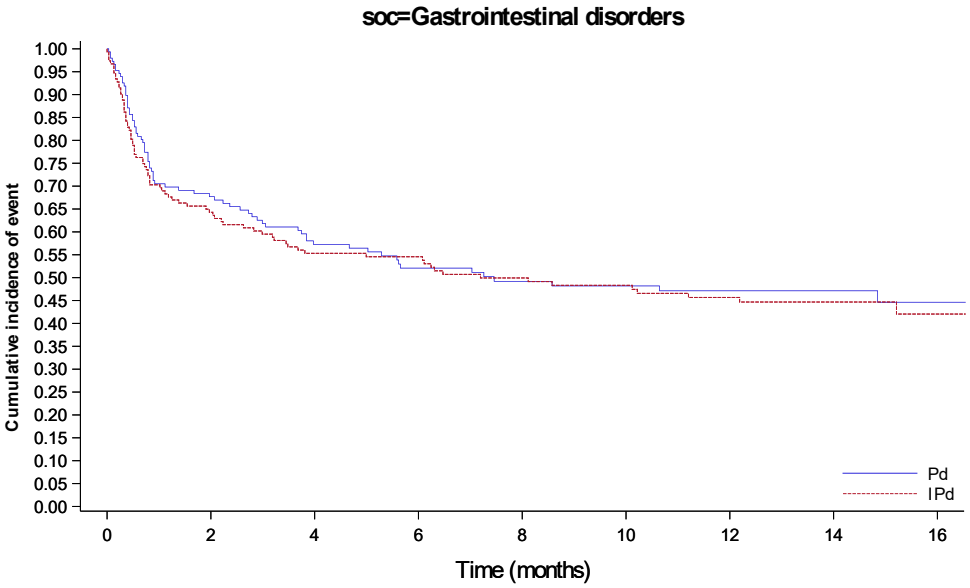
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	139	122	104	94	91	77	47	24
IPd	152	147	138	125	115	105	91	63	29

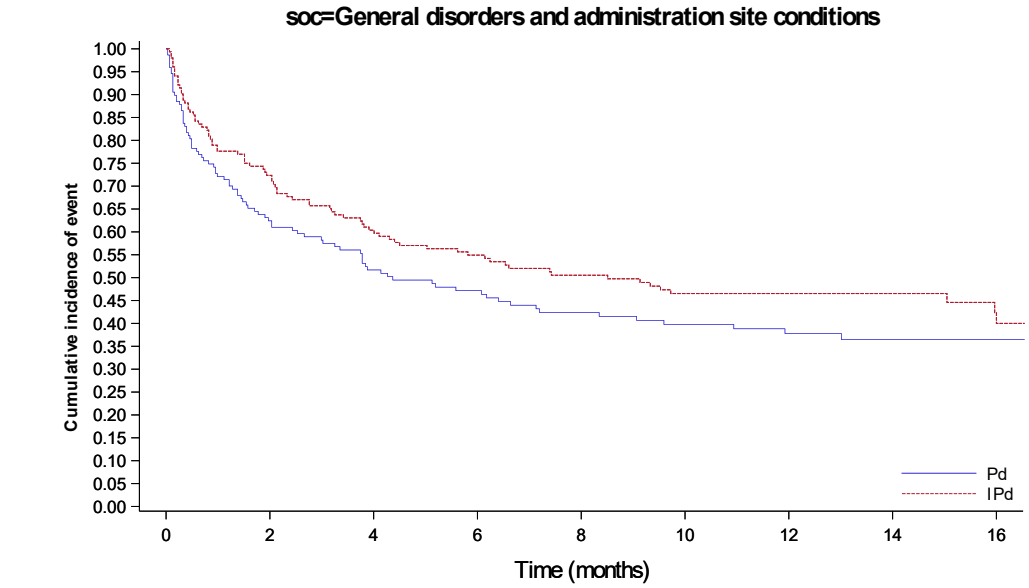
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



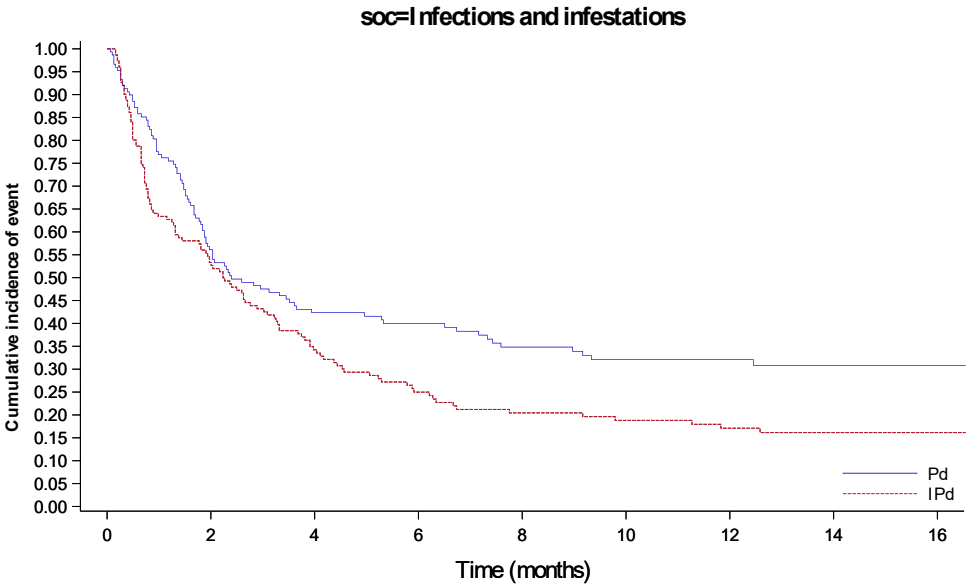
Number at Risk

Pd	148	95	75	58	48	46	41	26	13
IPd	152	95	78	71	63	55	46	30	12

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



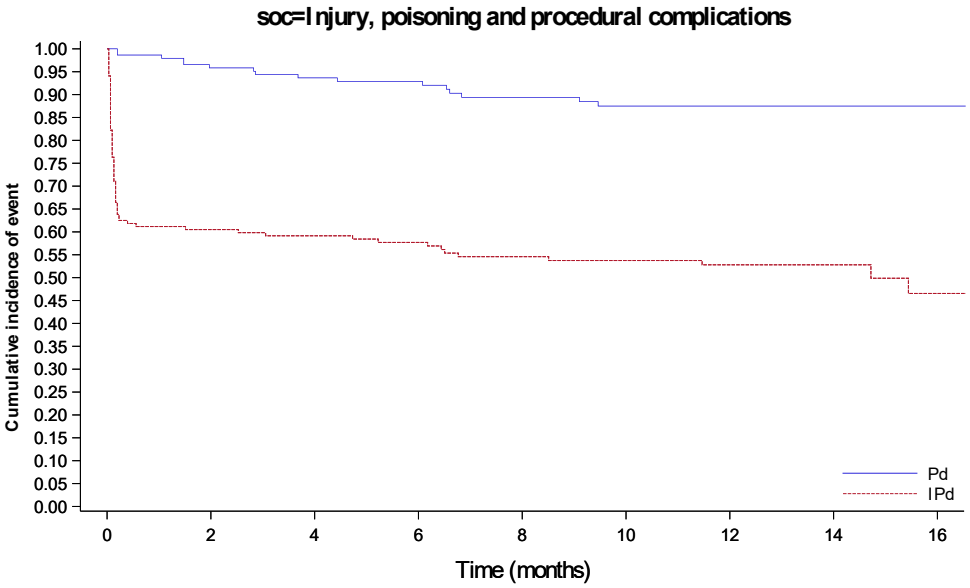
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	80	57	49	39	35	28	17	9
IPd	151	79	49	33	27	23	19	13	8

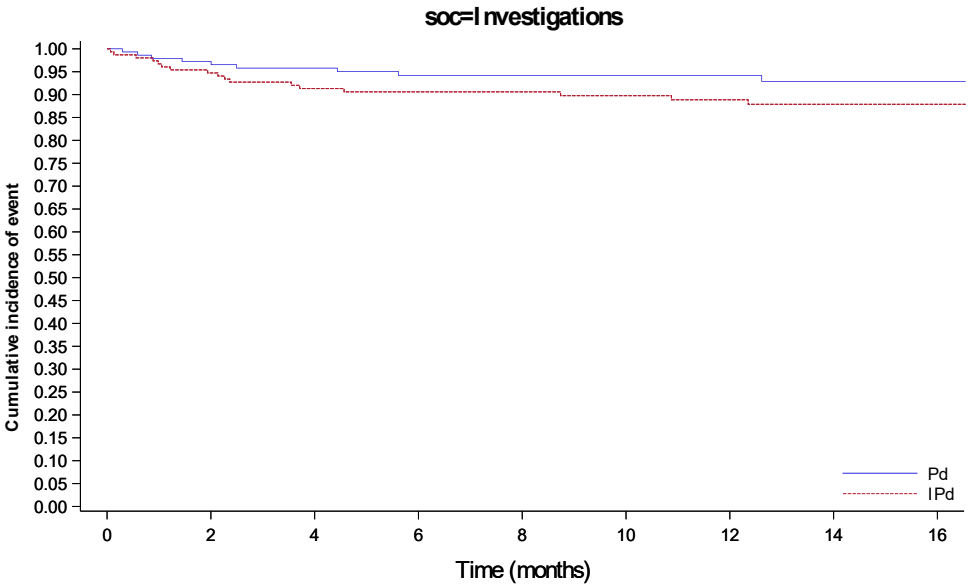
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	148	135	127	111	96	91	76	46	22
IPd	152	91	85	75	67	61	52	30	10

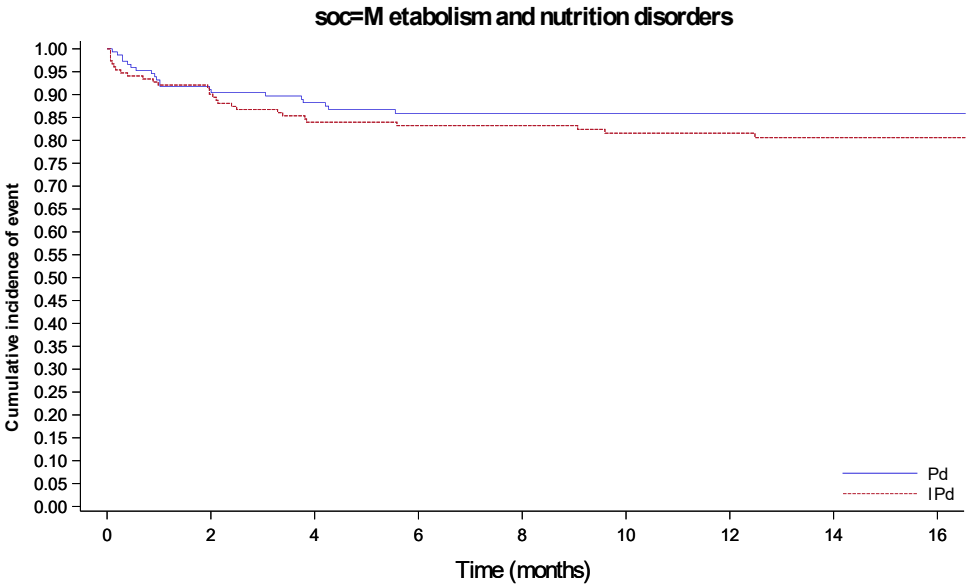
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	148	137	127	109	98	95	81	49	23
IPd	152	142	129	116	112	104	92	64	29

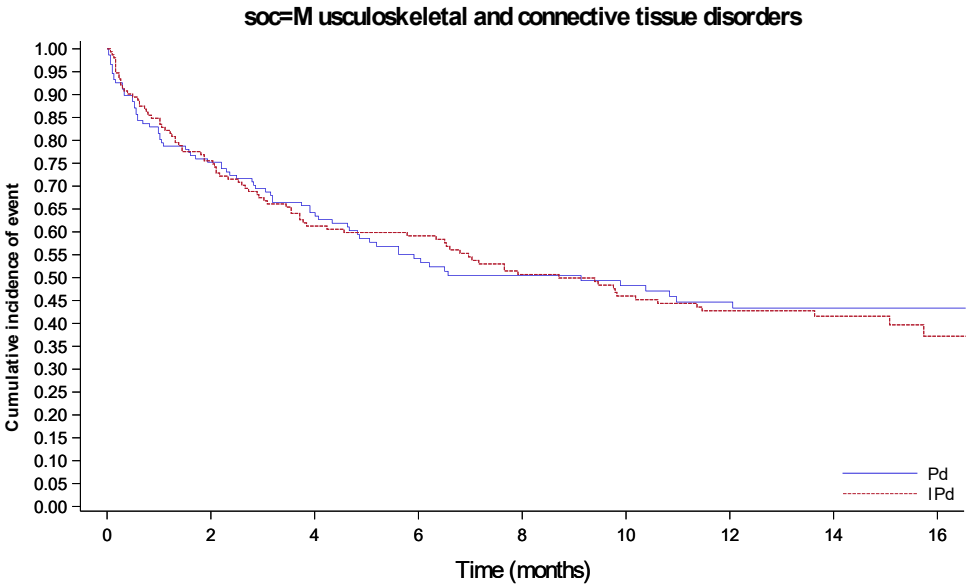
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	130	121	103	94	91	77	49	24
IPd	152	135	120	109	105	97	87	58	25

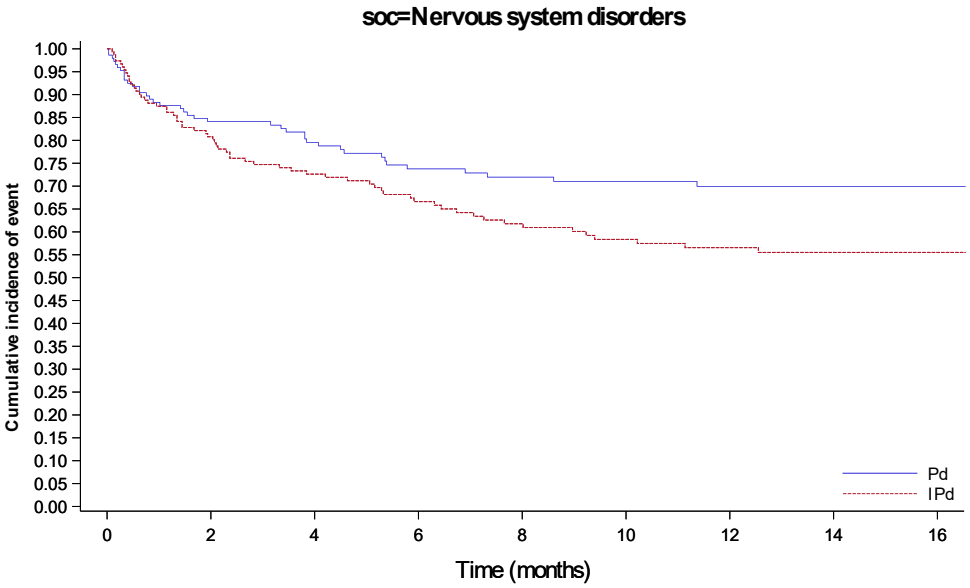
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	148	107	85	60	48	44	34	19	8
IPd	152	113	88	78	66	58	49	34	13

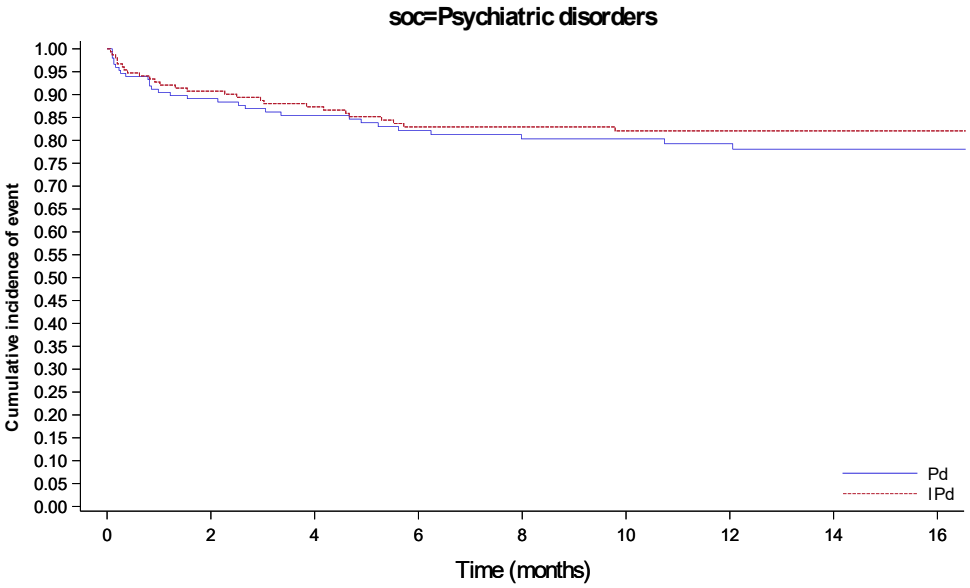
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	147	118	105	86	77	72	62	35	16
IPd	152	120	103	85	75	66	57	39	18

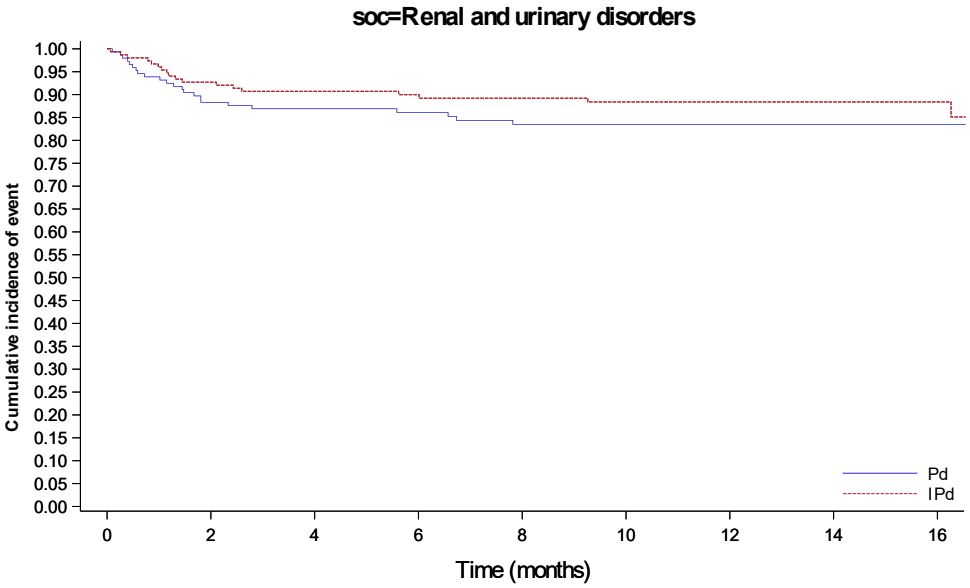
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	126	114	95	85	82	68	41	19
IPd	152	135	124	108	103	95	86	60	24

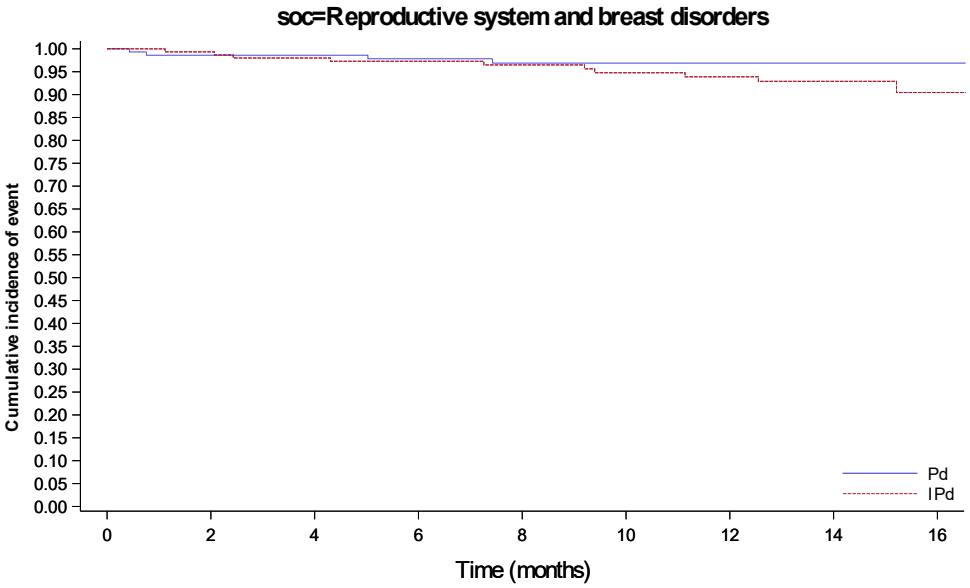
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	126	119	105	92	89	78	48	23
IPd	152	139	130	118	113	106	95	64	28

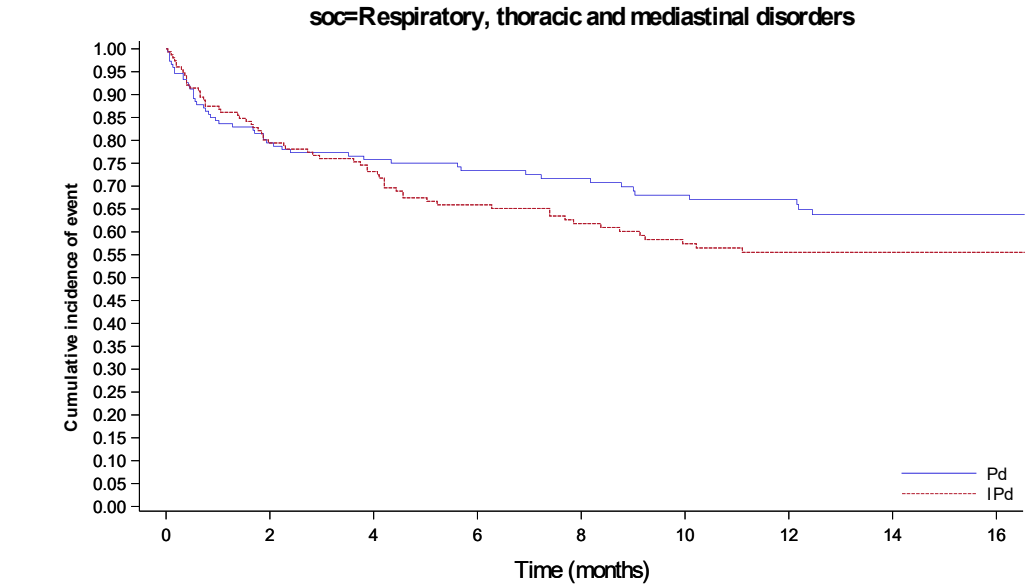
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	140	132	114	103	99	85	52	25
IPd	152	148	138	125	119	111	98	67	26

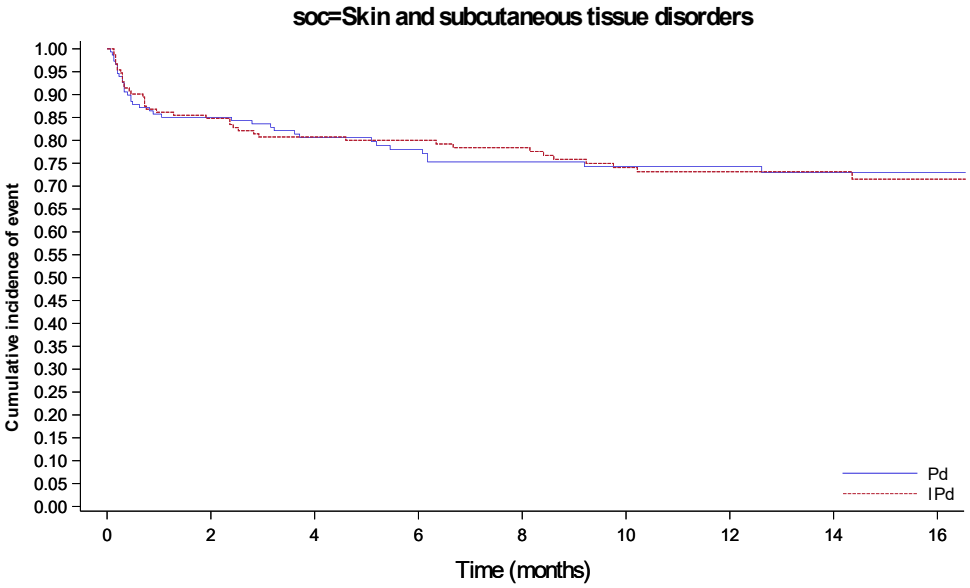
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	113	101	87	81	74	62	36	17
IPd	152	118	103	83	74	63	54	41	19

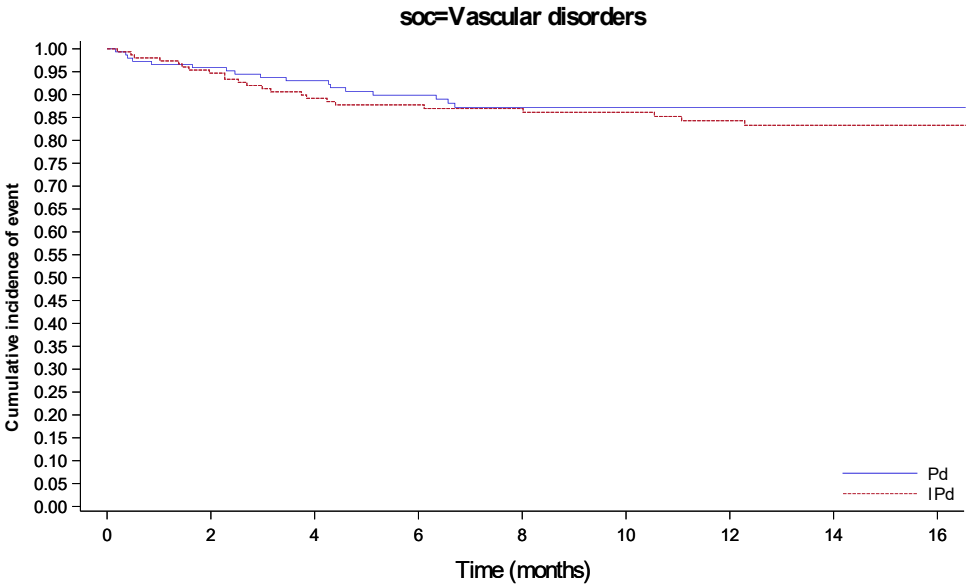
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	120	107	87	76	72	62	38	17
IPd	152	126	114	101	94	82	73	49	25

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	136	126	106	92	88	76	46	24
IPd	152	141	125	111	105	97	85	57	24

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Arthralgia (days)		
Number (%) of events	13 (8.7)	16 (10.5)
Number (%) of patients censored	136 (91.3)	136 (89.5)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.7341
Hazard ratio (95% CI) vs Pd	-	1.135 (0.546 to 2.361)
P-value	-	0.7343
Events probability (95% CI)[b]		
2 Months	0.966 (0.920 to 0.986)	0.954 (0.906 to 0.978)
4 Months	0.937 (0.882 to 0.967)	0.926 (0.870 to 0.958)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	0.929 (0.871 to 0.961)	0.926 (0.870 to 0.958)
8 Months	0.901 (0.835 to 0.942)	0.909 (0.849 to 0.947)
10 Months	0.901 (0.835 to 0.942)	0.909 (0.849 to 0.947)
12 Months	0.901 (0.835 to 0.942)	0.892 (0.826 to 0.934)
14 Months	0.901 (0.835 to 0.942)	0.881 (0.812 to 0.926)
16 Months	0.901 (0.835 to 0.942)	0.881 (0.812 to 0.926)
Number of patients at risk[b]		
2 Months	137	142
4 Months	125	130
6 Months	107	119
8 Months	94	112
10 Months	91	105
12 Months	76	92
14 Months	49	61
16 Months	25	25
Asthenia (days)		
Number (%) of events	27 (18.1)	23 (15.1)
Number (%) of patients censored	122 (81.9)	129 (84.9)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (9.593 to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.4967
Hazard ratio (95% CI) vs Pd	-	0.823 (0.470 to 1.443)
P-value	-	0.4973
Events probability (95% CI)[b]		
2 Months	0.904 (0.843 to 0.942)	0.927 (0.873 to 0.959)
4 Months	0.881 (0.816 to 0.925)	0.873 (0.808 to 0.917)
6 Months	0.865 (0.796 to 0.912)	0.858 (0.791 to 0.905)
8 Months	0.847 (0.775 to 0.898)	0.843 (0.772 to 0.893)
10 Months	0.818 (0.740 to 0.875)	0.843 (0.772 to 0.893)
12 Months	0.807 (0.726 to 0.866)	0.843 (0.772 to 0.893)
14 Months	0.793 (0.708 to 0.856)	0.843 (0.772 to 0.893)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	0.793 (0.708 to 0.856)	0.843 (0.772 to 0.893)
Number of patients at risk[b]		
2 Months	128	139
4 Months	118	123
6 Months	102	111
8 Months	91	105
10 Months	84	98
12 Months	71	87
14 Months	45	58
16 Months	24	28
Back pain (days)		
Number (%) of events	22 (14.8)	25 (16.4)
Number (%) of patients censored	127 (85.2)	127 (83.6)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (11.795 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.8643
Hazard ratio (95% CI) vs Pd	-	1.051 (0.593 to 1.864)
P-value	-	0.8644
Events probability (95% CI)[b]		
2 Months	0.931 (0.876 to 0.962)	0.954 (0.905 to 0.978)
4 Months	0.880 (0.813 to 0.923)	0.892 (0.830 to 0.932)
6 Months	0.864 (0.795 to 0.911)	0.870 (0.804 to 0.915)
8 Months	0.856 (0.785 to 0.905)	0.838 (0.766 to 0.890)
10 Months	0.856 (0.785 to 0.905)	0.830 (0.757 to 0.883)
12 Months	0.845 (0.772 to 0.897)	0.821 (0.746 to 0.876)
14 Months	0.834 (0.757 to 0.888)	0.821 (0.746 to 0.876)
16 Months	0.834 (0.757 to 0.888)	0.821 (0.746 to 0.876)
Number of patients at risk[b]		
2 Months	132	142
4 Months	117	126

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	102	111
8 Months	92	106
10 Months	88	101
12 Months	74	89
14 Months	45	61
16 Months	20	27
Bone pain (days)		
Number (%) of events	8 (5.4)	11 (7.2)
Number (%) of patients censored	141 (94.6)	141 (92.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.6057
Hazard ratio (95% CI) vs Pd	-	1.270 (0.511 to 3.160)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
P-value	-	0.6065
Events probability (95% CI)[b]		
2 Months	0.966 (0.920 to 0.986)	0.974 (0.931 to 0.990)
4 Months	0.966 (0.920 to 0.986)	0.946 (0.895 to 0.973)
6 Months	0.957 (0.907 to 0.981)	0.946 (0.895 to 0.973)
8 Months	0.957 (0.907 to 0.981)	0.946 (0.895 to 0.973)
10 Months	0.938 (0.878 to 0.969)	0.946 (0.895 to 0.973)
12 Months	0.938 (0.878 to 0.969)	0.929 (0.871 to 0.961)
14 Months	0.938 (0.878 to 0.969)	0.929 (0.871 to 0.961)
16 Months	0.938 (0.878 to 0.969)	0.900 (0.803 to 0.951)
Number of patients at risk[b]		
2 Months	138	145
4 Months	131	133
6 Months	113	120
8 Months	102	115
10 Months	96	112
12 Months	83	98
14 Months	51	67

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	24	26
Bronchitis (days)		
Number (%) of events	13 (8.7)	36 (23.7)
Number (%) of patients censored	136 (91.3)	116 (76.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	12.48 (4.501 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0007
Hazard ratio (95% CI) vs Pd	-	2.859 (1.516 to 5.392)
P-value	-	0.0012
Hazard ratio inverted (95% CI) vs IPd	0.350 (0.185 to 0.659)	-
Events probability (95% CI)[b]		
2 Months	0.972 (0.928 to 0.990)	0.901 (0.841 to 0.939)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.958 (0.908 to 0.981)	0.838 (0.768 to 0.889)
6 Months	0.934 (0.877 to 0.965)	0.787 (0.710 to 0.845)
8 Months	0.916 (0.853 to 0.953)	0.763 (0.684 to 0.825)
10 Months	0.916 (0.853 to 0.953)	0.763 (0.684 to 0.825)
12 Months	0.905 (0.837 to 0.945)	0.754 (0.673 to 0.817)
14 Months	0.892 (0.820 to 0.937)	0.743 (0.661 to 0.808)
16 Months	0.892 (0.820 to 0.937)	0.743 (0.661 to 0.808)
Number of patients at risk[b]		
2 Months	138	134
4 Months	128	117
6 Months	110	100
8 Months	97	93
10 Months	93	87
12 Months	77	76
14 Months	46	51
16 Months	22	22
Constipation (days)		
Number (%) of events	26 (17.4)	24 (15.8)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	123 (82.6)	128 (84.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (7.458 to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.5767
Hazard ratio (95% CI) vs Pd	-	0.854 (0.490 to 1.487)
P-value	-	0.5767
Events probability (95% CI)[b]		
2 Months	0.863 (0.796 to 0.909)	0.894 (0.833 to 0.934)
4 Months	0.841 (0.771 to 0.892)	0.867 (0.801 to 0.912)
6 Months	0.825 (0.752 to 0.878)	0.860 (0.793 to 0.906)
8 Months	0.816 (0.741 to 0.871)	0.843 (0.773 to 0.893)
10 Months	0.816 (0.741 to 0.871)	0.843 (0.773 to 0.893)
12 Months	0.816 (0.741 to 0.871)	0.843 (0.773 to 0.893)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.816 (0.741 to 0.871)	0.833 (0.760 to 0.885)
16 Months	0.816 (0.741 to 0.871)	0.833 (0.760 to 0.885)
Number of patients at risk[b]		
2 Months	122	133
4 Months	113	122
6 Months	98	108
8 Months	86	101
10 Months	82	95
12 Months	70	84
14 Months	45	57
16 Months	21	23
Cough (days)		
Number (%) of events	11 (7.4)	14 (9.2)
Number (%) of patients censored	138 (92.6)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.6675
Hazard ratio (95% CI) vs Pd	-	1.189 (0.540 to 2.619)
P-value	-	0.6679
Events probability (95% CI)[b]		
2 Months	0.959 (0.911 to 0.981)	0.973 (0.930 to 0.990)
4 Months	0.952 (0.901 to 0.977)	0.952 (0.903 to 0.977)
6 Months	0.936 (0.880 to 0.966)	0.938 (0.885 to 0.967)
8 Months	0.936 (0.880 to 0.966)	0.906 (0.843 to 0.944)
10 Months	0.926 (0.867 to 0.960)	0.897 (0.832 to 0.938)
12 Months	0.926 (0.867 to 0.960)	0.897 (0.832 to 0.938)
14 Months	0.915 (0.849 to 0.952)	0.897 (0.832 to 0.938)
16 Months	0.915 (0.849 to 0.952)	0.897 (0.832 to 0.938)
Number of patients at risk[b]		
2 Months	136	145

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	128	134
6 Months	111	120
8 Months	102	111
10 Months	97	103
12 Months	82	92
14 Months	49	63
16 Months	23	27
Decreased appetite (days)		
Number (%) of events	7 (4.7)	15 (9.9)
Number (%) of patients censored	142 (95.3)	137 (90.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1000

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	2.088 (0.851 to 5.120)
P-value	-	0.1079
Events probability (95% CI)[b]		
2 Months	0.979 (0.937 to 0.993)	0.947 (0.897 to 0.973)
4 Months	0.957 (0.908 to 0.981)	0.913 (0.854 to 0.948)
6 Months	0.949 (0.896 to 0.975)	0.913 (0.854 to 0.948)
8 Months	0.949 (0.896 to 0.975)	0.905 (0.845 to 0.943)
10 Months	0.949 (0.896 to 0.975)	0.897 (0.834 to 0.936)
12 Months	0.949 (0.896 to 0.975)	0.897 (0.834 to 0.936)
14 Months	0.949 (0.896 to 0.975)	0.897 (0.834 to 0.936)
16 Months	0.949 (0.896 to 0.975)	0.897 (0.834 to 0.936)
Number of patients at risk[b]		
2 Months	139	141
4 Months	129	130
6 Months	112	119
8 Months	101	114
10 Months	97	107
12 Months	82	96

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	51	65
16 Months	24	30
Diarrhoea (days)		
Number (%) of events	29 (19.5)	39 (25.7)
Number (%) of patients censored	120 (80.5)	113 (74.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (5.618 to NC)	10.12 (4.172 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2930
Hazard ratio (95% CI) vs Pd	-	1.293 (0.800 to 2.091)
P-value	-	0.2943
Events probability (95% CI)[b]		
2 Months	0.897 (0.835 to 0.937)	0.868 (0.803 to 0.913)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.839 (0.767 to 0.890)	0.826 (0.756 to 0.878)
6 Months	0.822 (0.747 to 0.876)	0.812 (0.739 to 0.866)
8 Months	0.813 (0.737 to 0.869)	0.773 (0.696 to 0.833)
10 Months	0.803 (0.725 to 0.861)	0.757 (0.678 to 0.819)
12 Months	0.793 (0.713 to 0.853)	0.731 (0.648 to 0.797)
14 Months	0.793 (0.713 to 0.853)	0.731 (0.648 to 0.797)
16 Months	0.768 (0.673 to 0.839)	0.710 (0.619 to 0.783)
Number of patients at risk[b]		
2 Months	127	129
4 Months	113	118
6 Months	96	106
8 Months	85	97
10 Months	82	88
12 Months	72	76
14 Months	45	51
16 Months	22	21
Dyspnoea (days)		
Number (%) of events	15 (10.1)	23 (15.1)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	134 (89.9)	129 (84.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2416
Hazard ratio (95% CI) vs Pd	-	1.471 (0.768 to 2.820)
P-value	-	0.2445
Events probability (95% CI)[b]		
2 Months	0.945 (0.893 to 0.972)	0.934 (0.881 to 0.964)
4 Months	0.930 (0.874 to 0.962)	0.914 (0.856 to 0.949)
6 Months	0.922 (0.863 to 0.956)	0.862 (0.795 to 0.909)
8 Months	0.913 (0.852 to 0.950)	0.854 (0.785 to 0.903)
10 Months	0.894 (0.827 to 0.936)	0.837 (0.764 to 0.889)
12 Months	0.894 (0.827 to 0.936)	0.837 (0.764 to 0.889)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.883 (0.812 to 0.929)	0.837 (0.764 to 0.889)
16 Months	0.883 (0.812 to 0.929)	0.837 (0.764 to 0.889)
Number of patients at risk[b]		
2 Months	134	139
4 Months	124	130
6 Months	109	112
8 Months	99	106
10 Months	93	97
12 Months	80	87
14 Months	48	61
16 Months	23	27
Fatigue (days)		
Number (%) of events	32 (21.5)	26 (17.1)
Number (%) of patients censored	117 (78.5)	126 (82.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (2.530 to NC)	NC (8.345 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2396
Hazard ratio (95% CI) vs Pd	-	0.734 (0.437 to 1.232)
P-value	-	0.2415
Events probability (95% CI)[b]		
2 Months	0.842 (0.772 to 0.892)	0.907 (0.849 to 0.944)
4 Months	0.806 (0.731 to 0.862)	0.887 (0.824 to 0.928)
6 Months	0.806 (0.731 to 0.862)	0.872 (0.806 to 0.916)
8 Months	0.780 (0.701 to 0.840)	0.831 (0.758 to 0.884)
10 Months	0.771 (0.690 to 0.832)	0.814 (0.738 to 0.870)
12 Months	0.771 (0.690 to 0.832)	0.814 (0.738 to 0.870)
14 Months	0.771 (0.690 to 0.832)	0.814 (0.738 to 0.870)
16 Months	0.771 (0.690 to 0.832)	0.814 (0.738 to 0.870)
Number of patients at risk[b]		
2 Months	119	135

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	107	124
6 Months	95	110
8 Months	84	101
10 Months	79	92
12 Months	68	83
14 Months	40	57
16 Months	19	26
Febrile neutropenia (days)		
Number (%) of events	3 (2.0)	18 (11.8)
Number (%) of patients censored	146 (98.0)	134 (88.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0011

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	6.001 (1.768 to 20.370)
P-value	-	0.0041
Hazard ratio inverted (95% CI) vs IPd	0.167 (0.049 to 0.566)	-
Events probability (95% CI)[b]		
2 Months	0.986 (0.945 to 0.996)	0.907 (0.848 to 0.944)
4 Months	0.986 (0.945 to 0.996)	0.900 (0.840 to 0.939)
6 Months	0.986 (0.945 to 0.996)	0.887 (0.824 to 0.928)
8 Months	0.986 (0.945 to 0.996)	0.887 (0.824 to 0.928)
10 Months	0.976 (0.927 to 0.992)	0.887 (0.824 to 0.928)
12 Months	0.976 (0.927 to 0.992)	0.878 (0.812 to 0.921)
14 Months	0.976 (0.927 to 0.992)	0.878 (0.812 to 0.921)
16 Months	0.976 (0.927 to 0.992)	0.878 (0.812 to 0.921)
Number of patients at risk[b]		
2 Months	140	135
4 Months	132	129
6 Months	116	114
8 Months	105	110
10 Months	100	107

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	86	94
14 Months	54	64
16 Months	26	26
Headache (days)		
Number (%) of events	8 (5.4)	15 (9.9)
Number (%) of patients censored	141 (94.6)	137 (90.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1316
Hazard ratio (95% CI) vs Pd	-	1.968 (0.802 to 4.828)
P-value	-	0.1391
Events probability (95% CI)[b]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	0.972 (0.927 to 0.989)	0.973 (0.931 to 0.990)
4 Months	0.972 (0.927 to 0.989)	0.967 (0.922 to 0.986)
6 Months	0.947 (0.892 to 0.975)	0.930 (0.873 to 0.962)
8 Months	0.947 (0.892 to 0.975)	0.922 (0.863 to 0.956)
10 Months	0.947 (0.892 to 0.975)	0.905 (0.842 to 0.944)
12 Months	0.947 (0.892 to 0.975)	0.897 (0.831 to 0.938)
14 Months	0.947 (0.892 to 0.975)	0.887 (0.819 to 0.931)
16 Months	0.947 (0.892 to 0.975)	0.887 (0.819 to 0.931)
Number of patients at risk[b]		
2 Months	137	145
4 Months	129	138
6 Months	111	121
8 Months	101	115
10 Months	97	107
12 Months	83	94
14 Months	52	65
16 Months	24	28
Infusion related reaction (days)		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of events	2 (1.3)	56 (36.8)
Number (%) of patients censored	147 (98.7)	96 (63.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	0.13 (0.099 to 0.164)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	<.0001
Hazard ratio (95% CI) vs Pd	-	33.139 (8.083 to 135.860)
P-value	-	<.0001
Hazard ratio inverted (95% CI) vs IPd	0.030 (0.007 to 0.124)	-
Events probability (95% CI)[b]		
2 Months	0.993 (0.952 to 0.999)	0.632 (0.550 to 0.703)
4 Months	0.993 (0.952 to 0.999)	0.632 (0.550 to 0.703)
6 Months	0.993 (0.952 to 0.999)	0.632 (0.550 to 0.703)
8 Months	0.984 (0.939 to 0.996)	0.632 (0.550 to 0.703)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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	Pd (N=149)	**IPd (N=152)**
10 Months	0.984 (0.939 to 0.996)	0.632 (0.550 to 0.703)
12 Months	0.984 (0.939 to 0.996)	0.632 (0.550 to 0.703)
14 Months	0.984 (0.939 to 0.996)	0.632 (0.550 to 0.703)
16 Months	0.984 (0.939 to 0.996)	0.632 (0.550 to 0.703)
Number of patients at risk[b]		
2 Months	141	95
4 Months	134	90
6 Months	117	81
8 Months	105	77
10 Months	101	71
12 Months	86	63
14 Months	53	40
16 Months	26	15
Insomnia (days)		
Number (%) of events	12 (8.1)	13 (8.6)
Number (%) of patients censored	137 (91.9)	139 (91.4)
Kaplan-Meier estimates of Events in months		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.9973
Hazard ratio (95% CI) vs Pd	-	0.999 (0.456 to 2.189)
P-value	-	0.9973
Events probability (95% CI)[b]		
2 Months	0.939 (0.886 to 0.968)	0.967 (0.922 to 0.986)
4 Months	0.931 (0.876 to 0.963)	0.960 (0.913 to 0.982)
6 Months	0.923 (0.866 to 0.957)	0.930 (0.874 to 0.962)
8 Months	0.923 (0.866 to 0.957)	0.914 (0.853 to 0.950)
10 Months	0.923 (0.866 to 0.957)	0.905 (0.842 to 0.944)
12 Months	0.913 (0.850 to 0.950)	0.905 (0.842 to 0.944)
14 Months	0.913 (0.850 to 0.950)	0.905 (0.842 to 0.944)
16 Months	0.913 (0.850 to 0.950)	0.905 (0.842 to 0.944)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[b]		
2 Months	133	144
4 Months	124	135
6 Months	107	118
8 Months	97	111
10 Months	93	103
12 Months	77	92
14 Months	48	63
16 Months	23	26
Muscle spasms (days)		
Number (%) of events	15 (10.1)	14 (9.2)
Number (%) of patients censored	134 (89.9)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Log-Rank test p-value[a] vs Pd	-	0.6642
Hazard ratio (95% CI) vs Pd	-	0.851 (0.411 to 1.763)
P-value	-	0.6641
Events probability (95% CI)[b]		
2 Months	0.958 (0.910 to 0.981)	0.967 (0.922 to 0.986)
4 Months	0.929 (0.873 to 0.961)	0.939 (0.886 to 0.968)
6 Months	0.905 (0.841 to 0.944)	0.932 (0.876 to 0.963)
8 Months	0.905 (0.841 to 0.944)	0.907 (0.845 to 0.945)
10 Months	0.884 (0.814 to 0.929)	0.907 (0.845 to 0.945)
12 Months	0.884 (0.814 to 0.929)	0.907 (0.845 to 0.945)
14 Months	0.884 (0.814 to 0.929)	0.894 (0.826 to 0.937)
16 Months	0.884 (0.814 to 0.929)	0.894 (0.826 to 0.937)
Number of patients at risk[b]		
2 Months	136	144
4 Months	124	132
6 Months	104	118
8 Months	93	110

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
10 Months	87	103
12 Months	74	93
14 Months	46	65
16 Months	20	26
Muscular weakness (days)		
Number (%) of events	7 (4.7)	11 (7.2)
Number (%) of patients censored	142 (95.3)	141 (92.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.4604
Hazard ratio (95% CI) vs Pd	-	1.426 (0.553 to 3.681)
P-value	-	0.4628

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[b]		
2 Months	0.987 (0.947 to 0.997)	0.987 (0.948 to 0.997)
4 Months	0.965 (0.917 to 0.985)	0.966 (0.921 to 0.986)
6 Months	0.957 (0.907 to 0.980)	0.952 (0.901 to 0.977)
8 Months	0.957 (0.907 to 0.980)	0.944 (0.890 to 0.972)
10 Months	0.957 (0.907 to 0.980)	0.944 (0.890 to 0.972)
12 Months	0.947 (0.890 to 0.974)	0.926 (0.867 to 0.960)
14 Months	0.947 (0.890 to 0.974)	0.926 (0.867 to 0.960)
16 Months	0.947 (0.890 to 0.974)	0.897 (0.800 to 0.949)
Number of patients at risk[b]		
2 Months	140	147
4 Months	129	137
6 Months	111	123
8 Months	100	118
10 Months	96	111
12 Months	81	97
14 Months	50	66
16 Months	24	28

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Musculoskeletal chest pain (days)		
Number (%) of events	7 (4.7)	13 (8.6)
Number (%) of patients censored	142 (95.3)	139 (91.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2138
Hazard ratio (95% CI) vs Pd	-	1.777 (0.709 to 4.454)
P-value	-	0.2201
Events probability (95% CI)[b]		
2 Months	0.993 (0.951 to 0.999)	0.967 (0.922 to 0.986)
4 Months	0.971 (0.926 to 0.989)	0.932 (0.877 to 0.963)
6 Months	0.963 (0.914 to 0.985)	0.925 (0.868 to 0.958)
8 Months	0.955 (0.902 to 0.979)	0.925 (0.868 to 0.958)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
10 Months	0.955 (0.902 to 0.979)	0.908 (0.846 to 0.946)
12 Months	0.944 (0.885 to 0.973)	0.908 (0.846 to 0.946)
14 Months	0.944 (0.885 to 0.973)	0.908 (0.846 to 0.946)
16 Months	0.944 (0.885 to 0.973)	0.908 (0.846 to 0.946)
Number of patients at risk[b]		
2 Months	141	144
4 Months	130	131
6 Months	112	119
8 Months	100	115
10 Months	98	106
12 Months	82	95
14 Months	50	65
16 Months	25	29
Myalgia (days)		
Number (%) of events	5 (3.4)	10 (6.6)
Number (%) of patients censored	144 (96.6)	142 (93.4)
Kaplan-Meier estimates of Events in months		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1371
Hazard ratio (95% CI) vs Pd	-	2.348 (0.736 to 7.491)
P-value	-	0.1491
Events probability (95% CI)[b]		
2 Months	0.986 (0.946 to 0.997)	0.967 (0.922 to 0.986)
4 Months	0.986 (0.946 to 0.997)	0.953 (0.904 to 0.977)
6 Months	0.978 (0.932 to 0.993)	0.946 (0.895 to 0.973)
8 Months	0.969 (0.918 to 0.988)	0.946 (0.895 to 0.973)
10 Months	0.969 (0.918 to 0.988)	0.946 (0.895 to 0.973)
12 Months	0.969 (0.918 to 0.988)	0.946 (0.895 to 0.973)
14 Months	0.969 (0.918 to 0.988)	0.937 (0.881 to 0.967)
16 Months	0.969 (0.918 to 0.988)	0.922 (0.855 to 0.959)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[b]		
2 Months	139	144
4 Months	131	134
6 Months	113	120
8 Months	102	117
10 Months	98	110
12 Months	84	99
14 Months	52	67
16 Months	26	27
Nasopharyngitis (days)		
Number (%) of events	7 (4.7)	14 (9.2)
Number (%) of patients censored	142 (95.3)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Log-Rank test p-value[a] vs Pd	-	0.1712
Hazard ratio (95% CI) vs Pd	-	1.865 (0.753 to 4.622)
P-value	-	0.1782
Events probability (95% CI)[b]		
2 Months	0.979 (0.937 to 0.993)	0.973 (0.931 to 0.990)
4 Months	0.965 (0.918 to 0.985)	0.946 (0.895 to 0.973)
6 Months	0.965 (0.918 to 0.985)	0.931 (0.876 to 0.962)
8 Months	0.956 (0.905 to 0.980)	0.923 (0.866 to 0.957)
10 Months	0.956 (0.905 to 0.980)	0.906 (0.844 to 0.945)
12 Months	0.946 (0.889 to 0.974)	0.906 (0.844 to 0.945)
14 Months	0.946 (0.889 to 0.974)	0.894 (0.825 to 0.937)
16 Months	0.946 (0.889 to 0.974)	0.894 (0.825 to 0.937)
Number of patients at risk[b]		
2 Months	139	145
4 Months	129	134
6 Months	112	119
8 Months	100	114

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
10 Months	96	105
12 Months	80	93
14 Months	49	64
16 Months	23	28
Nausea (days)		
Number (%) of events	14 (9.4)	23 (15.1)
Number (%) of patients censored	135 (90.6)	129 (84.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1444
Hazard ratio (95% CI) vs Pd	-	1.632 (0.840 to 3.172)
P-value	-	0.1485

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[b]		
2 Months	0.952 (0.902 to 0.977)	0.888 (0.826 to 0.929)
4 Months	0.923 (0.865 to 0.956)	0.874 (0.809 to 0.918)
6 Months	0.914 (0.854 to 0.951)	0.867 (0.801 to 0.912)
8 Months	0.905 (0.842 to 0.944)	0.859 (0.791 to 0.906)
10 Months	0.895 (0.829 to 0.937)	0.859 (0.791 to 0.906)
12 Months	0.895 (0.829 to 0.937)	0.841 (0.770 to 0.892)
14 Months	0.895 (0.829 to 0.937)	0.841 (0.770 to 0.892)
16 Months	0.895 (0.829 to 0.937)	0.841 (0.770 to 0.892)
Number of patients at risk[b]		
2 Months	135	132
4 Months	123	122
6 Months	105	111
8 Months	96	105
10 Months	91	98
12 Months	77	87
14 Months	48	58
16 Months	24	25

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Neutropenia (days)		
Number (%) of events	50 (33.6)	71 (46.7)
Number (%) of patients censored	99 (66.4)	81 (53.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	2.04 (0.986 to 4.665)	0.85 (0.756 to 0.986)
Median (95% CI)	NC (NC to NC)	NC (2.891 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0213
Hazard ratio (95% CI) vs Pd	-	1.525 (1.062 to 2.191)
P-value	-	0.0223
Hazard ratio inverted (95% CI) vs IPd	0.656 (0.456 to 0.942)	-
Events probability (95% CI)[b]		
2 Months	0.753 (0.675 to 0.815)	0.616 (0.533 to 0.688)
4 Months	0.703 (0.621 to 0.770)	0.575 (0.492 to 0.649)
6 Months	0.654 (0.569 to 0.727)	0.568 (0.485 to 0.643)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.645 (0.559 to 0.719)	0.551 (0.468 to 0.627)
10 Months	0.645 (0.559 to 0.719)	0.533 (0.448 to 0.610)
12 Months	0.645 (0.559 to 0.719)	0.524 (0.439 to 0.602)
14 Months	0.645 (0.559 to 0.719)	0.510 (0.423 to 0.590)
16 Months	0.645 (0.559 to 0.719)	0.510 (0.423 to 0.590)
Number of patients at risk[b]		
2 Months	109	92
4 Months	94	81
6 Months	78	70
8 Months	69	65
10 Months	67	57
12 Months	59	51
14 Months	38	34
16 Months	23	14
Oedema peripheral (days)		
Number (%) of events	16 (10.7)	20 (13.2)
Number (%) of patients censored	133 (89.3)	132 (86.8)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.7321
Hazard ratio (95% CI) vs Pd	-	1.122 (0.581 to 2.165)
P-value	-	0.7322
Events probability (95% CI)[b]		
2 Months	0.924 (0.868 to 0.957)	0.987 (0.948 to 0.997)
4 Months	0.910 (0.850 to 0.947)	0.953 (0.903 to 0.977)
6 Months	0.894 (0.830 to 0.935)	0.938 (0.885 to 0.968)
8 Months	0.894 (0.830 to 0.935)	0.906 (0.844 to 0.945)
10 Months	0.884 (0.818 to 0.928)	0.864 (0.792 to 0.913)
12 Months	0.884 (0.818 to 0.928)	0.847 (0.771 to 0.899)
14 Months	0.884 (0.818 to 0.928)	0.847 (0.771 to 0.899)
16 Months	0.884 (0.818 to 0.928)	0.847 (0.771 to 0.899)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[b]		
2 Months	132	147
4 Months	123	136
6 Months	104	121
8 Months	95	112
10 Months	90	100
12 Months	76	86
14 Months	48	60
16 Months	23	27
Peripheral sensory neuropathy (days)		
Number (%) of events	9 (6.0)	11 (7.2)
Number (%) of patients censored	140 (94.0)	141 (92.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.5809
Hazard ratio (95% CI) vs Pd	-	1.292 (0.519 to 3.212)
P-value	-	0.5819
Events probability (95% CI)[b]		
2 Months	0.986 (0.946 to 0.997)	0.960 (0.914 to 0.982)
4 Months	0.972 (0.926 to 0.989)	0.954 (0.905 to 0.978)
6 Months	0.963 (0.913 to 0.984)	0.931 (0.875 to 0.962)
8 Months	0.954 (0.899 to 0.979)	0.931 (0.875 to 0.962)
10 Months	0.944 (0.885 to 0.973)	0.922 (0.864 to 0.956)
12 Months	0.933 (0.868 to 0.966)	0.922 (0.864 to 0.956)
14 Months	0.933 (0.868 to 0.966)	0.922 (0.864 to 0.956)
16 Months	0.933 (0.868 to 0.966)	0.922 (0.864 to 0.956)
Number of patients at risk[b]		
2 Months	139	143
4 Months	129	134
6 Months	111	118

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	99	113
10 Months	94	105
12 Months	80	94
14 Months	47	62
16 Months	23	27
Pneumonia (days)		
Number (%) of events	26 (17.4)	31 (20.4)
Number (%) of patients censored	123 (82.6)	121 (79.6)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (5.421 to NC)	NC (6.275 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.6603
Hazard ratio (95% CI) vs Pd	-	1.124 (0.667 to 1.892)
P-value	-	0.6614

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[b]		
2 Months	0.911 (0.851 to 0.947)	0.921 (0.865 to 0.954)
4 Months	0.846 (0.775 to 0.896)	0.859 (0.792 to 0.906)
6 Months	0.815 (0.740 to 0.870)	0.830 (0.758 to 0.882)
8 Months	0.815 (0.740 to 0.870)	0.807 (0.732 to 0.862)
10 Months	0.815 (0.740 to 0.870)	0.799 (0.723 to 0.856)
12 Months	0.815 (0.740 to 0.870)	0.790 (0.713 to 0.848)
14 Months	0.815 (0.740 to 0.870)	0.790 (0.713 to 0.848)
16 Months	0.815 (0.740 to 0.870)	0.769 (0.681 to 0.836)
Number of patients at risk[b]		
2 Months	130	137
4 Months	114	122
6 Months	100	109
8 Months	91	103
10 Months	89	98
12 Months	76	88
14 Months	47	60
16 Months	23	25

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Pyrexia (days)		
Number (%) of events	21 (14.1)	22 (14.5)
Number (%) of patients censored	128 (85.9)	130 (85.5)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (16.000 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.9094
Hazard ratio (95% CI) vs Pd	-	0.966 (0.531 to 1.757)
P-value	-	0.9094
Events probability (95% CI)[b]		
2 Months	0.917 (0.859 to 0.952)	0.941 (0.889 to 0.969)
4 Months	0.895 (0.832 to 0.935)	0.914 (0.856 to 0.949)
6 Months	0.871 (0.803 to 0.917)	0.906 (0.847 to 0.943)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.862 (0.792 to 0.910)	0.883 (0.818 to 0.926)
10 Months	0.853 (0.781 to 0.903)	0.866 (0.798 to 0.913)
12 Months	0.843 (0.769 to 0.895)	0.858 (0.788 to 0.906)
14 Months	0.843 (0.769 to 0.895)	0.846 (0.771 to 0.897)
16 Months	0.843 (0.769 to 0.895)	0.816 (0.717 to 0.884)
Number of patients at risk[b]		
2 Months	130	141
4 Months	121	132
6 Months	104	119
8 Months	96	111
10 Months	91	102
12 Months	76	91
14 Months	48	63
16 Months	24	29
Stomatitis (days)		
Number (%) of events	4 (2.7)	10 (6.6)
Number (%) of patients censored	145 (97.3)	142 (93.4)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1249
Hazard ratio (95% CI) vs Pd	-	2.409 (0.756 to 7.683)
P-value	-	0.1372
Events probability (95% CI)[b]		
2 Months	0.986 (0.945 to 0.996)	0.960 (0.913 to 0.982)
4 Months	0.986 (0.945 to 0.996)	0.939 (0.887 to 0.968)
6 Months	0.977 (0.931 to 0.993)	0.939 (0.887 to 0.968)
8 Months	0.977 (0.931 to 0.993)	0.939 (0.887 to 0.968)
10 Months	0.968 (0.916 to 0.988)	0.931 (0.875 to 0.962)
12 Months	0.968 (0.916 to 0.988)	0.931 (0.875 to 0.962)
14 Months	0.968 (0.916 to 0.988)	0.931 (0.875 to 0.962)
16 Months	0.968 (0.916 to 0.988)	0.931 (0.875 to 0.962)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[b]		
2 Months	140	143
4 Months	132	133
6 Months	114	120
8 Months	103	116
10 Months	99	108
12 Months	84	97
14 Months	53	68
16 Months	26	29
Thrombocytopenia (days)		
Number (%) of events	18 (12.1)	19 (12.5)
Number (%) of patients censored	131 (87.9)	133 (87.5)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.9746
Hazard ratio (95% CI) vs Pd	-	1.011 (0.530 to 1.925)
P-value	-	0.9746
Events probability (95% CI)[b]		
2 Months	0.897 (0.836 to 0.937)	0.894 (0.833 to 0.934)
4 Months	0.890 (0.827 to 0.931)	0.881 (0.817 to 0.923)
6 Months	0.875 (0.809 to 0.920)	0.881 (0.817 to 0.923)
8 Months	0.875 (0.809 to 0.920)	0.873 (0.808 to 0.917)
10 Months	0.875 (0.809 to 0.920)	0.873 (0.808 to 0.917)
12 Months	0.875 (0.809 to 0.920)	0.873 (0.808 to 0.917)
14 Months	0.875 (0.809 to 0.920)	0.873 (0.808 to 0.917)
16 Months	0.875 (0.809 to 0.920)	0.873 (0.808 to 0.917)
Number of patients at risk[b]		
2 Months	128	134
4 Months	121	125
6 Months	109	114

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	100	109
10 Months	96	102
12 Months	82	92
14 Months	51	62
16 Months	24	27
Tremor (days)		
Number (%) of events	6 (4.0)	12 (7.9)
Number (%) of patients censored	143 (96.0)	140 (92.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1879
Hazard ratio (95% CI) vs Pd	-	1.910 (0.717 to 5.089)
P-value	-	0.1957

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[b]		
2 Months	0.986 (0.945 to 0.996)	0.973 (0.931 to 0.990)
4 Months	0.964 (0.915 to 0.985)	0.932 (0.878 to 0.963)
6 Months	0.964 (0.915 to 0.985)	0.932 (0.878 to 0.963)
8 Months	0.955 (0.902 to 0.980)	0.932 (0.878 to 0.963)
10 Months	0.955 (0.902 to 0.980)	0.924 (0.866 to 0.957)
12 Months	0.955 (0.902 to 0.980)	0.915 (0.854 to 0.951)
14 Months	0.955 (0.902 to 0.980)	0.915 (0.854 to 0.951)
16 Months	0.955 (0.902 to 0.980)	0.915 (0.854 to 0.951)
Number of patients at risk[b]		
2 Months	140	145
4 Months	129	131
6 Months	114	119
8 Months	102	115
10 Months	98	107
12 Months	83	94
14 Months	51	68
16 Months	23	29

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Upper respiratory tract infection (days)		
Number (%) of events	26 (17.4)	43 (28.3)
Number (%) of patients censored	123 (82.6)	109 (71.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (8.936 to NC)	7.82 (5.290 to 15.869)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0577
Hazard ratio (95% CI) vs Pd	-	1.596 (0.981 to 2.597)
P-value	-	0.0600
Events probability (95% CI)[b]		
2 Months	0.903 (0.842 to 0.942)	0.914 (0.856 to 0.949)
4 Months	0.874 (0.808 to 0.919)	0.845 (0.775 to 0.894)
6 Months	0.858 (0.788 to 0.906)	0.776 (0.698 to 0.836)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.830 (0.755 to 0.884)	0.734 (0.651 to 0.800)
10 Months	0.811 (0.731 to 0.869)	0.716 (0.632 to 0.785)
12 Months	0.811 (0.731 to 0.869)	0.706 (0.620 to 0.776)
14 Months	0.793 (0.705 to 0.857)	0.685 (0.596 to 0.758)
16 Months	0.793 (0.705 to 0.857)	0.655 (0.549 to 0.741)
Number of patients at risk[b]		
2 Months	128	136
4 Months	116	119
6 Months	98	97
8 Months	87	87
10 Months	82	79
12 Months	70	68
14 Months	42	47
16 Months	20	19
Urinary tract infection (days)		
Number (%) of events	14 (9.4)	15 (9.9)
Number (%) of patients censored	135 (90.6)	137 (90.1)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (16.920 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.9749
Hazard ratio (95% CI) vs Pd	-	1.012 (0.488 to 2.097)
P-value	-	0.9749
Events probability (95% CI)[b]		
2 Months	0.958 (0.910 to 0.981)	0.954 (0.905 to 0.978)
4 Months	0.929 (0.872 to 0.961)	0.913 (0.855 to 0.949)
6 Months	0.921 (0.862 to 0.956)	0.913 (0.855 to 0.949)
8 Months	0.894 (0.827 to 0.936)	0.913 (0.855 to 0.949)
10 Months	0.894 (0.827 to 0.936)	0.913 (0.855 to 0.949)
12 Months	0.894 (0.827 to 0.936)	0.904 (0.844 to 0.942)
14 Months	0.894 (0.827 to 0.936)	0.904 (0.844 to 0.942)
16 Months	0.894 (0.827 to 0.936)	0.904 (0.844 to 0.942)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[b]		
2 Months	136	143
4 Months	125	130
6 Months	108	119
8 Months	94	115
10 Months	90	108
12 Months	78	95
14 Months	48	65
16 Months	24	27
Vomiting (days)		
Number (%) of events	5 (3.4)	18 (11.8)
Number (%) of patients censored	144 (96.6)	134 (88.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0078
Hazard ratio (95% CI) vs Pd	-	3.525 (1.309 to 9.495)
P-value	-	0.0127
Hazard ratio inverted (95% CI) vs IPd	0.284 (0.105 to 0.764)	-
Events probability (95% CI)[b]		
2 Months	0.986 (0.947 to 0.997)	0.947 (0.897 to 0.973)
4 Months	0.986 (0.947 to 0.997)	0.919 (0.861 to 0.953)
6 Months	0.978 (0.934 to 0.993)	0.919 (0.861 to 0.953)
8 Months	0.960 (0.907 to 0.983)	0.895 (0.831 to 0.935)
10 Months	0.960 (0.907 to 0.983)	0.887 (0.821 to 0.929)
12 Months	0.960 (0.907 to 0.983)	0.878 (0.810 to 0.922)
14 Months	0.960 (0.907 to 0.983)	0.864 (0.791 to 0.913)
16 Months	0.960 (0.907 to 0.983)	0.864 (0.791 to 0.913)
Number of patients at risk[b]		
2 Months	141	141
4 Months	133	129

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	115	117
8 Months	102	110
10 Months	98	102
12 Months	83	90
14 Months	50	57
16 Months	23	25
Weight decreased (days)		
Number (%) of events	2 (1.3)	10 (6.6)
Number (%) of patients censored	147 (98.7)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0084
Hazard ratio (95% CI) vs Pd	-	9.543 (1.222 to 74.547)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
P-value	-	0.0315
Hazard ratio inverted (95% CI) vs IPd	0.105 (0.013 to 0.819)	-
Events probability (95% CI)[b]		
2 Months	0.993 (0.952 to 0.999)	0.967 (0.923 to 0.986)
4 Months	0.993 (0.952 to 0.999)	0.947 (0.896 to 0.973)
6 Months	0.993 (0.952 to 0.999)	0.939 (0.887 to 0.968)
8 Months	0.993 (0.952 to 0.999)	0.939 (0.887 to 0.968)
10 Months	0.993 (0.952 to 0.999)	0.931 (0.875 to 0.962)
12 Months	0.993 (0.952 to 0.999)	0.931 (0.875 to 0.962)
14 Months	0.993 (0.952 to 0.999)	0.931 (0.875 to 0.962)
16 Months	0.993 (0.952 to 0.999)	0.931 (0.875 to 0.962)
Number of patients at risk[b]		
2 Months	140	145
4 Months	132	134
6 Months	116	121
8 Months	105	116
10 Months	101	108
12 Months	86	97

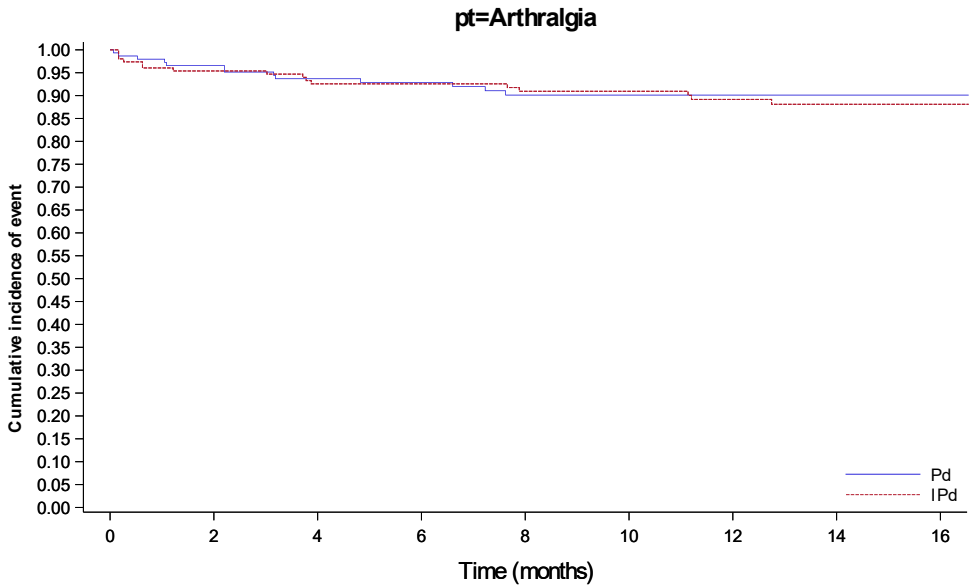
PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.3 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	54	67
16 Months	26	29

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

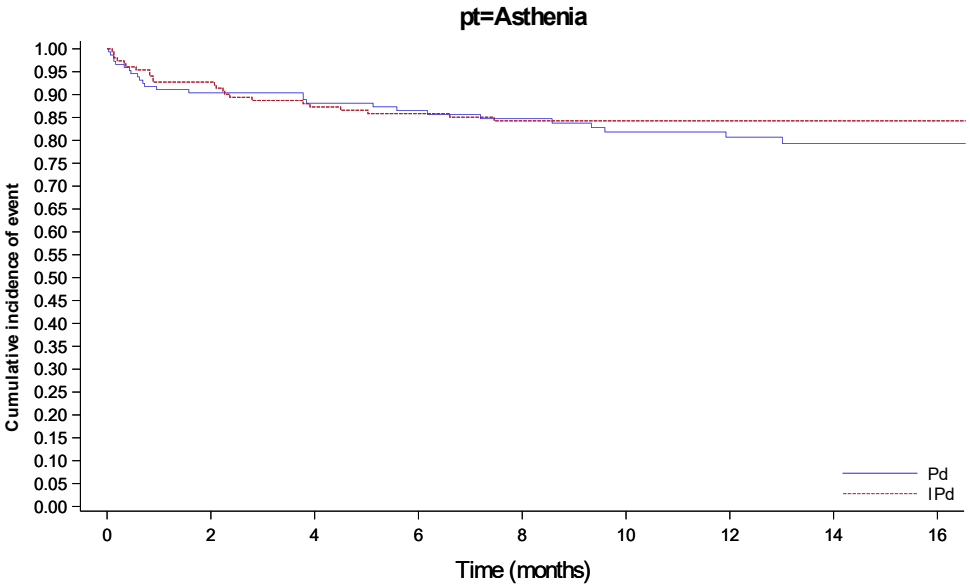
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	137	125	107	94	91	76	49	25
IPd	152	142	130	119	112	105	92	61	25

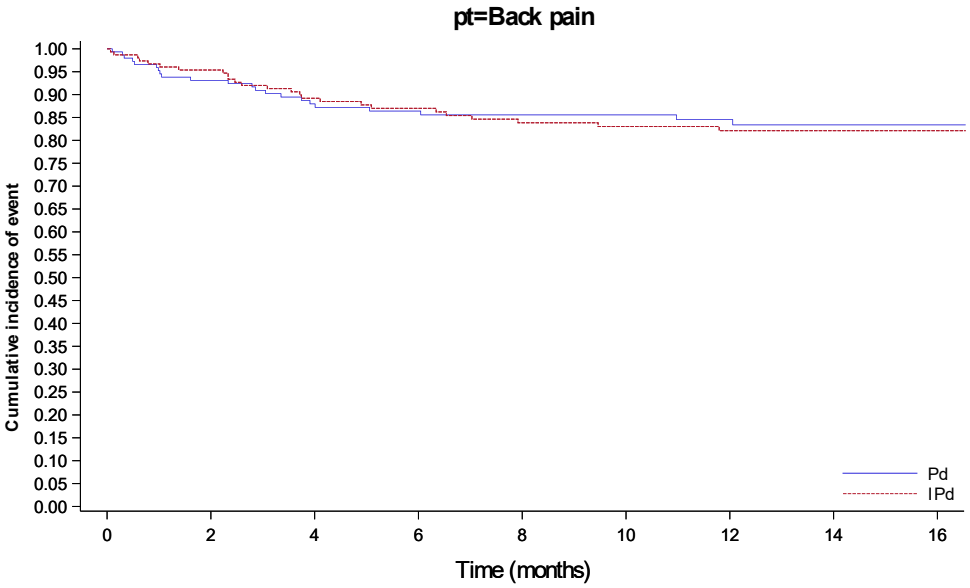
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	148	128	118	102	91	84	71	45	24
IPd	152	139	123	111	105	98	87	58	28

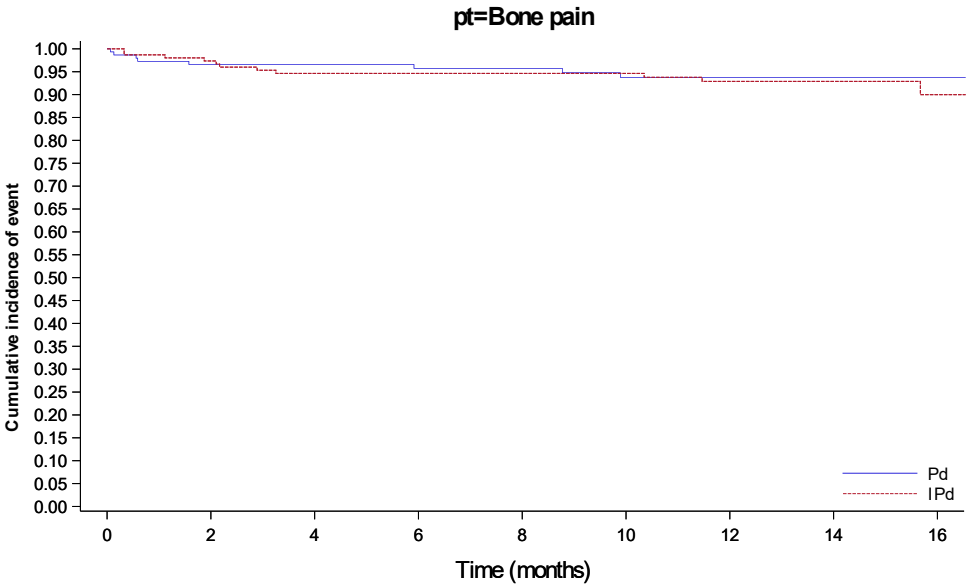
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	132	117	102	92	88	74	45	20
IPd	152	142	126	111	106	101	89	61	27

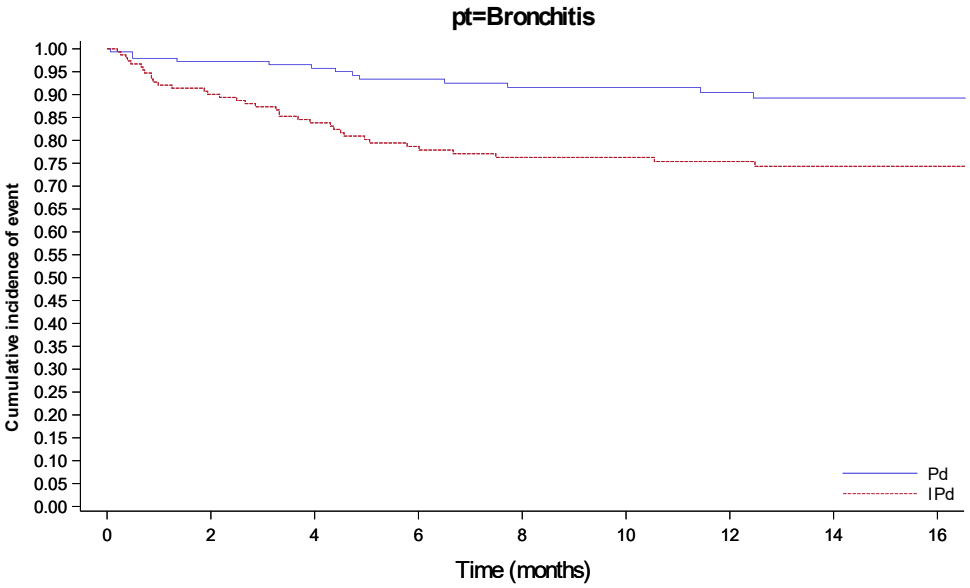
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	138	131	113	102	96	83	51	24
IPd	152	145	133	120	115	112	98	67	26

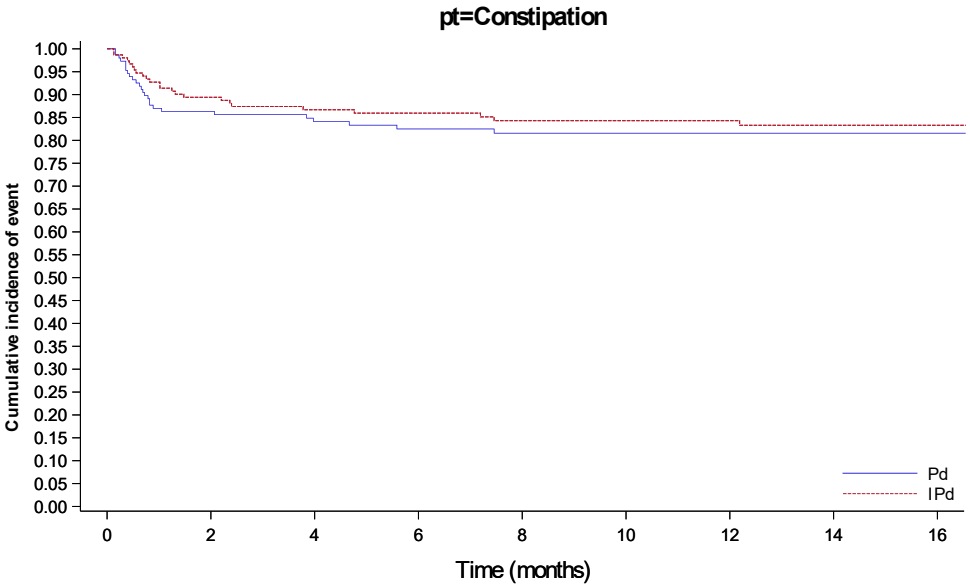
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



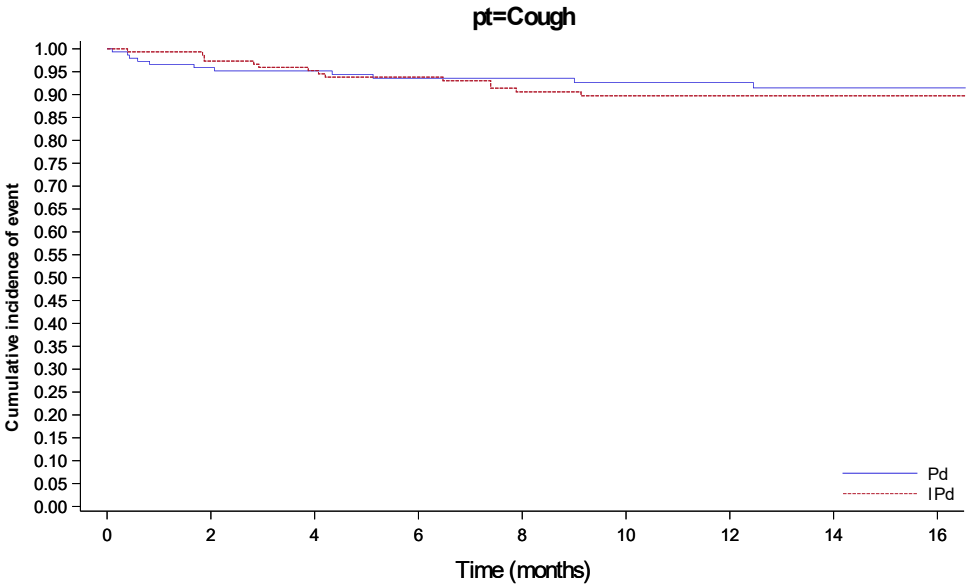
Number at Risk

Pd	149	138	128	110	97	93	77	46	22
IPd	152	134	117	100	93	87	76	51	22

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



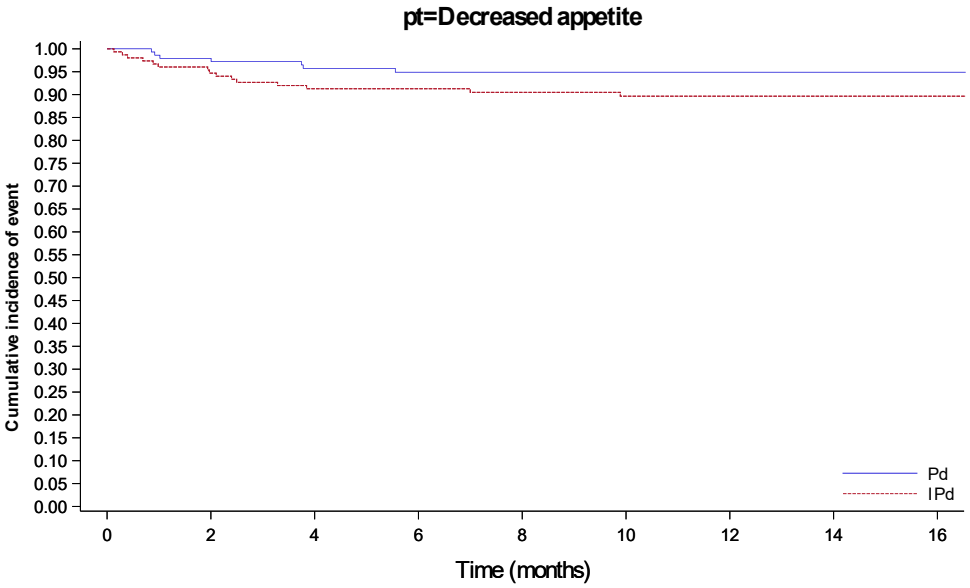
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	136	128	111	102	97	82	49	23
IPd	152	145	134	120	111	103	92	63	27

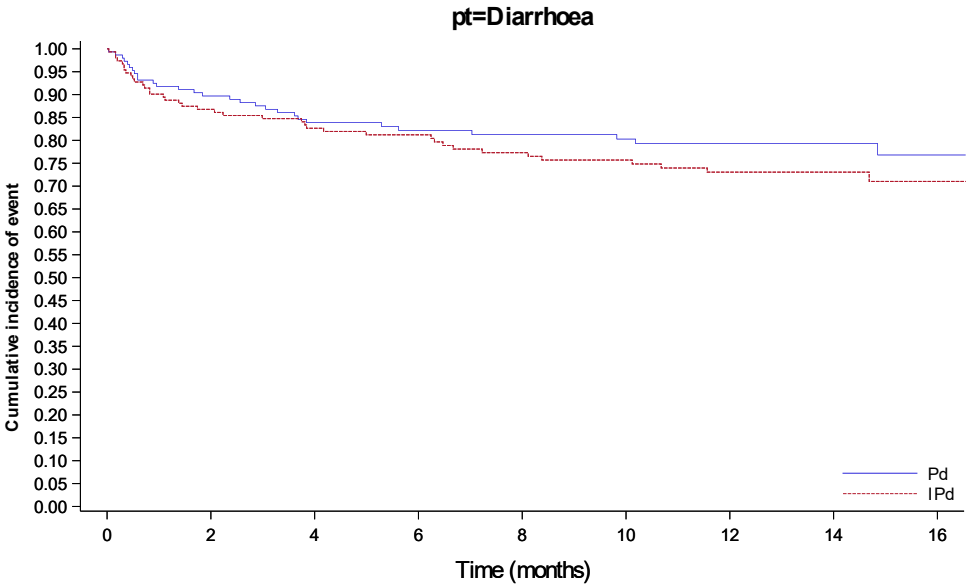
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	139	129	112	101	97	82	51	24
IPd	152	141	130	119	114	107	96	65	30

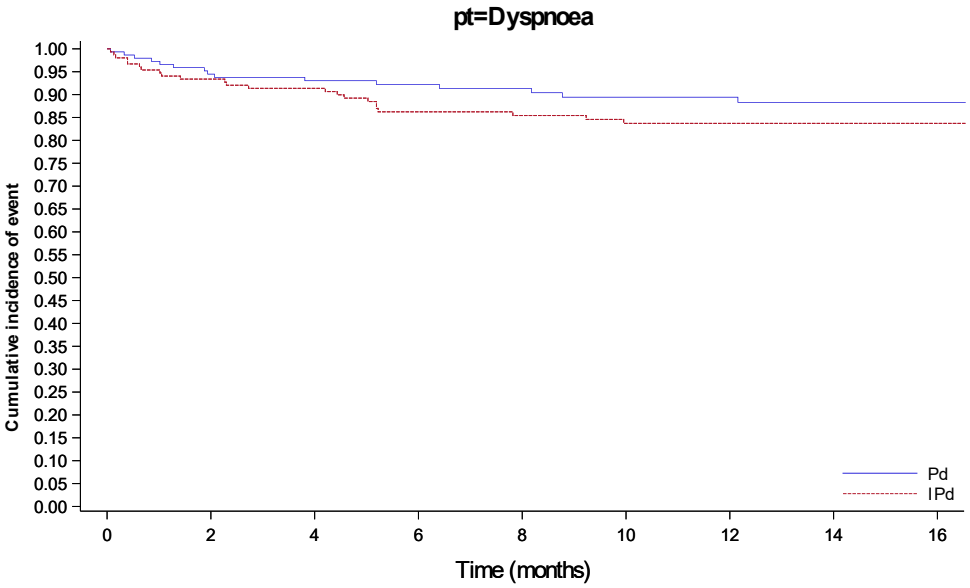
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	127	113	96	85	82	72	45	22
IPd	152	129	118	106	97	88	76	51	21

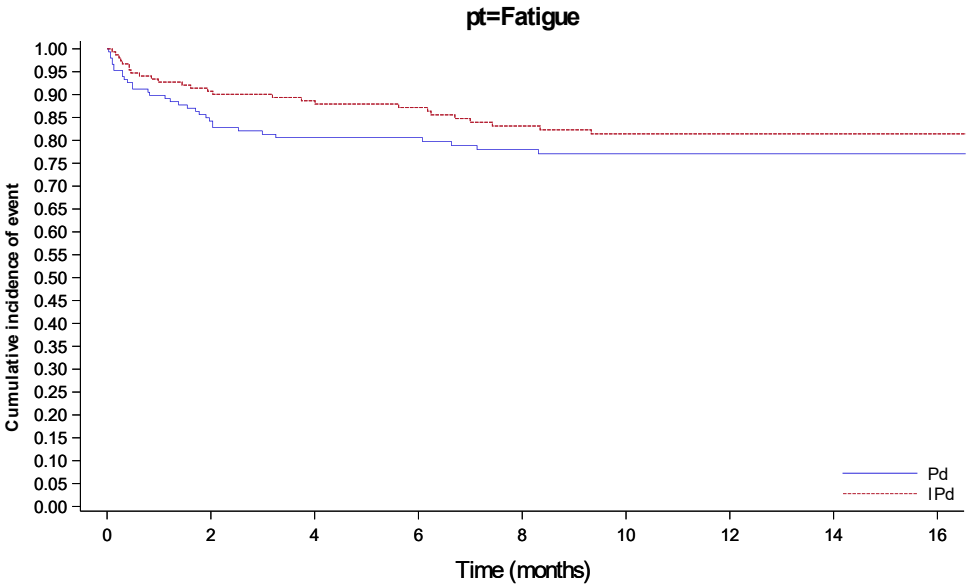
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	134	124	109	99	93	80	48	23
IPd	152	139	130	112	106	97	87	61	27

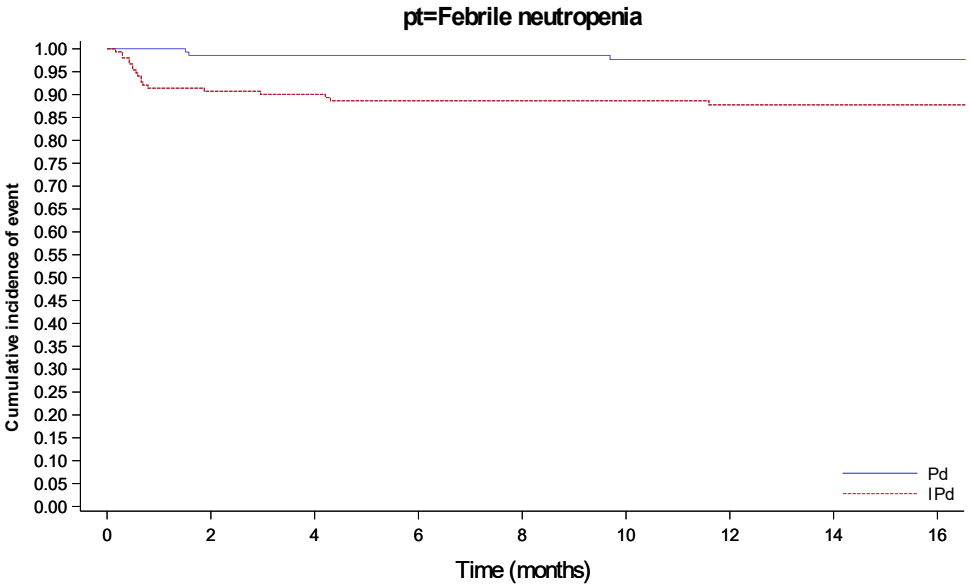
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	119	107	95	84	79	68	40	19
IPd	152	135	124	110	101	92	83	57	26

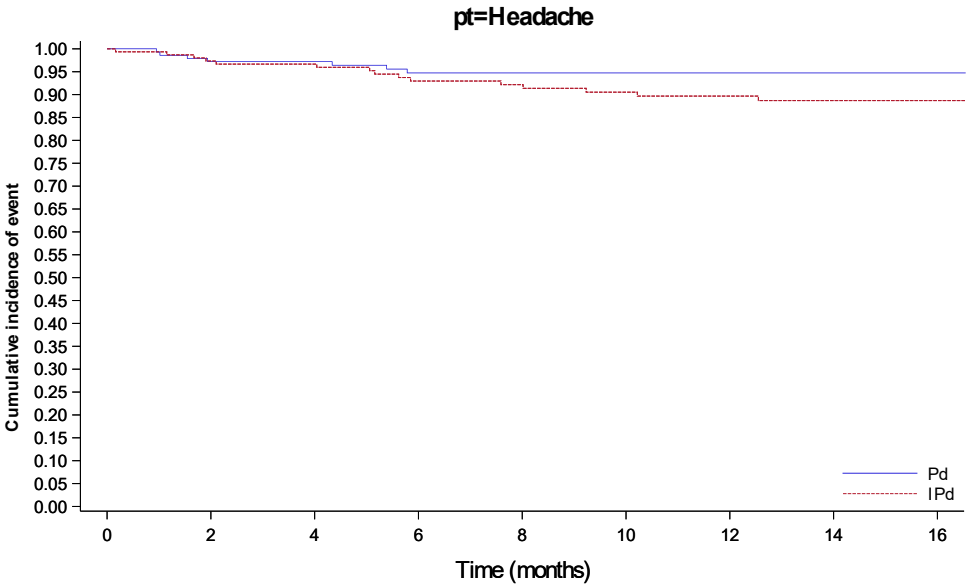
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	140	132	116	105	100	86	54	26
IPd	152	135	129	114	110	107	94	64	26

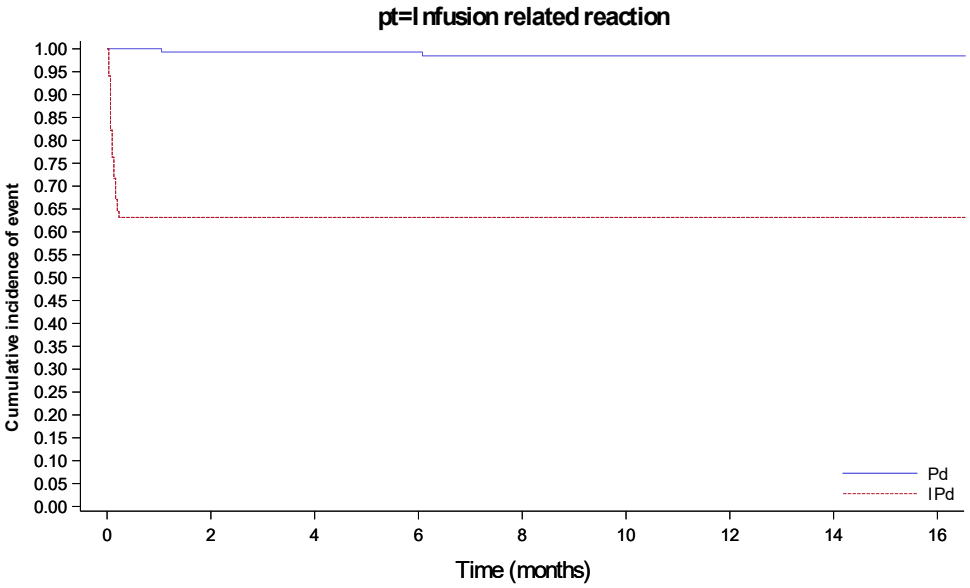
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	148	137	129	111	101	97	83	52	24
IPd	152	145	138	121	115	107	94	65	28

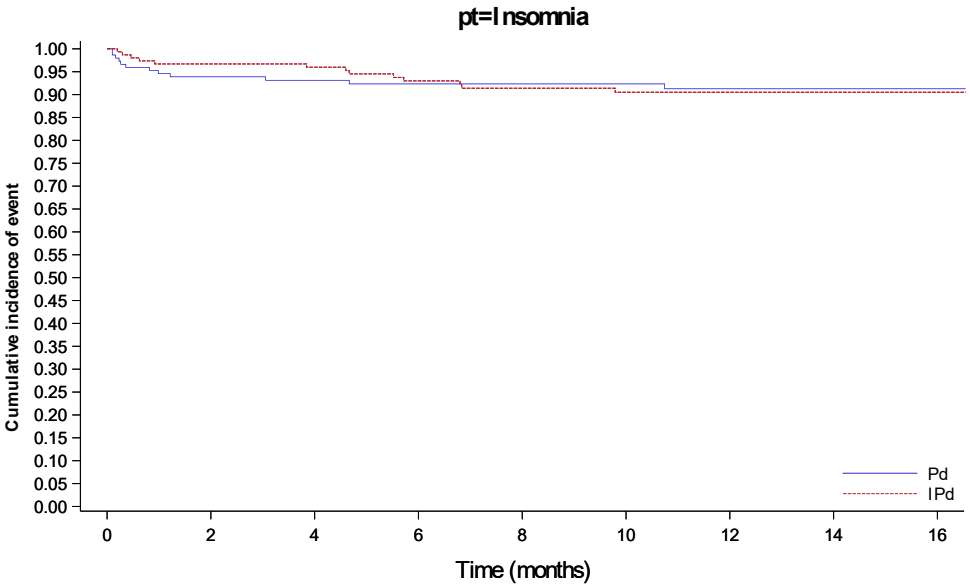
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	141	134	117	105	101	86	53	26
IPd	152	95	90	81	77	71	63	40	15

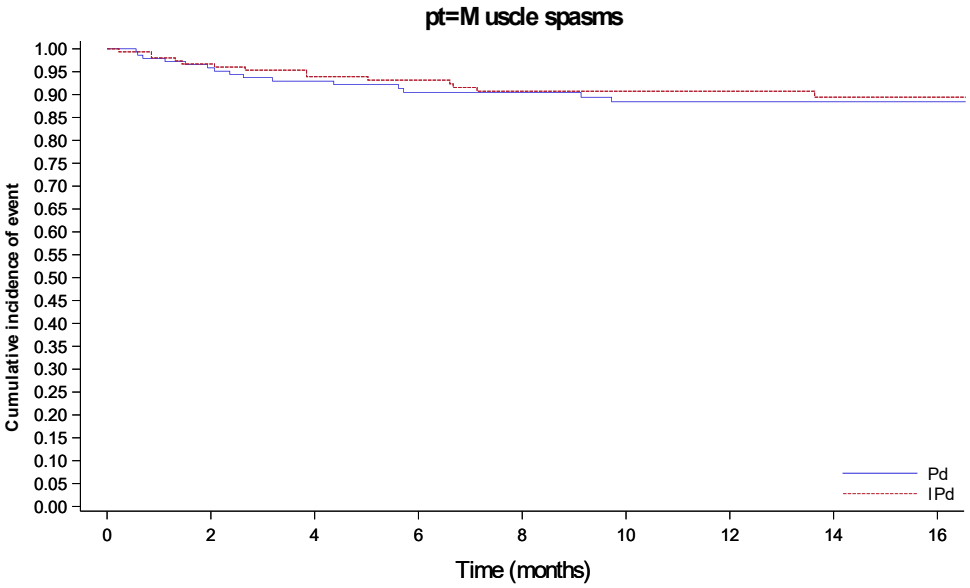
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	133	124	107	97	93	77	48	23
IPd	152	144	135	118	111	103	92	63	26

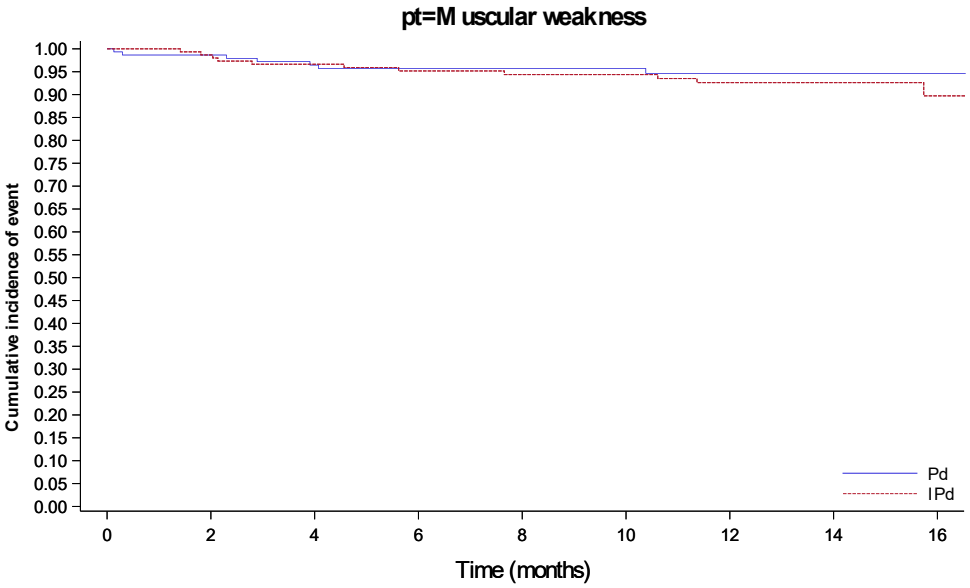
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	136	124	104	93	87	74	46	20
IPd	152	144	132	118	110	103	93	65	26

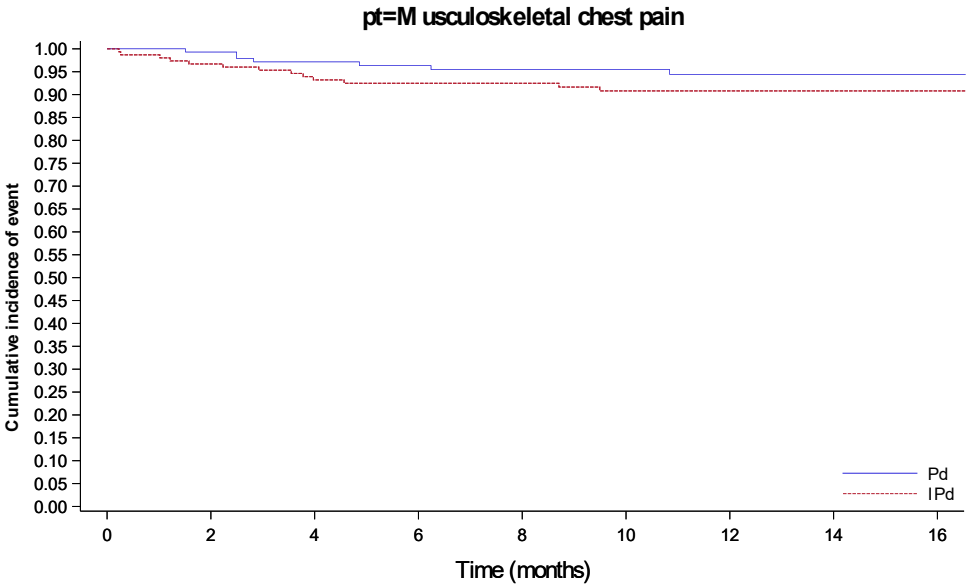
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	140	129	111	100	96	81	50	24
IPd	152	147	137	123	118	111	97	66	28

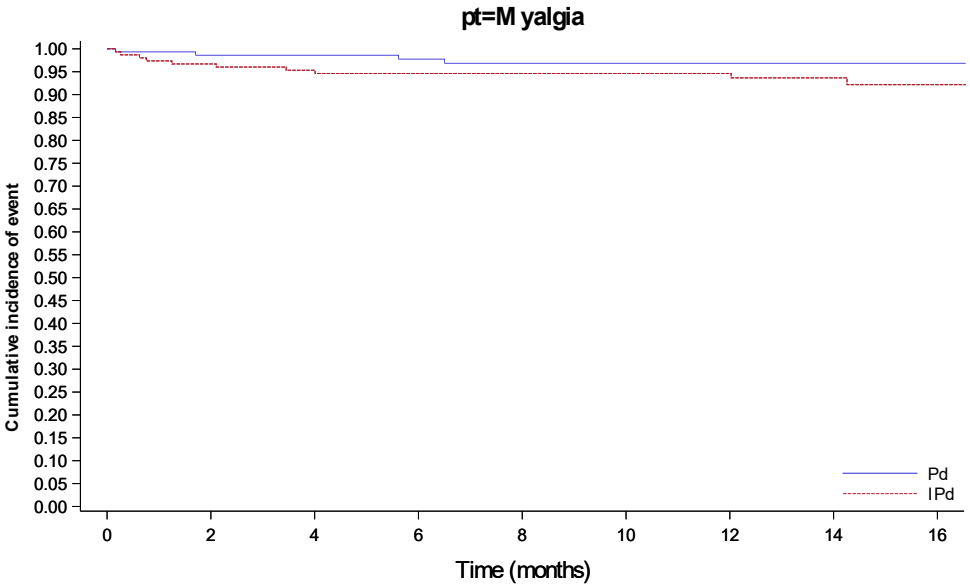
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	141	130	112	100	98	82	50	25
IPd	152	144	131	119	115	106	95	65	29

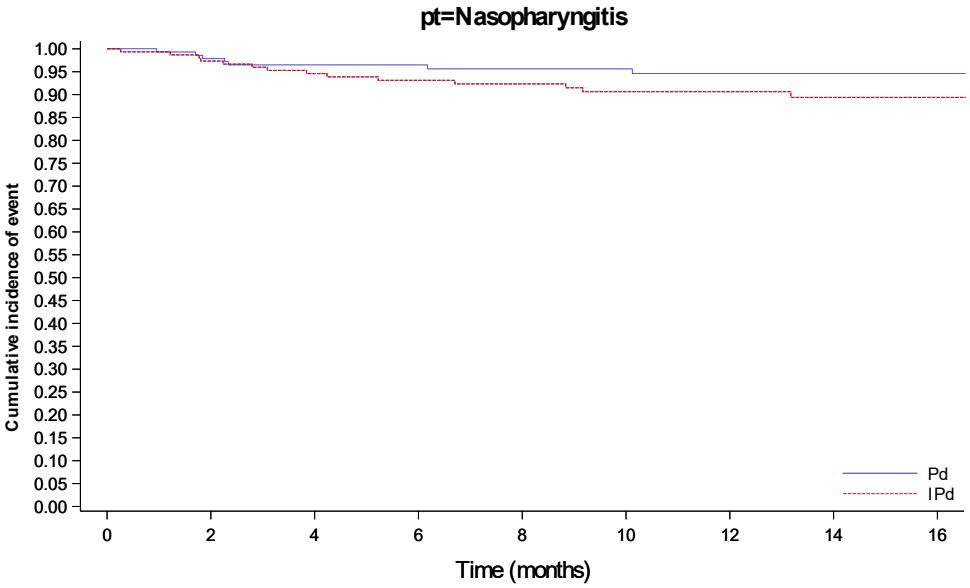
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	148	139	131	113	102	98	84	52	26
IPd	152	144	134	120	117	110	99	67	27

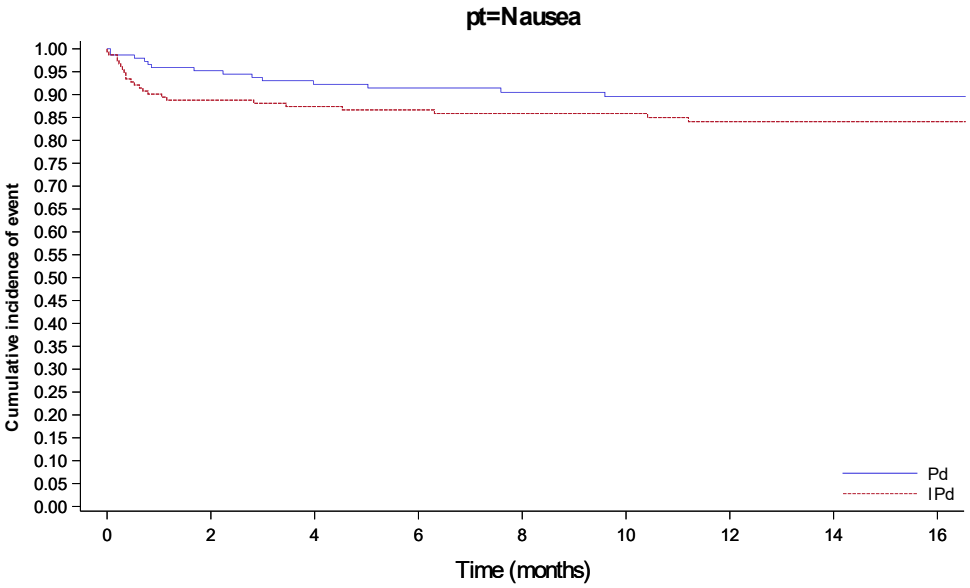
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	139	129	112	100	96	80	49	23
IPd	152	145	134	119	114	105	93	64	28

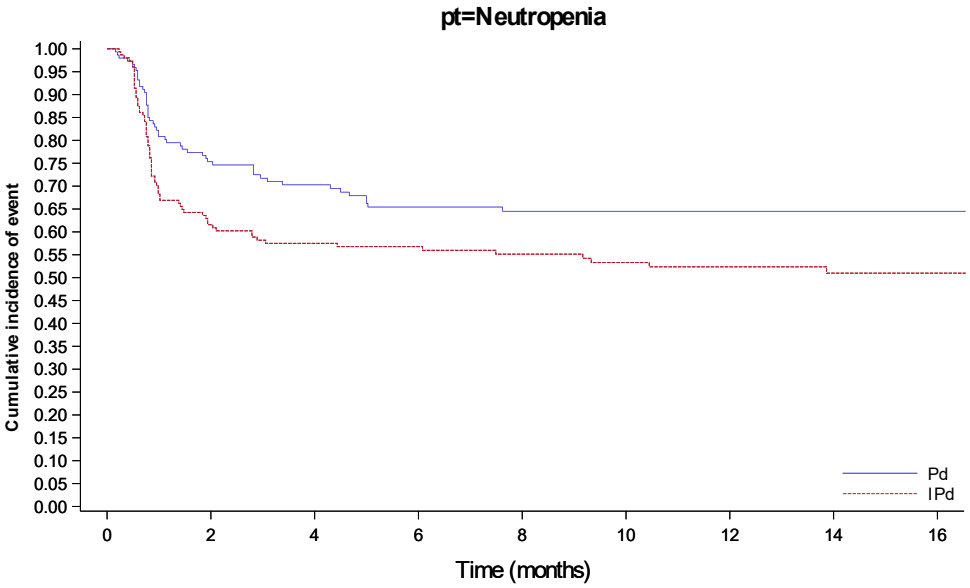
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	135	123	105	96	91	77	48	24
IPd	152	132	122	111	105	98	87	58	25

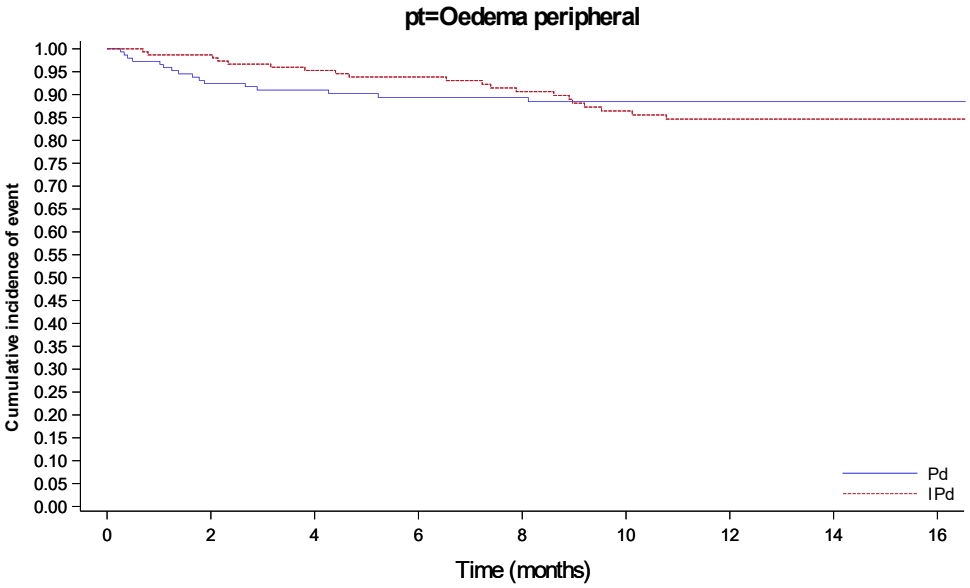
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	109	94	78	69	67	59	38	23
IPd	152	92	81	70	65	57	51	34	14

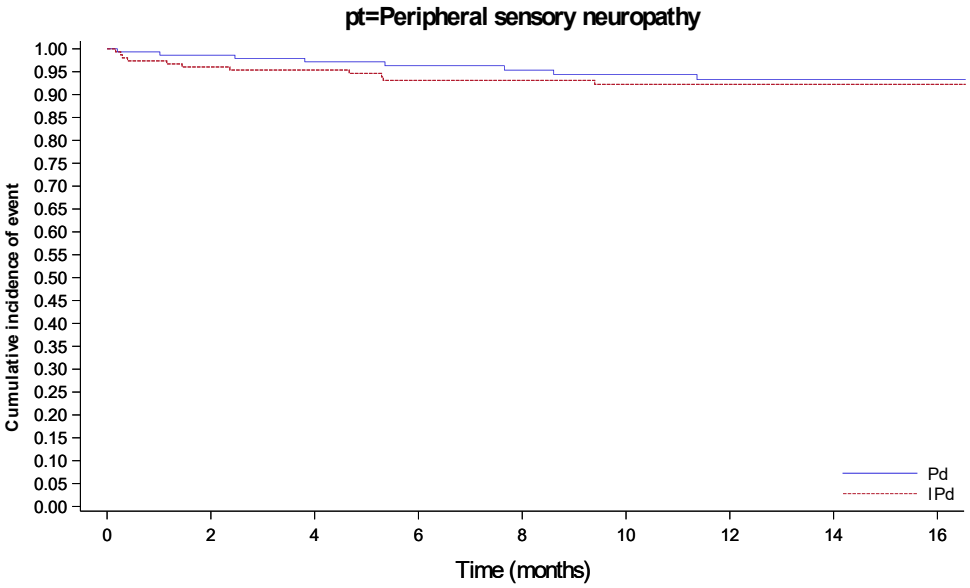
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	132	123	104	95	90	76	48	23
IPd	152	147	136	121	112	100	86	60	27

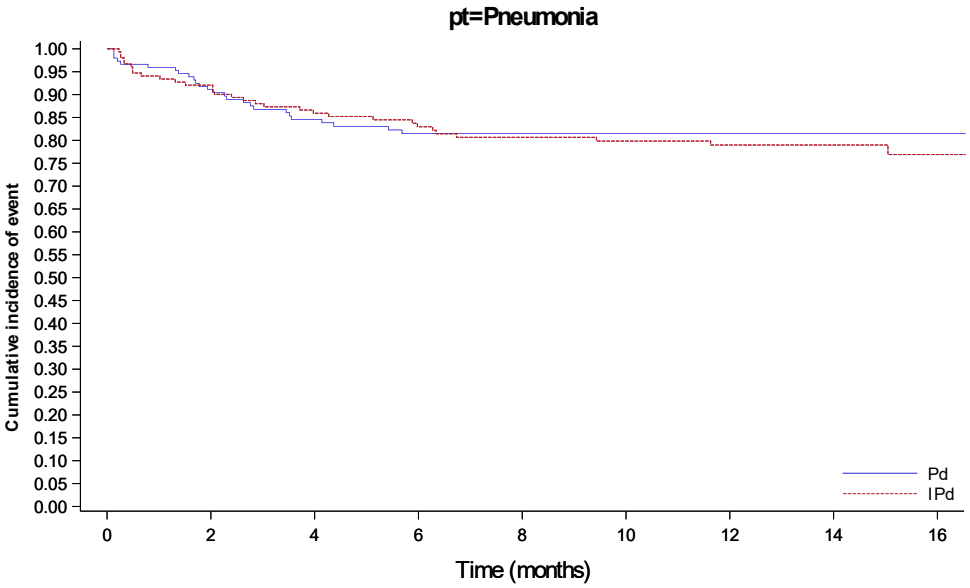
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	148	139	129	111	99	94	80	47	23
IPd	152	143	134	118	113	105	94	62	27

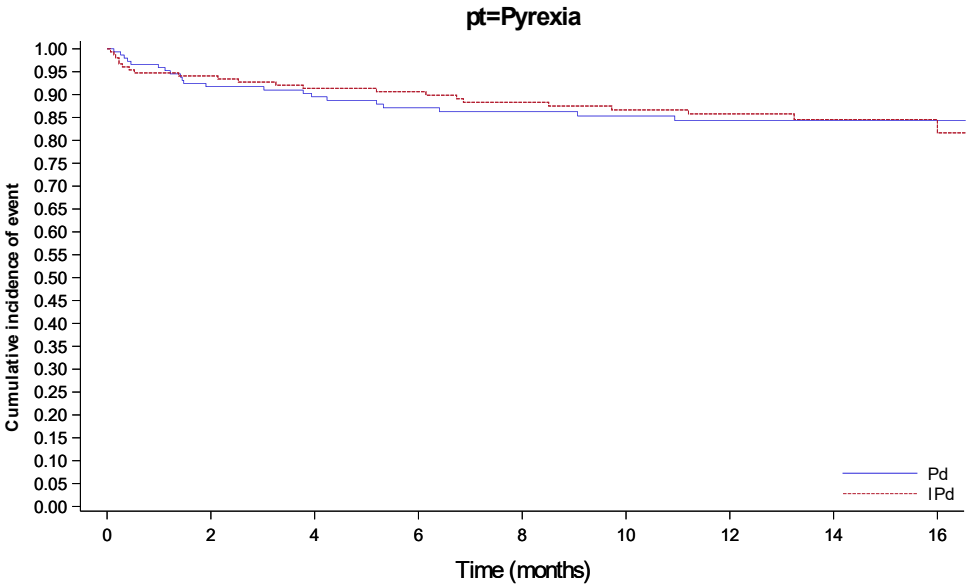
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	130	114	100	91	89	76	47	23
IPd	152	137	122	109	103	98	88	60	25

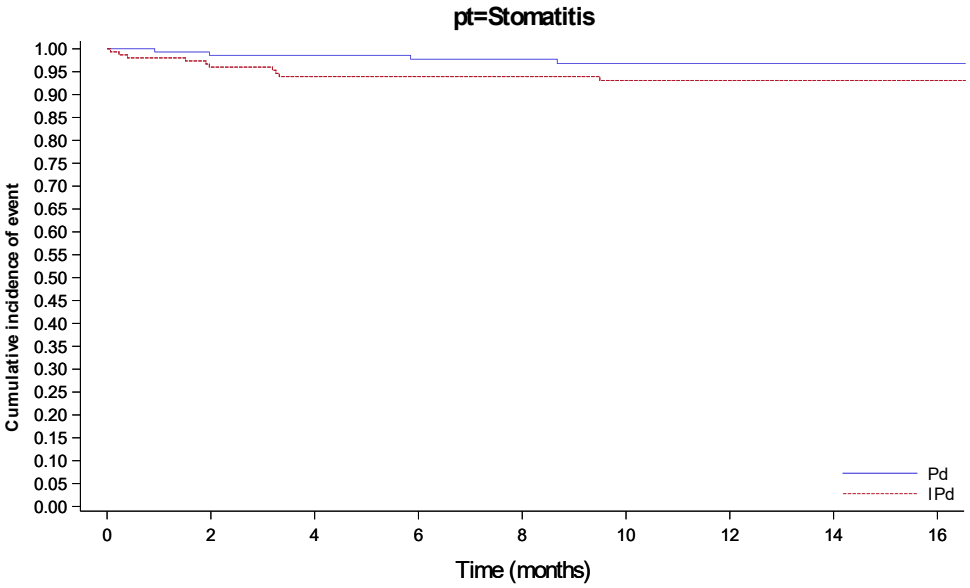
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	130	121	104	96	91	76	48	24
IPd	152	141	132	119	111	102	91	63	29

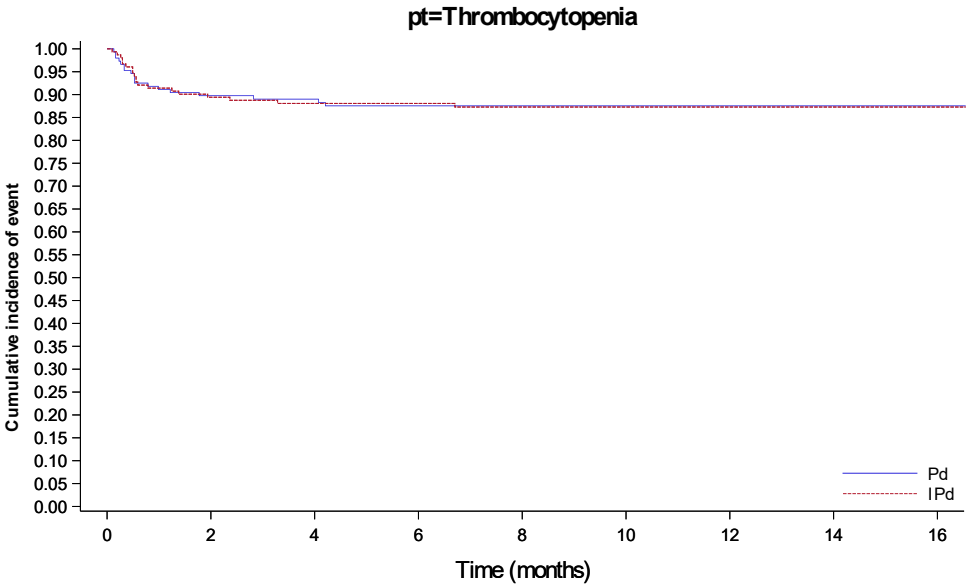
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	140	132	114	103	99	84	53	26
IPd	152	143	133	120	116	108	97	68	29

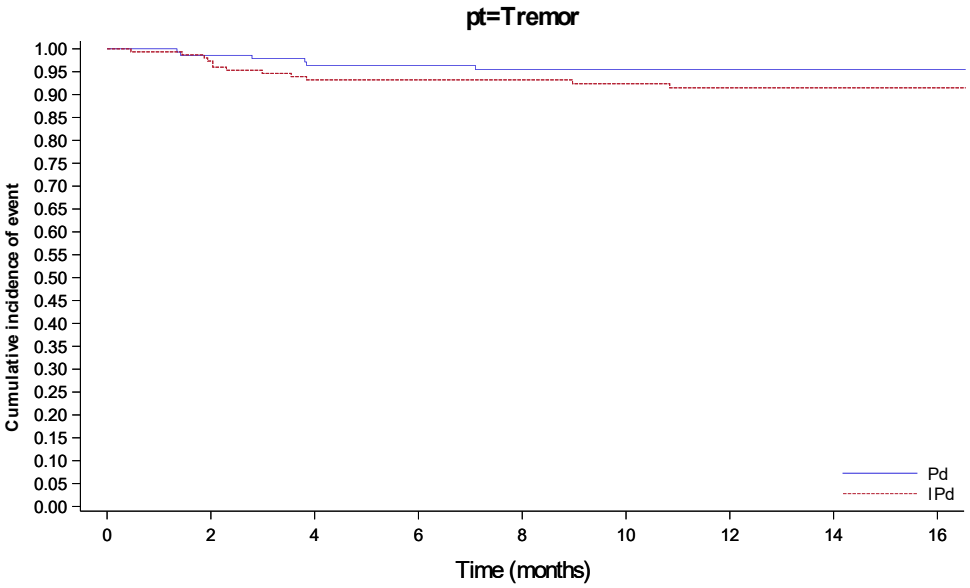
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	128	121	109	100	96	82	51	24
IPd	152	134	125	114	109	102	92	62	27

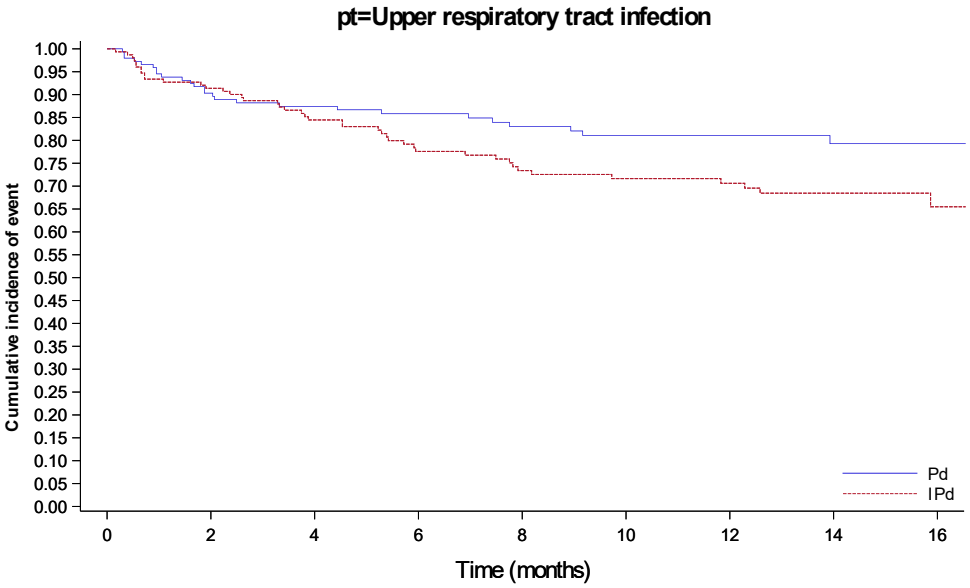
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	140	129	114	102	98	83	51	23
IPd	152	145	131	119	115	107	94	68	29

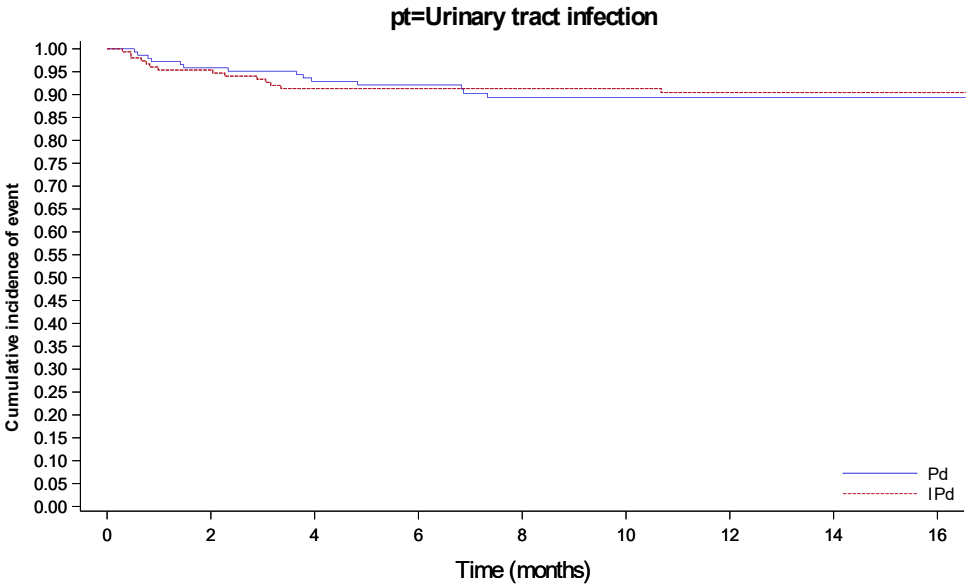
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	128	116	98	87	82	70	42	20
IPd	152	136	119	97	87	79	68	47	19

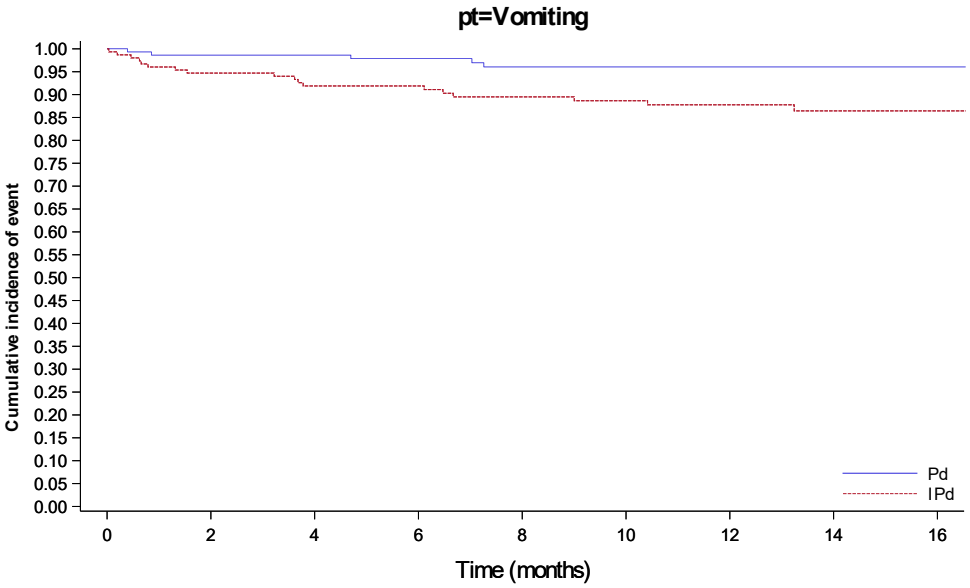
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	136	125	108	94	90	78	48	24
IPd	152	143	130	119	115	108	95	65	27

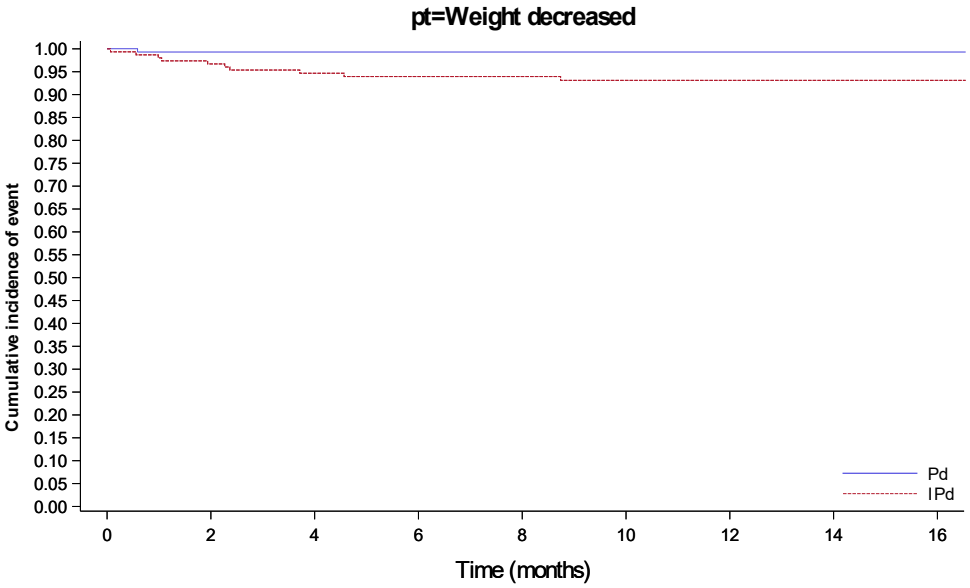
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	141	133	115	102	98	83	50	23
IPd	152	141	129	117	110	102	90	57	25

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	148	140	132	116	105	101	86	54	26
IPd	152	145	134	121	116	108	97	67	29

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.5 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Blood and lymphatic system disorders (days)		
Number (%) of events	10 (6.7)	18 (11.8)
Number (%) of patients censored	139 (93.3)	134 (88.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1370
Hazard ratio (95% CI) vs Pd	-	1.783 (0.823 to 3.863)
P-value	-	0.1425
Events probability (95% CI)[b]		
2 Months	0.945 (0.893 to 0.972)	0.901 (0.841 to 0.939)
4 Months	0.938 (0.884 to 0.967)	0.887 (0.825 to 0.928)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.5 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	0.938 (0.884 to 0.967)	0.887 (0.825 to 0.928)
8 Months	0.938 (0.884 to 0.967)	0.887 (0.825 to 0.928)
10 Months	0.929 (0.871 to 0.961)	0.879 (0.814 to 0.922)
12 Months	0.929 (0.871 to 0.961)	0.879 (0.814 to 0.922)
14 Months	0.929 (0.871 to 0.961)	0.879 (0.814 to 0.922)
16 Months	0.929 (0.871 to 0.961)	0.879 (0.814 to 0.922)
Number of patients at risk[b]		
2 Months	135	135
4 Months	128	126
6 Months	114	115
8 Months	104	111
10 Months	99	106
12 Months	85	94
14 Months	53	63
16 Months	25	26
General disorders and administration site conditions (days)		
Number (%) of events	13 (8.7)	16 (10.5)
Number (%) of patients censored	136 (91.3)	136 (89.5)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.5 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (15.967 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.7563
Hazard ratio (95% CI) vs Pd	-	1.122 (0.540 to 2.334)
P-value	-	0.7574
Events probability (95% CI)[b]		
2 Months	0.966 (0.920 to 0.986)	0.974 (0.931 to 0.990)
4 Months	0.937 (0.882 to 0.967)	0.953 (0.904 to 0.977)
6 Months	0.906 (0.844 to 0.944)	0.933 (0.878 to 0.963)
8 Months	0.906 (0.844 to 0.944)	0.918 (0.859 to 0.952)
10 Months	0.906 (0.844 to 0.944)	0.902 (0.839 to 0.941)
12 Months	0.906 (0.844 to 0.944)	0.902 (0.839 to 0.941)
14 Months	0.906 (0.844 to 0.944)	0.902 (0.839 to 0.941)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.5 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	0.906 (0.844 to 0.944)	0.853 (0.749 to 0.916)
Number of patients at risk[b]		
2 Months	139	146
4 Months	128	139
6 Months	112	126
8 Months	102	121
10 Months	98	113
12 Months	83	102
14 Months	52	70
16 Months	26	28
Infections and infestations (days)		
Number (%) of events	46 (30.9)	60 (39.5)
Number (%) of patients censored	103 (69.1)	92 (60.5)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	4.37 (2.267 to 11.433)	4.44 (2.267 to 7.524)
Median (95% CI)	NC (NC to NC)	NC (11.302 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.5 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2628
Hazard ratio (95% CI) vs Pd	-	1.246 (0.847 to 1.832)
P-value	-	0.2637
Events probability (95% CI)[b]		
2 Months	0.850 (0.781 to 0.898)	0.833 (0.763 to 0.884)
4 Months	0.750 (0.671 to 0.813)	0.779 (0.703 to 0.837)
6 Months	0.720 (0.638 to 0.786)	0.701 (0.619 to 0.768)
8 Months	0.704 (0.621 to 0.772)	0.663 (0.580 to 0.734)
10 Months	0.695 (0.611 to 0.764)	0.617 (0.531 to 0.691)
12 Months	0.677 (0.591 to 0.748)	0.585 (0.498 to 0.662)
14 Months	0.677 (0.591 to 0.748)	0.585 (0.498 to 0.662)
16 Months	0.657 (0.564 to 0.735)	0.585 (0.498 to 0.662)
Number of patients at risk[b]		
2 Months	122	124
4 Months	104	112

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.5 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	92	94
8 Months	81	88
10 Months	79	79
12 Months	66	68
14 Months	41	45
16 Months	20	19
Injury, poisoning and procedural complications (days)		
Number (%) of events	2 (1.3)	11 (7.2)
Number (%) of patients censored	147 (98.7)	141 (92.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0137
Hazard ratio (95% CI) vs Pd	-	5.402 (1.197 to 24.366)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.5 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
P-value	-	0.0282
Hazard ratio inverted (95% CI) vs IPd	0.185 (0.041 to 0.835)	-
Events probability (95% CI)[b]		
2 Months	0.986 (0.946 to 0.997)	0.954 (0.906 to 0.978)
4 Months	0.986 (0.946 to 0.997)	0.934 (0.880 to 0.964)
6 Months	0.986 (0.946 to 0.997)	0.934 (0.880 to 0.964)
8 Months	0.986 (0.946 to 0.997)	0.926 (0.870 to 0.958)
10 Months	0.986 (0.946 to 0.997)	0.926 (0.870 to 0.958)
12 Months	0.986 (0.946 to 0.997)	0.926 (0.870 to 0.958)
14 Months	0.986 (0.946 to 0.997)	0.926 (0.870 to 0.958)
16 Months	0.986 (0.946 to 0.997)	0.926 (0.870 to 0.958)
Number of patients at risk[b]		
2 Months	140	143
4 Months	133	134
6 Months	116	121
8 Months	105	115
10 Months	101	108
12 Months	86	96

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.5 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	53	65
16 Months	26	27
Metabolism and nutrition disorders (days)		
Number (%) of events	6 (4.0)	8 (5.3)
Number (%) of patients censored	143 (96.0)	144 (94.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.6405
Hazard ratio (95% CI) vs Pd	-	1.286 (0.446 to 3.707)
P-value	-	0.6413
Events probability (95% CI)[b]		
2 Months	0.966 (0.920 to 0.986)	0.967 (0.922 to 0.986)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.5 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.966 (0.920 to 0.986)	0.953 (0.905 to 0.977)
6 Months	0.958 (0.909 to 0.981)	0.953 (0.905 to 0.977)
8 Months	0.958 (0.909 to 0.981)	0.953 (0.905 to 0.977)
10 Months	0.958 (0.909 to 0.981)	0.945 (0.893 to 0.972)
12 Months	0.958 (0.909 to 0.981)	0.945 (0.893 to 0.972)
14 Months	0.958 (0.909 to 0.981)	0.945 (0.893 to 0.972)
16 Months	0.958 (0.909 to 0.981)	0.945 (0.893 to 0.972)
Number of patients at risk[b]		
2 Months	137	144
4 Months	131	135
6 Months	113	124
8 Months	103	119
10 Months	100	111
12 Months	85	101
14 Months	52	69
16 Months	26	28
Musculoskeletal and connective tissue disorders (days)		
Number (%) of events	6 (4.0)	13 (8.6)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.5 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	143 (96.0)	139 (91.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1443
Hazard ratio (95% CI) vs Pd	-	2.025 (0.770 to 5.331)
P-value	-	0.1528
Events probability (95% CI)[b]		
2 Months	0.972 (0.928 to 0.990)	0.954 (0.905 to 0.978)
4 Months	0.972 (0.928 to 0.990)	0.947 (0.897 to 0.973)
6 Months	0.964 (0.916 to 0.985)	0.940 (0.887 to 0.968)
8 Months	0.955 (0.903 to 0.980)	0.932 (0.877 to 0.963)
10 Months	0.955 (0.903 to 0.980)	0.932 (0.877 to 0.963)
12 Months	0.955 (0.903 to 0.980)	0.923 (0.866 to 0.957)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.5 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.955 (0.903 to 0.980)	0.923 (0.866 to 0.957)
16 Months	0.955 (0.903 to 0.980)	0.882 (0.788 to 0.936)
Number of patients at risk[b]		
2 Months	138	142
4 Months	130	134
6 Months	112	123
8 Months	100	120
10 Months	96	113
12 Months	83	100
14 Months	52	67
16 Months	25	26
Nervous system disorders (days)		
Number (%) of events	6 (4.0)	8 (5.3)
Number (%) of patients censored	143 (96.0)	144 (94.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.5 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.6860
Hazard ratio (95% CI) vs Pd	-	1.243 (0.431 to 3.585)
P-value	-	0.6866
Events probability (95% CI)[b]		
2 Months	0.980 (0.938 to 0.993)	0.987 (0.948 to 0.997)
4 Months	0.980 (0.938 to 0.993)	0.973 (0.930 to 0.990)
6 Months	0.964 (0.915 to 0.985)	0.973 (0.930 to 0.990)
8 Months	0.955 (0.901 to 0.980)	0.949 (0.896 to 0.976)
10 Months	0.955 (0.901 to 0.980)	0.949 (0.896 to 0.976)
12 Months	0.955 (0.901 to 0.980)	0.940 (0.884 to 0.970)
14 Months	0.955 (0.901 to 0.980)	0.940 (0.884 to 0.970)
16 Months	0.955 (0.901 to 0.980)	0.940 (0.884 to 0.970)
Number of patients at risk[b]		
2 Months	140	147

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.5 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	132	137
6 Months	114	124
8 Months	102	116
10 Months	98	110
12 Months	84	97
14 Months	52	66
16 Months	25	27
Renal and urinary disorders (days)		
Number (%) of events	10 (6.7)	9 (5.9)
Number (%) of patients censored	139 (93.3)	143 (94.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.7143

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.5 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	0.845 (0.343 to 2.081)
P-value	-	0.7146
Events probability (95% CI)[b]		
2 Months	0.945 (0.893 to 0.972)	0.960 (0.914 to 0.982)
4 Months	0.945 (0.893 to 0.972)	0.954 (0.905 to 0.978)
6 Months	0.937 (0.882 to 0.967)	0.954 (0.905 to 0.978)
8 Months	0.928 (0.870 to 0.961)	0.954 (0.905 to 0.978)
10 Months	0.928 (0.870 to 0.961)	0.945 (0.893 to 0.972)
12 Months	0.928 (0.870 to 0.961)	0.937 (0.882 to 0.967)
14 Months	0.928 (0.870 to 0.961)	0.937 (0.882 to 0.967)
16 Months	0.928 (0.870 to 0.961)	0.937 (0.882 to 0.967)
Number of patients at risk[b]		
2 Months	135	144
4 Months	128	136
6 Months	113	125
8 Months	102	121
10 Months	98	113
12 Months	83	101

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.5 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	51	69
16 Months	24	29
Respiratory, thoracic and mediastinal disorders (days)		
Number (%) of events	8 (5.4)	10 (6.6)
Number (%) of patients censored	141 (94.6)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.7483
Hazard ratio (95% CI) vs Pd	-	1.164 (0.459 to 2.951)
P-value	-	0.7485
Events probability (95% CI)[b]		
2 Months	0.986 (0.947 to 0.997)	0.974 (0.931 to 0.990)

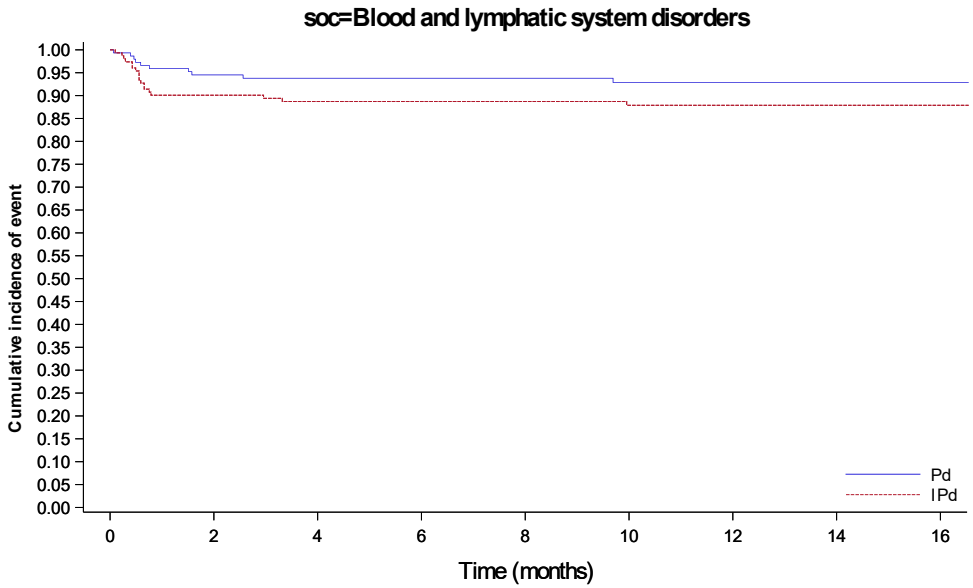
SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.5 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

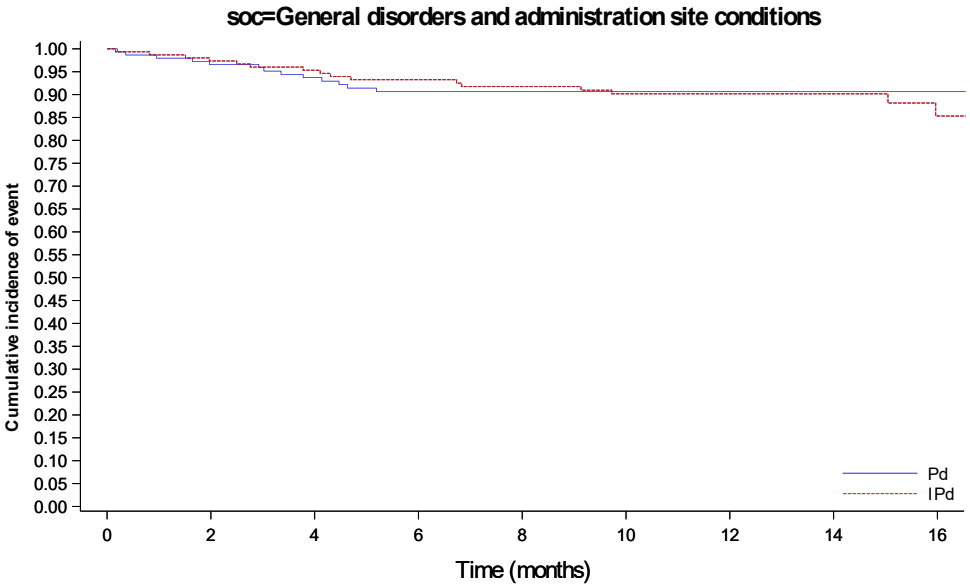
	Pd (N=149)	**IPd (N=152)**
4 Months	0.986 (0.947 to 0.997)	0.960 (0.912 to 0.982)
6 Months	0.970 (0.922 to 0.989)	0.952 (0.902 to 0.977)
8 Months	0.961 (0.909 to 0.984)	0.936 (0.880 to 0.966)
10 Months	0.952 (0.896 to 0.978)	0.936 (0.880 to 0.966)
12 Months	0.952 (0.896 to 0.978)	0.927 (0.868 to 0.960)
14 Months	0.929 (0.861 to 0.964)	0.927 (0.868 to 0.960)
16 Months	0.929 (0.861 to 0.964)	0.927 (0.868 to 0.960)
Number of patients at risk[b]		
2 Months	141	145
4 Months	133	135
6 Months	114	122
8 Months	104	115
10 Months	99	108
12 Months	84	97
14 Months	50	66
16 Months	25	28

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event according to SOC by treatment group - Safety population



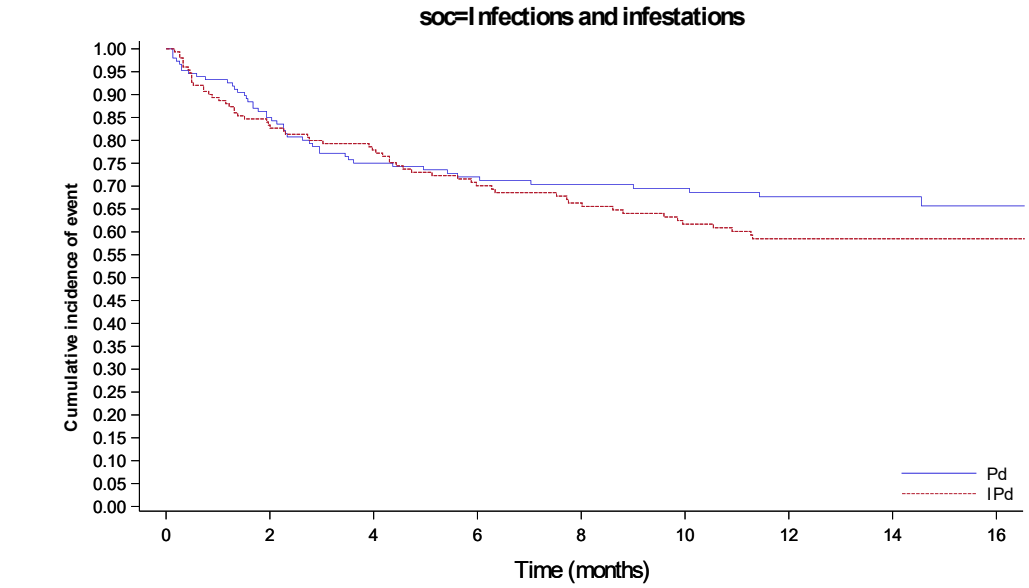
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event according to SOC by treatment group - Safety population



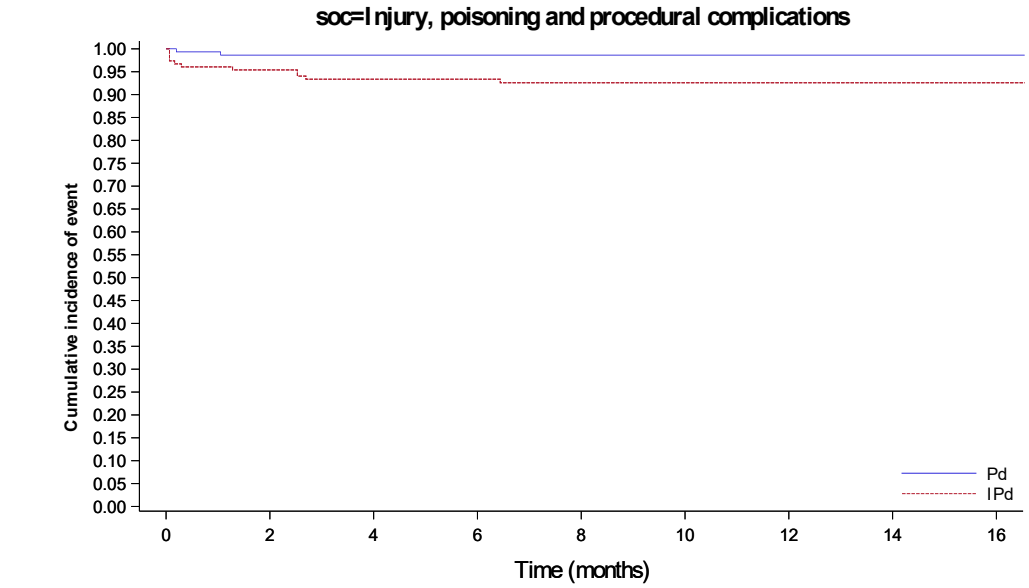
Number at Risk

Pd	149	139	128	112	102	98	83	52	26
IPd	152	146	139	126	121	113	102	70	28

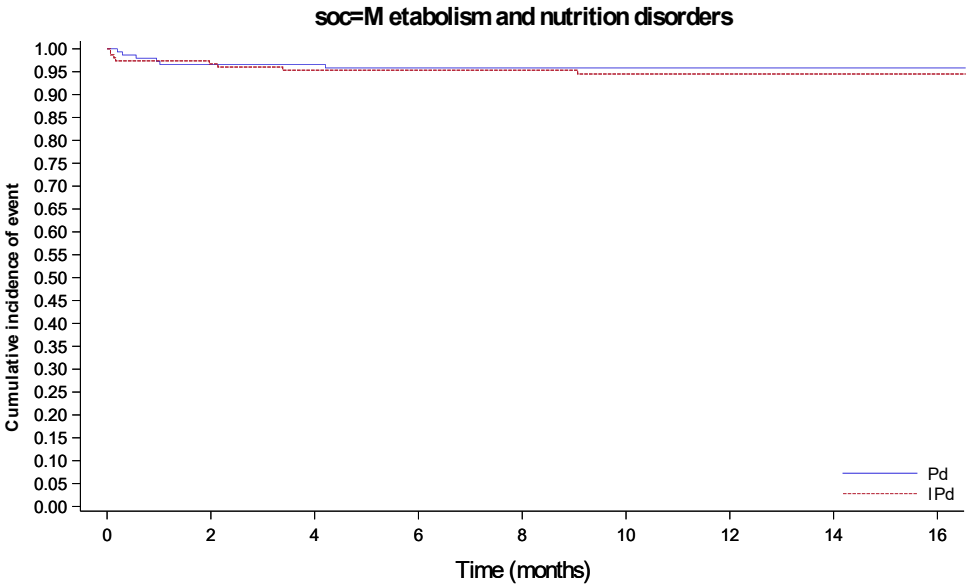
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event according to SOC by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event according to SOC by treatment group - Safety population



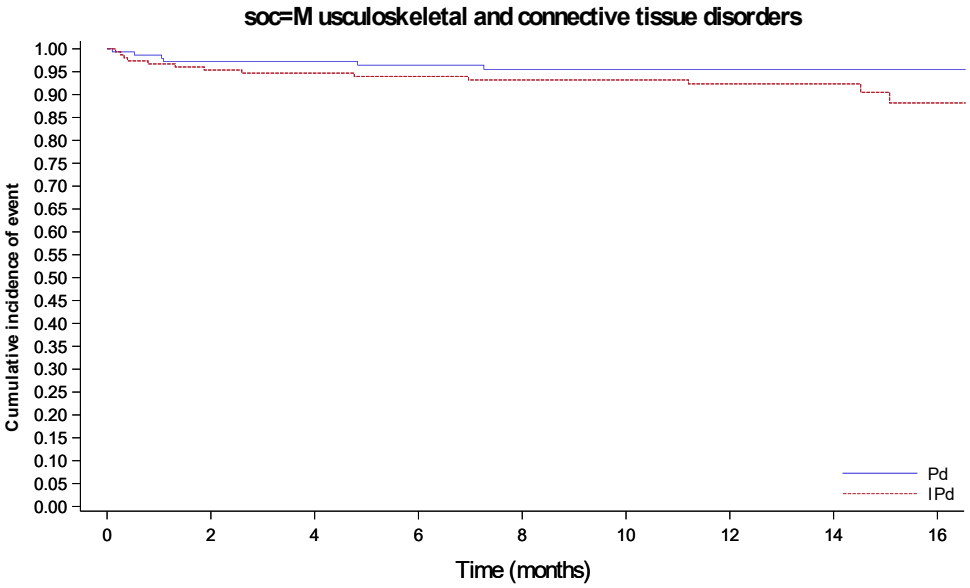
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	137	131	113	103	100	85	52	26
IPd	152	144	135	124	119	111	101	69	28

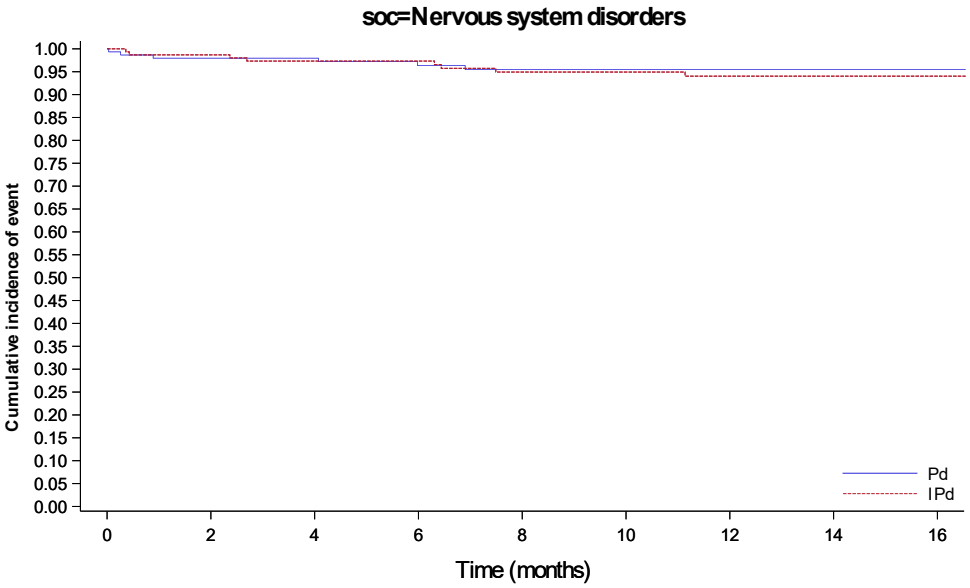
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event according to SOC by treatment group - Safety population



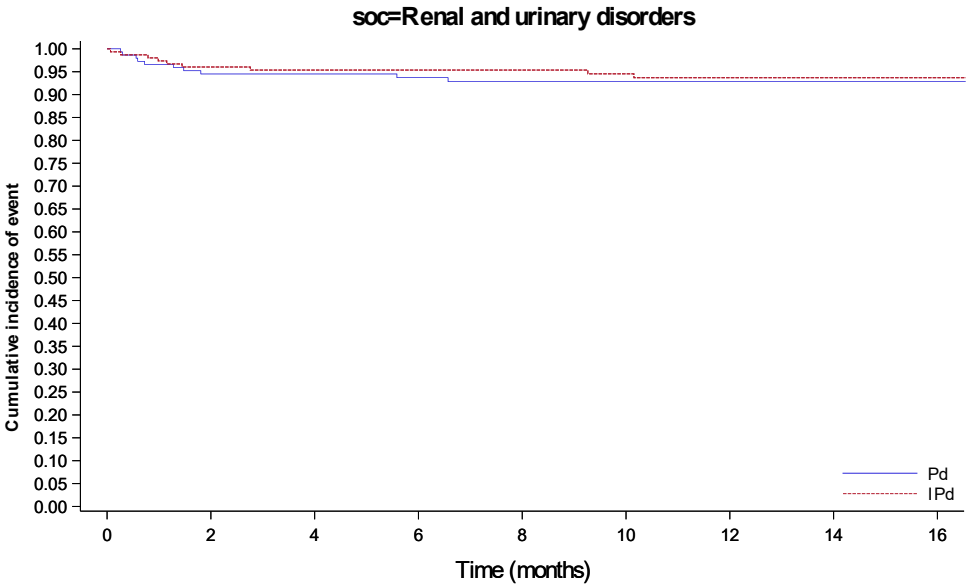
Number at Risk

Pd	149	138	130	112	100	96	83	52	25
IPd	152	142	134	123	120	113	100	67	26

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event according to SOC by treatment group - Safety population



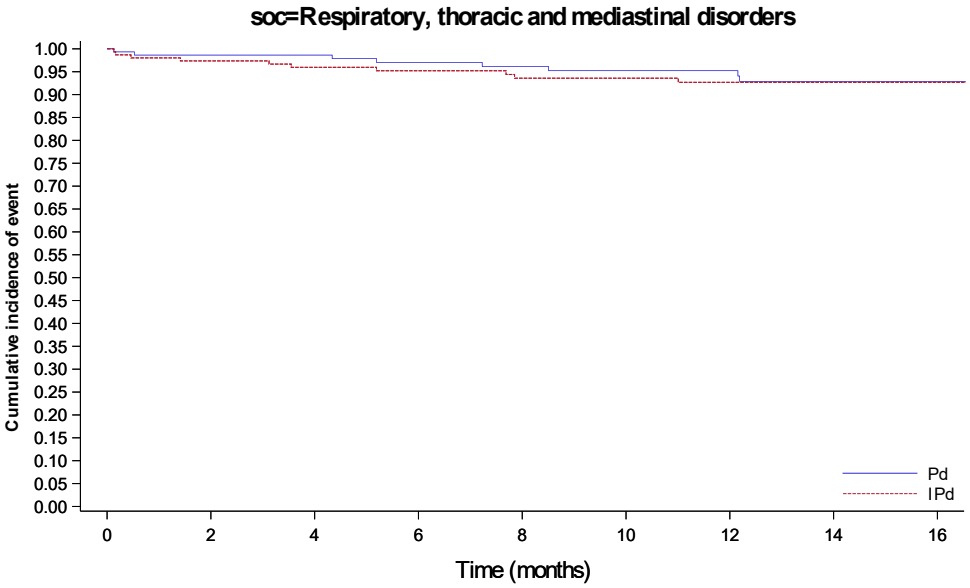
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	135	128	113	102	98	83	51	24
IPd	152	144	136	125	121	113	101	69	29

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	141	133	114	104	99	84	50	25
IPd	152	145	135	122	115	108	97	66	28

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.7 Treatment emergent serious adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Febrile neutropenia (days)		
Number (%) of events	3 (2.0)	10 (6.6)
Number (%) of patients censored	146 (98.0)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0584
Hazard ratio (95% CI) vs Pd	-	3.245 (0.893 to 11.792)
P-value	-	0.0738
Events probability (95% CI)[b]		
2 Months	0.986 (0.945 to 0.996)	0.947 (0.897 to 0.973)
4 Months	0.986 (0.945 to 0.996)	0.940 (0.888 to 0.968)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.7 Treatment emergent serious adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	0.986 (0.945 to 0.996)	0.940 (0.888 to 0.968)
8 Months	0.986 (0.945 to 0.996)	0.940 (0.888 to 0.968)
10 Months	0.976 (0.927 to 0.992)	0.940 (0.888 to 0.968)
12 Months	0.976 (0.927 to 0.992)	0.931 (0.875 to 0.962)
14 Months	0.976 (0.927 to 0.992)	0.931 (0.875 to 0.962)
16 Months	0.976 (0.927 to 0.992)	0.931 (0.875 to 0.962)
Number of patients at risk[b]		
2 Months	140	141
4 Months	132	132
6 Months	116	119
8 Months	105	114
10 Months	100	110
12 Months	86	97
14 Months	54	65
16 Months	26	27
Pneumonia (days)		
Number (%) of events	23 (15.4)	23 (15.1)
Number (%) of patients censored	126 (84.6)	129 (84.9)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.7 Treatment emergent serious adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.8112
Hazard ratio (95% CI) vs Pd	-	0.932 (0.523 to 1.661)
P-value	-	0.8111
Events probability (95% CI)[b]		
2 Months	0.924 (0.868 to 0.957)	0.941 (0.889 to 0.969)
4 Months	0.867 (0.799 to 0.913)	0.906 (0.847 to 0.943)
6 Months	0.836 (0.763 to 0.888)	0.869 (0.802 to 0.915)
8 Months	0.836 (0.763 to 0.888)	0.854 (0.784 to 0.902)
10 Months	0.836 (0.763 to 0.888)	0.846 (0.775 to 0.896)
12 Months	0.836 (0.763 to 0.888)	0.837 (0.764 to 0.889)
14 Months	0.836 (0.763 to 0.888)	0.837 (0.764 to 0.889)

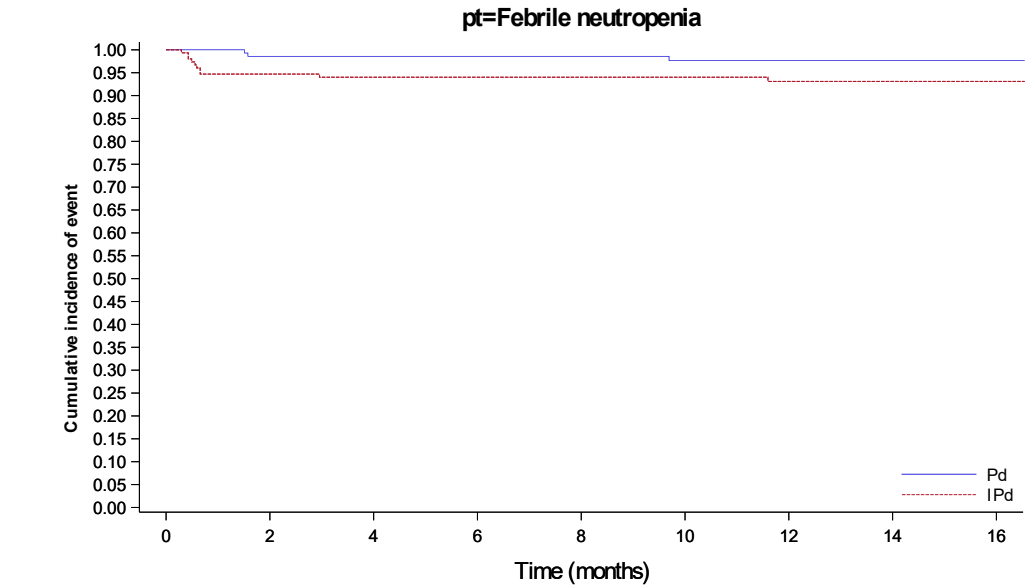
PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.7 Treatment emergent serious adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	0.836 (0.763 to 0.888)	0.837 (0.764 to 0.889)
Number of patients at risk[b]		
2 Months	132	140
4 Months	117	129
6 Months	103	113
8 Months	94	107
10 Months	92	102
12 Months	79	91
14 Months	50	60
16 Months	25	26

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_s_t_x.rtf (16FEB2021 22:47)

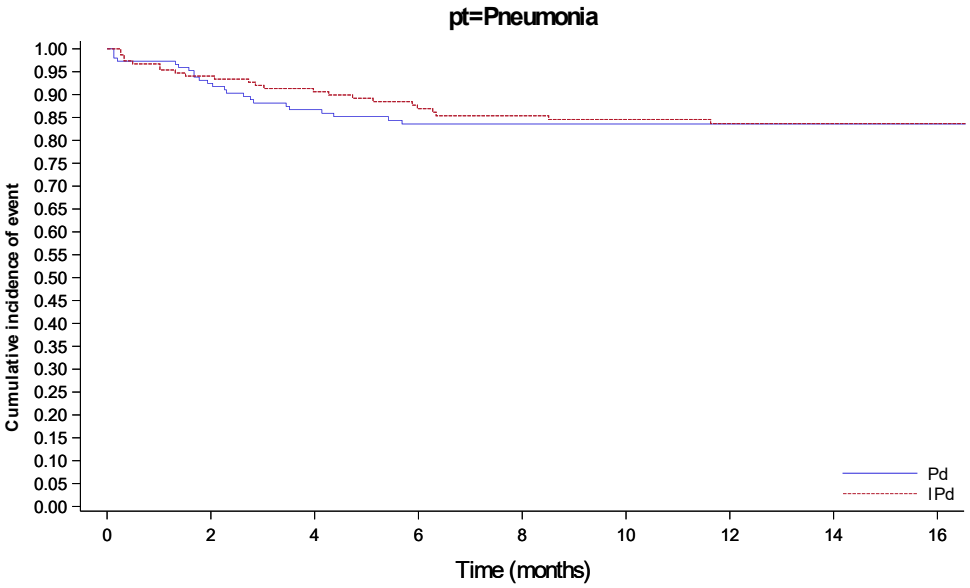
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.8 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	140	132	116	105	100	86	54	26
IPd	152	141	132	119	114	110	97	65	27

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.8 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	132	117	103	94	92	79	50	25
IPd	152	140	129	113	107	102	91	60	26

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.9 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Blood and lymphatic system disorders (days)		
Number (%) of events	7 (4.7)	1 (0.7)
Number (%) of patients censored	142 (95.3)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0278
Hazard ratio (95% CI) vs Pd	-	0.135 (0.017 to 1.099)
P-value	-	0.0612
Events probability (95% CI)[b]		
2 Months	0.952 (0.903 to 0.977)	1.000 (1.000 to 1.000)
4 Months	0.952 (0.903 to 0.977)	0.993 (0.953 to 0.999)
6 Months	0.952 (0.903 to 0.977)	0.993 (0.953 to 0.999)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.9 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.952 (0.903 to 0.977)	0.993 (0.953 to 0.999)
10 Months	0.952 (0.903 to 0.977)	0.993 (0.953 to 0.999)
12 Months	0.952 (0.903 to 0.977)	0.993 (0.953 to 0.999)
14 Months	0.952 (0.903 to 0.977)	0.993 (0.953 to 0.999)
16 Months	0.952 (0.903 to 0.977)	0.993 (0.953 to 0.999)
Number of patients at risk[b]		
2 Months	136	149
4 Months	130	140
6 Months	114	127
8 Months	105	122
10 Months	101	115
12 Months	86	103
14 Months	53	70
16 Months	25	29
General disorders and administration site conditions (days)		
Number (%) of events	2 (1.3)	4 (2.6)
Number (%) of patients censored	147 (98.7)	148 (97.4)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.9 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.4811
Hazard ratio (95% CI) vs Pd	-	1.824 (0.334 to 9.964)
P-value	-	0.4877
Events probability (95% CI)[b]		
2 Months	0.993 (0.953 to 0.999)	1.000 (1.000 to 1.000)
4 Months	0.993 (0.953 to 0.999)	0.993 (0.953 to 0.999)
6 Months	0.986 (0.944 to 0.996)	0.986 (0.946 to 0.997)
8 Months	0.986 (0.944 to 0.996)	0.986 (0.946 to 0.997)
10 Months	0.986 (0.944 to 0.996)	0.978 (0.932 to 0.993)
12 Months	0.986 (0.944 to 0.996)	0.978 (0.932 to 0.993)
14 Months	0.986 (0.944 to 0.996)	0.978 (0.932 to 0.993)
16 Months	0.986 (0.944 to 0.996)	0.947 (0.829 to 0.984)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.9 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	29
Hepatobiliary disorders (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.9 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3370
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
4 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
6 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
8 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
10 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
12 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
14 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
16 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	117	128

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.9 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	30
Infections and infestations (days)		
Number (%) of events	8 (5.4)	4 (2.6)
Number (%) of patients censored	141 (94.6)	148 (97.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2028
Hazard ratio (95% CI) vs Pd	-	0.467 (0.141 to 1.551)
P-value	-	0.2138

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.9 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[b]		
2 Months	0.966 (0.920 to 0.986)	0.993 (0.954 to 0.999)
4 Months	0.959 (0.910 to 0.981)	0.993 (0.954 to 0.999)
6 Months	0.951 (0.901 to 0.977)	0.979 (0.937 to 0.993)
8 Months	0.943 (0.889 to 0.971)	0.979 (0.937 to 0.993)
10 Months	0.943 (0.889 to 0.971)	0.979 (0.937 to 0.993)
12 Months	0.943 (0.889 to 0.971)	0.970 (0.923 to 0.989)
14 Months	0.943 (0.889 to 0.971)	0.970 (0.923 to 0.989)
16 Months	0.943 (0.889 to 0.971)	0.970 (0.923 to 0.989)
Number of patients at risk[b]		
2 Months	139	148
4 Months	131	141
6 Months	117	127
8 Months	105	122
10 Months	101	115
12 Months	87	102
14 Months	54	70
16 Months	26	30

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.9 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3441
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
4 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
6 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.9 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	1.000 (1.000 to 1.000)	0.992 (0.944 to 0.999)
10 Months	1.000 (1.000 to 1.000)	0.992 (0.944 to 0.999)
12 Months	1.000 (1.000 to 1.000)	0.992 (0.944 to 0.999)
14 Months	1.000 (1.000 to 1.000)	0.992 (0.944 to 0.999)
16 Months	1.000 (1.000 to 1.000)	0.992 (0.944 to 0.999)
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	122
10 Months	102	115
12 Months	87	103
14 Months	54	70
16 Months	26	30
Nervous system disorders (days)		
Number (%) of events	2 (1.3)	0 (0.0)
Number (%) of patients censored	147 (98.7)	152 (100.0)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.9 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1285
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9964
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
4 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
6 Months	0.992 (0.947 to 0.999)	1.000 (1.000 to 1.000)
8 Months	0.992 (0.947 to 0.999)	1.000 (1.000 to 1.000)
10 Months	0.992 (0.947 to 0.999)	1.000 (1.000 to 1.000)
12 Months	0.992 (0.947 to 0.999)	1.000 (1.000 to 1.000)
14 Months	0.979 (0.913 to 0.995)	1.000 (1.000 to 1.000)
16 Months	0.979 (0.913 to 0.995)	1.000 (1.000 to 1.000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.9 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	116	128
8 Months	105	123
10 Months	101	116
12 Months	86	104
14 Months	53	71
16 Months	25	30
Skin and subcutaneous tissue disorders (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.9 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3324
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
4 Months	1.000 (1.000 to 1.000)	0.993 (0.953 to 0.999)
6 Months	1.000 (1.000 to 1.000)	0.993 (0.953 to 0.999)
8 Months	1.000 (1.000 to 1.000)	0.993 (0.953 to 0.999)
10 Months	1.000 (1.000 to 1.000)	0.993 (0.953 to 0.999)
12 Months	1.000 (1.000 to 1.000)	0.993 (0.953 to 0.999)
14 Months	1.000 (1.000 to 1.000)	0.993 (0.953 to 0.999)
16 Months	1.000 (1.000 to 1.000)	0.993 (0.953 to 0.999)
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	140
6 Months	117	128

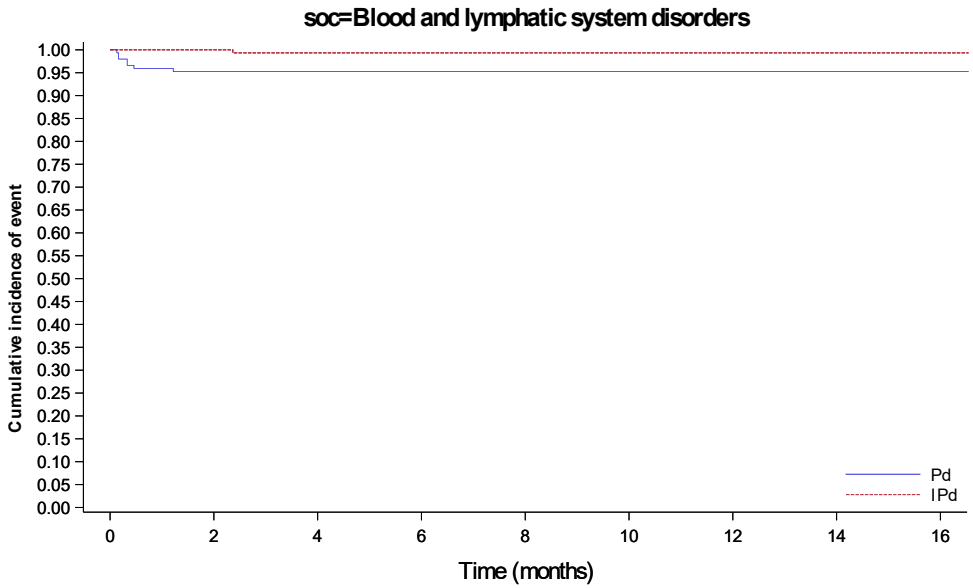
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.9 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

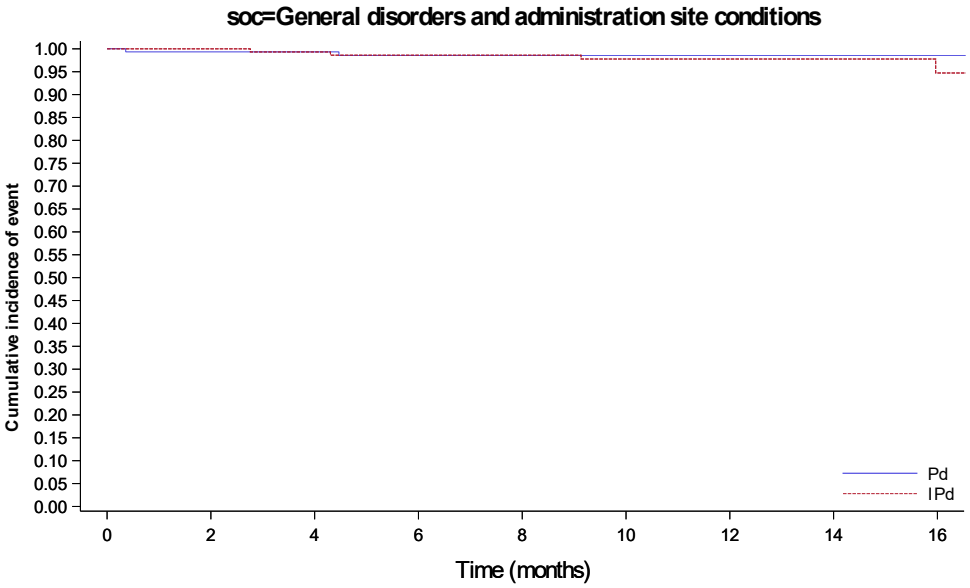
	Pd (N=149)	**IPd (N=152)**
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	30

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16FEB2021 22:48)

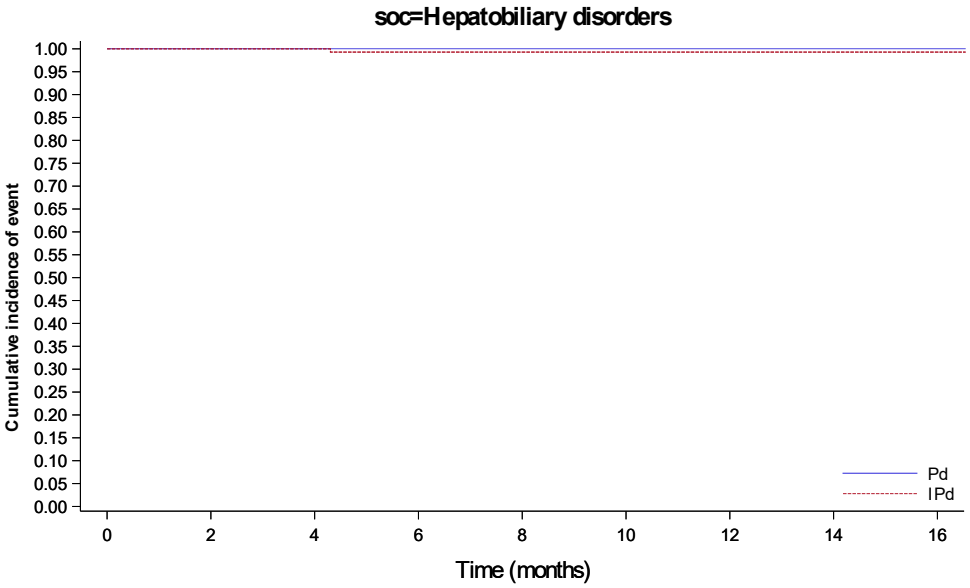
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.10 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population



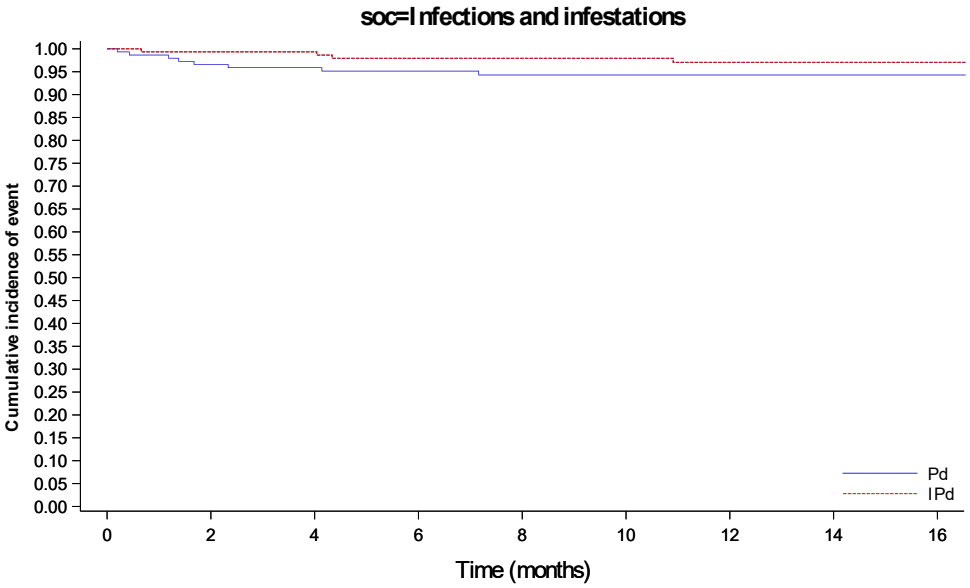
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.10 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.10 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population



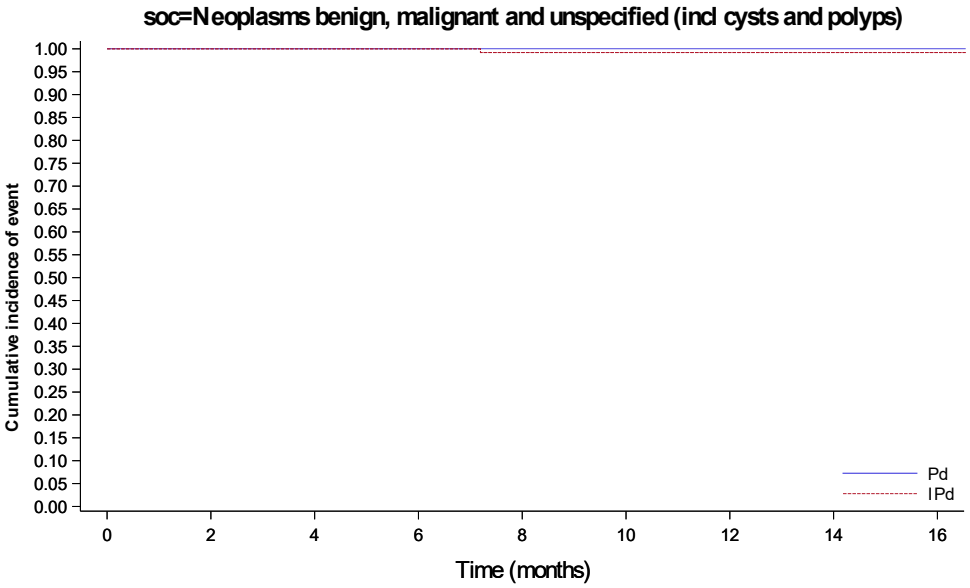
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.10 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population



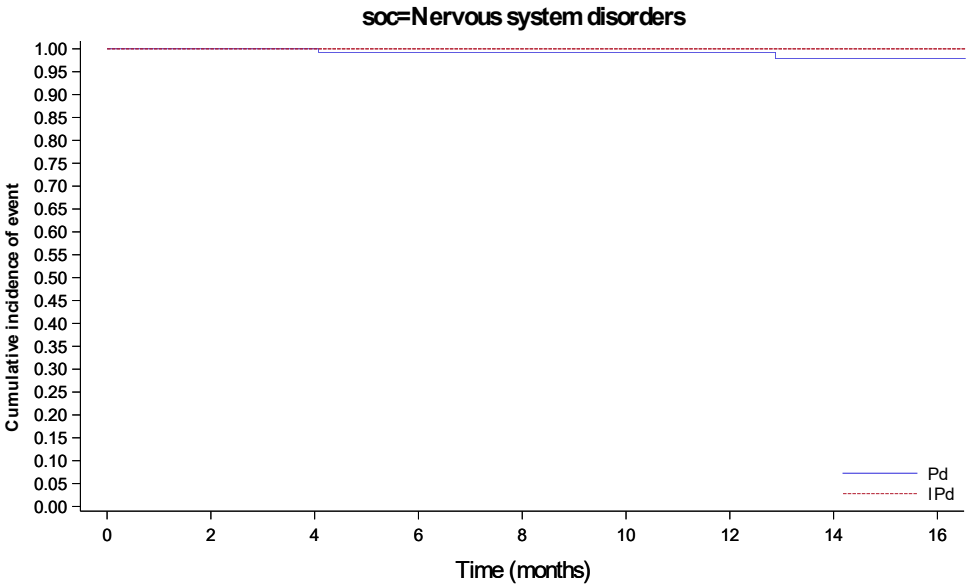
Number at Risk

Pd	149	139	131	117	105	101	87	54	26
IPd	152	148	141	127	122	115	102	70	30

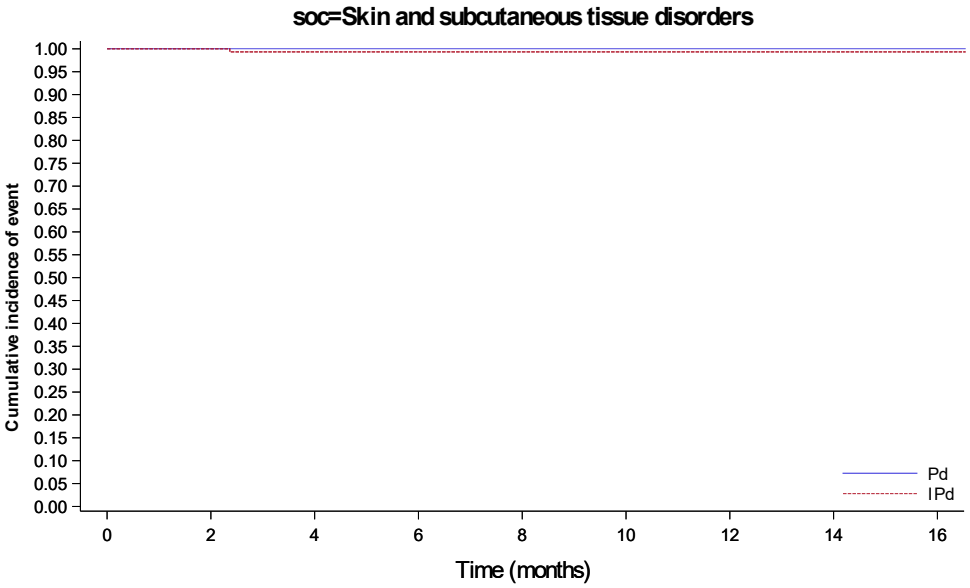
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.10 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.10 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.10 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population



Number at Risk

Pd	149	142	134	117	106	102	87	54	26
IPd	152	149	140	128	123	116	104	71	30

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Atypical pneumonia (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3314
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
4 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
6 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
10 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
12 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
14 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
16 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	117	127
8 Months	106	122
10 Months	102	115
12 Months	87	103
14 Months	54	70
16 Months	26	30
Bronchopulmonary aspergillosis (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3271
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	0.993 (0.954 to 0.999)
4 Months	1.000 (1.000 to 1.000)	0.993 (0.954 to 0.999)
6 Months	1.000 (1.000 to 1.000)	0.993 (0.954 to 0.999)
8 Months	1.000 (1.000 to 1.000)	0.993 (0.954 to 0.999)
10 Months	1.000 (1.000 to 1.000)	0.993 (0.954 to 0.999)
12 Months	1.000 (1.000 to 1.000)	0.993 (0.954 to 0.999)
14 Months	1.000 (1.000 to 1.000)	0.993 (0.954 to 0.999)
16 Months	1.000 (1.000 to 1.000)	0.993 (0.954 to 0.999)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[b]		
2 Months	142	148
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	30
Death (days)		
Number (%) of events	1 (0.7)	2 (1.3)
Number (%) of patients censored	148 (99.3)	150 (98.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.6101
Hazard ratio (95% CI) vs Pd	-	1.850 (0.168 to 20.410)
P-value	-	0.6157
Events probability (95% CI)[b]		
2 Months	0.993 (0.953 to 0.999)	1.000 (1.000 to 1.000)
4 Months	0.993 (0.953 to 0.999)	0.993 (0.953 to 0.999)
6 Months	0.993 (0.953 to 0.999)	0.993 (0.953 to 0.999)
8 Months	0.993 (0.953 to 0.999)	0.993 (0.953 to 0.999)
10 Months	0.993 (0.953 to 0.999)	0.985 (0.940 to 0.996)
12 Months	0.993 (0.953 to 0.999)	0.985 (0.940 to 0.996)
14 Months	0.993 (0.953 to 0.999)	0.985 (0.940 to 0.996)
16 Months	0.993 (0.953 to 0.999)	0.985 (0.940 to 0.996)
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	117	128

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	30
Decubitus ulcer (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3324
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
4 Months	1.000 (1.000 to 1.000)	0.993 (0.953 to 0.999)
6 Months	1.000 (1.000 to 1.000)	0.993 (0.953 to 0.999)
8 Months	1.000 (1.000 to 1.000)	0.993 (0.953 to 0.999)
10 Months	1.000 (1.000 to 1.000)	0.993 (0.953 to 0.999)
12 Months	1.000 (1.000 to 1.000)	0.993 (0.953 to 0.999)
14 Months	1.000 (1.000 to 1.000)	0.993 (0.953 to 0.999)
16 Months	1.000 (1.000 to 1.000)	0.993 (0.953 to 0.999)
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	140
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	30

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Echinococciasis (days)		
Number (%) of events	1 (0.7)	0 (0.0)
Number (%) of patients censored	148 (99.3)	152 (100.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2905
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
4 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
6 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.991 (0.938 to 0.999)	1.000 (1.000 to 1.000)
10 Months	0.991 (0.938 to 0.999)	1.000 (1.000 to 1.000)
12 Months	0.991 (0.938 to 0.999)	1.000 (1.000 to 1.000)
14 Months	0.991 (0.938 to 0.999)	1.000 (1.000 to 1.000)
16 Months	0.991 (0.938 to 0.999)	1.000 (1.000 to 1.000)
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	105	123
10 Months	101	116
12 Months	87	104
14 Months	54	71
16 Months	26	30
General physical health deterioration (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3583
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
4 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
6 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
8 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
10 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
12 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
14 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
16 Months	1.000 (1.000 to 1.000)	0.969 (0.798 to 0.996)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	29
Haemorrhage intracranial (days)		
Number (%) of events	1 (0.7)	0 (0.0)
Number (%) of patients censored	148 (99.3)	152 (100.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2675
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
4 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
6 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
8 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
10 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
12 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
14 Months	0.986 (0.908 to 0.998)	1.000 (1.000 to 1.000)
16 Months	0.986 (0.908 to 0.998)	1.000 (1.000 to 1.000)
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	117	128

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	30
Hepatic failure (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3370
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
4 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
6 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
8 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
10 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
12 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
14 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
16 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	30

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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	Pd (N=149)	**IPd (N=152)**
Medical device site infection (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3571
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
4 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
6 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
10 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
12 Months	1.000 (1.000 to 1.000)	0.991 (0.938 to 0.999)
14 Months	1.000 (1.000 to 1.000)	0.991 (0.938 to 0.999)
16 Months	1.000 (1.000 to 1.000)	0.991 (0.938 to 0.999)
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	87	103
14 Months	54	71
16 Months	26	30
Multiple organ dysfunction syndrome (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3370
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
4 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
6 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
8 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
10 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
12 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
14 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
16 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	30
Myelodysplastic syndrome (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3441
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
4 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
6 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
8 Months	1.000 (1.000 to 1.000)	0.992 (0.944 to 0.999)
10 Months	1.000 (1.000 to 1.000)	0.992 (0.944 to 0.999)
12 Months	1.000 (1.000 to 1.000)	0.992 (0.944 to 0.999)
14 Months	1.000 (1.000 to 1.000)	0.992 (0.944 to 0.999)
16 Months	1.000 (1.000 to 1.000)	0.992 (0.944 to 0.999)
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	117	128

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	106	122
10 Months	102	115
12 Months	87	103
14 Months	54	70
16 Months	26	30
Neutropenia (days)		
Number (%) of events	2 (1.3)	0 (0.0)
Number (%) of patients censored	147 (98.7)	152 (100.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1504
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9964

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

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16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[b]		
2 Months	0.986 (0.947 to 0.997)	1.000 (1.000 to 1.000)
4 Months	0.986 (0.947 to 0.997)	1.000 (1.000 to 1.000)
6 Months	0.986 (0.947 to 0.997)	1.000 (1.000 to 1.000)
8 Months	0.986 (0.947 to 0.997)	1.000 (1.000 to 1.000)
10 Months	0.986 (0.947 to 0.997)	1.000 (1.000 to 1.000)
12 Months	0.986 (0.947 to 0.997)	1.000 (1.000 to 1.000)
14 Months	0.986 (0.947 to 0.997)	1.000 (1.000 to 1.000)
16 Months	0.986 (0.947 to 0.997)	1.000 (1.000 to 1.000)
Number of patients at risk[b]		
2 Months	140	149
4 Months	132	141
6 Months	115	128
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	30

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

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16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Pneumonia (days)		
Number (%) of events	3 (2.0)	0 (0.0)
Number (%) of patients censored	146 (98.0)	152 (100.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0745
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9956
Events probability (95% CI)[b]		
2 Months	0.986 (0.945 to 0.996)	1.000 (1.000 to 1.000)
4 Months	0.986 (0.945 to 0.996)	1.000 (1.000 to 1.000)
6 Months	0.978 (0.935 to 0.993)	1.000 (1.000 to 1.000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
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16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.978 (0.935 to 0.993)	1.000 (1.000 to 1.000)
10 Months	0.978 (0.935 to 0.993)	1.000 (1.000 to 1.000)
12 Months	0.978 (0.935 to 0.993)	1.000 (1.000 to 1.000)
14 Months	0.978 (0.935 to 0.993)	1.000 (1.000 to 1.000)
16 Months	0.978 (0.935 to 0.993)	1.000 (1.000 to 1.000)
Number of patients at risk[b]		
2 Months	140	149
4 Months	132	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	30
Pneumonia influenzal (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

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16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3370
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
4 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
6 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
8 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
10 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
12 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
14 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)
16 Months	1.000 (1.000 to 1.000)	0.993 (0.951 to 0.999)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	30
Pneumonia streptococcal (days)		
Number (%) of events	1 (0.7)	0 (0.0)
Number (%) of patients censored	148 (99.3)	152 (100.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3092
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[b]		
2 Months	0.993 (0.952 to 0.999)	1.000 (1.000 to 1.000)
4 Months	0.993 (0.952 to 0.999)	1.000 (1.000 to 1.000)
6 Months	0.993 (0.952 to 0.999)	1.000 (1.000 to 1.000)
8 Months	0.993 (0.952 to 0.999)	1.000 (1.000 to 1.000)
10 Months	0.993 (0.952 to 0.999)	1.000 (1.000 to 1.000)
12 Months	0.993 (0.952 to 0.999)	1.000 (1.000 to 1.000)
14 Months	0.993 (0.952 to 0.999)	1.000 (1.000 to 1.000)
16 Months	0.993 (0.952 to 0.999)	1.000 (1.000 to 1.000)
Number of patients at risk[b]		
2 Months	141	149
4 Months	133	141
6 Months	117	128

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	30
Sepsis (days)		
Number (%) of events	1 (0.7)	0 (0.0)
Number (%) of patients censored	148 (99.3)	152 (100.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3022
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
4 Months	0.993 (0.950 to 0.999)	1.000 (1.000 to 1.000)
6 Months	0.993 (0.950 to 0.999)	1.000 (1.000 to 1.000)
8 Months	0.993 (0.950 to 0.999)	1.000 (1.000 to 1.000)
10 Months	0.993 (0.950 to 0.999)	1.000 (1.000 to 1.000)
12 Months	0.993 (0.950 to 0.999)	1.000 (1.000 to 1.000)
14 Months	0.993 (0.950 to 0.999)	1.000 (1.000 to 1.000)
16 Months	0.993 (0.950 to 0.999)	1.000 (1.000 to 1.000)
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	30

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Septic shock (days)		
Number (%) of events	2 (1.3)	0 (0.0)
Number (%) of patients censored	147 (98.7)	152 (100.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1504
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9964
Events probability (95% CI)[b]		
2 Months	0.986 (0.947 to 0.997)	1.000 (1.000 to 1.000)
4 Months	0.986 (0.947 to 0.997)	1.000 (1.000 to 1.000)
6 Months	0.986 (0.947 to 0.997)	1.000 (1.000 to 1.000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.986 (0.947 to 0.997)	1.000 (1.000 to 1.000)
10 Months	0.986 (0.947 to 0.997)	1.000 (1.000 to 1.000)
12 Months	0.986 (0.947 to 0.997)	1.000 (1.000 to 1.000)
14 Months	0.986 (0.947 to 0.997)	1.000 (1.000 to 1.000)
16 Months	0.986 (0.947 to 0.997)	1.000 (1.000 to 1.000)
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	30
Spinal subdural haematoma (days)		
Number (%) of events	1 (0.7)	0 (0.0)
Number (%) of patients censored	148 (99.3)	152 (100.0)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3014
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
4 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
6 Months	0.992 (0.947 to 0.999)	1.000 (1.000 to 1.000)
8 Months	0.992 (0.947 to 0.999)	1.000 (1.000 to 1.000)
10 Months	0.992 (0.947 to 0.999)	1.000 (1.000 to 1.000)
12 Months	0.992 (0.947 to 0.999)	1.000 (1.000 to 1.000)
14 Months	0.992 (0.947 to 0.999)	1.000 (1.000 to 1.000)
16 Months	0.992 (0.947 to 0.999)	1.000 (1.000 to 1.000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	116	128
8 Months	105	123
10 Months	101	116
12 Months	86	104
14 Months	53	71
16 Months	25	30
Sudden death (days)		
Number (%) of events	1 (0.7)	0 (0.0)
Number (%) of patients censored	148 (99.3)	152 (100.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2994
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
4 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
6 Months	0.992 (0.947 to 0.999)	1.000 (1.000 to 1.000)
8 Months	0.992 (0.947 to 0.999)	1.000 (1.000 to 1.000)
10 Months	0.992 (0.947 to 0.999)	1.000 (1.000 to 1.000)
12 Months	0.992 (0.947 to 0.999)	1.000 (1.000 to 1.000)
14 Months	0.992 (0.947 to 0.999)	1.000 (1.000 to 1.000)
16 Months	0.992 (0.947 to 0.999)	1.000 (1.000 to 1.000)
Number of patients at risk[b]		
2 Months	142	149
4 Months	134	141
6 Months	117	128

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	106	123
10 Months	102	116
12 Months	87	104
14 Months	54	71
16 Months	26	30
Thrombocytopenia (days)		
Number (%) of events	7 (4.7)	1 (0.7)
Number (%) of patients censored	142 (95.3)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0278
Hazard ratio (95% CI) vs Pd	-	0.135 (0.017 to 1.099)
P-value	-	0.0612

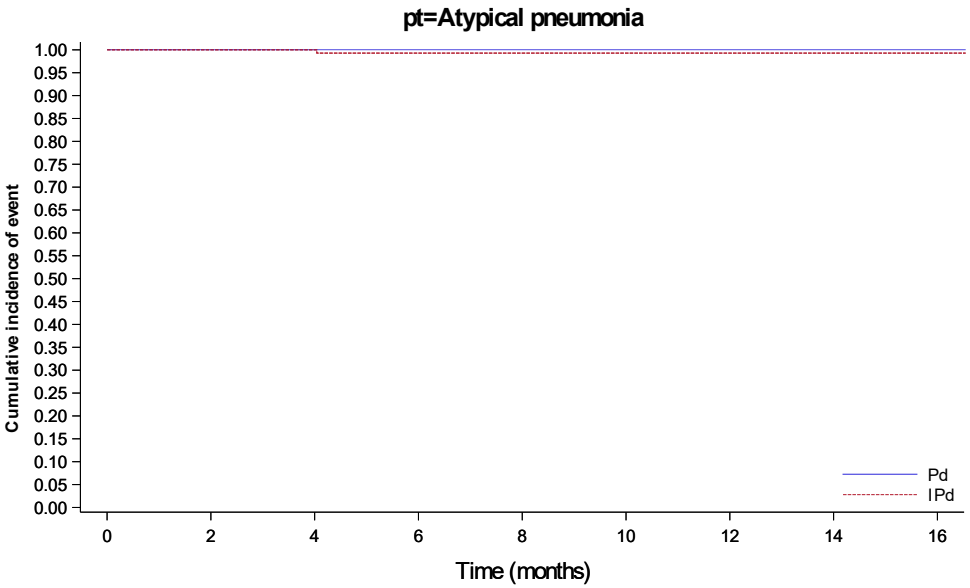
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.11 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[b]		
2 Months	0.952 (0.903 to 0.977)	1.000 (1.000 to 1.000)
4 Months	0.952 (0.903 to 0.977)	0.993 (0.953 to 0.999)
6 Months	0.952 (0.903 to 0.977)	0.993 (0.953 to 0.999)
8 Months	0.952 (0.903 to 0.977)	0.993 (0.953 to 0.999)
10 Months	0.952 (0.903 to 0.977)	0.993 (0.953 to 0.999)
12 Months	0.952 (0.903 to 0.977)	0.993 (0.953 to 0.999)
14 Months	0.952 (0.903 to 0.977)	0.993 (0.953 to 0.999)
16 Months	0.952 (0.903 to 0.977)	0.993 (0.953 to 0.999)
Number of patients at risk[b]		
2 Months	136	149
4 Months	130	140
6 Months	114	127
8 Months	105	122
10 Months	101	115
12 Months	86	103
14 Months	53	70
16 Months	25	29

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16FEB2021 22:48)

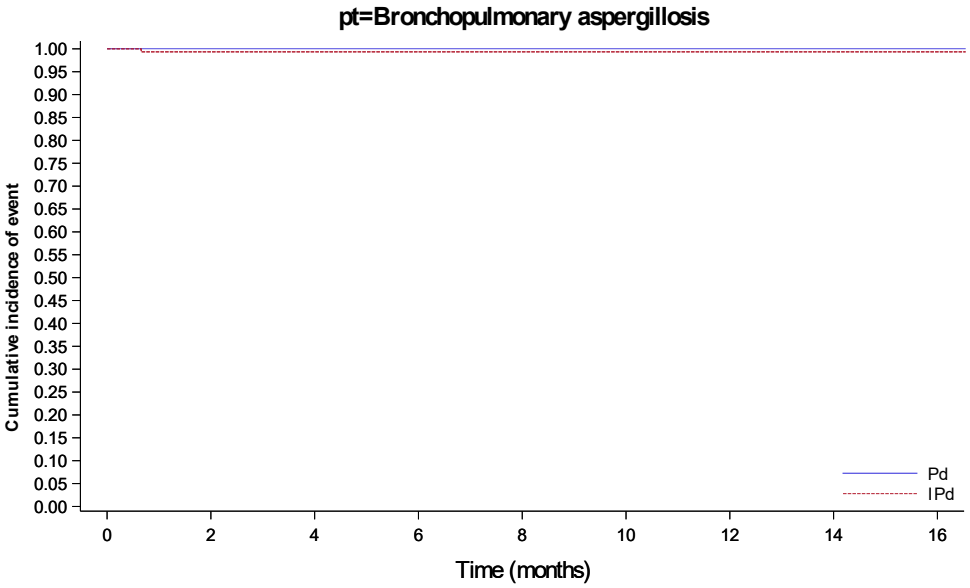
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.12 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population



Number at Risk

Pd	149	142	134	117	106	102	87	54	26
IPd	152	149	141	127	122	115	103	70	30

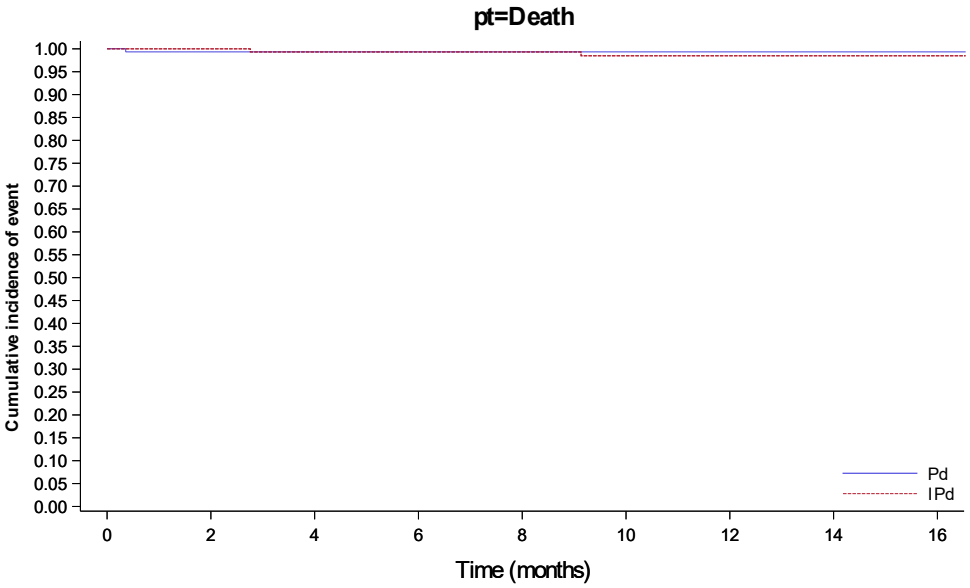
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.12 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population



Number at Risk

Pd	149	142	134	117	106	102	87	54	26
IPd	152	148	141	128	123	116	104	71	30

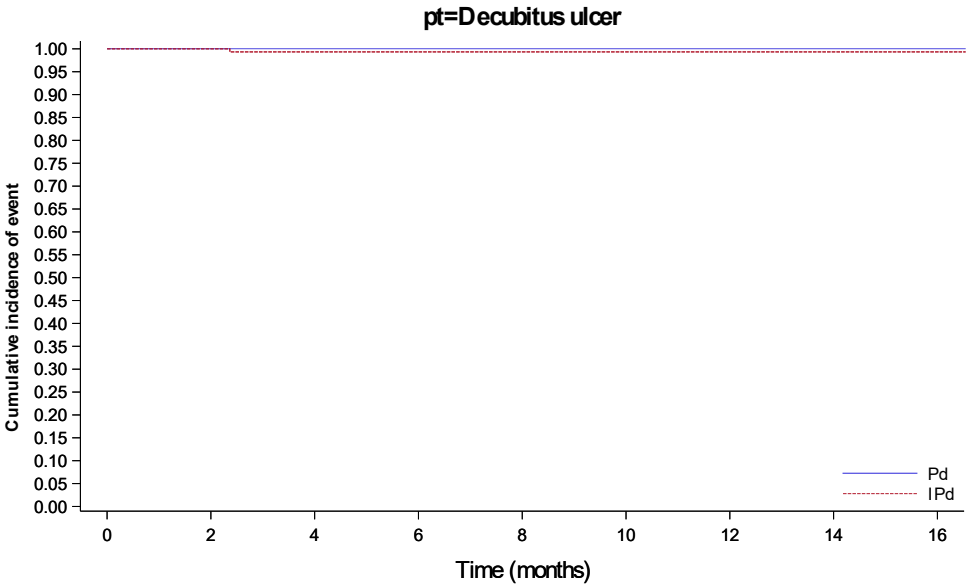
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.12 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population



Number at Risk

Pd	149	142	134	117	106	102	87	54	26
IPd	152	149	141	128	123	116	104	71	30

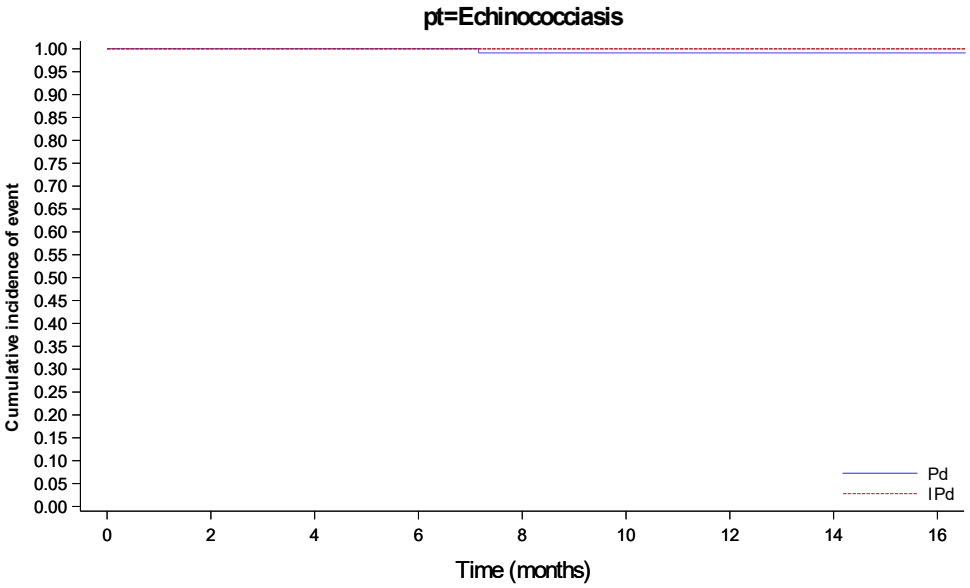
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.12 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population



Number at Risk

Pd	149	142	134	117	106	102	87	54	26
IPd	152	149	140	128	123	116	104	71	30

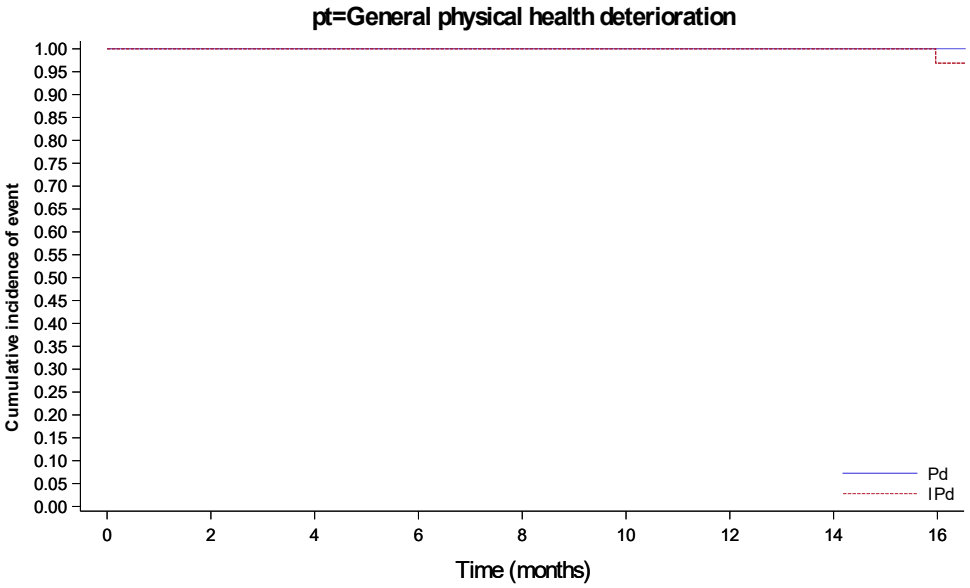
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.12 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population



Number at Risk

Pd	149	142	134	117	105	101	87	54	26
IPd	152	149	141	128	123	116	104	71	30

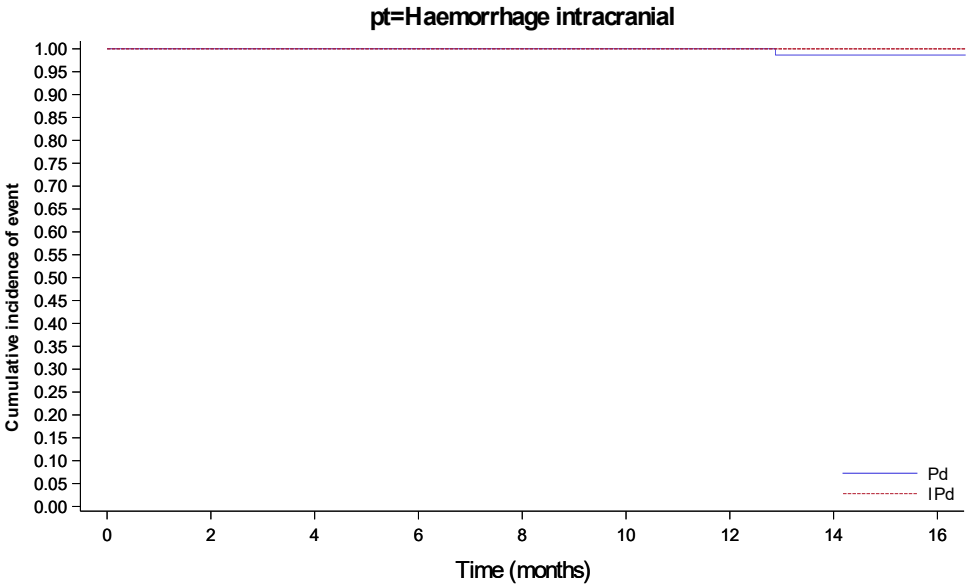
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.12 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population



Number at Risk

Pd	149	142	134	117	106	102	87	54	26
IPd	152	149	141	128	123	116	104	71	29

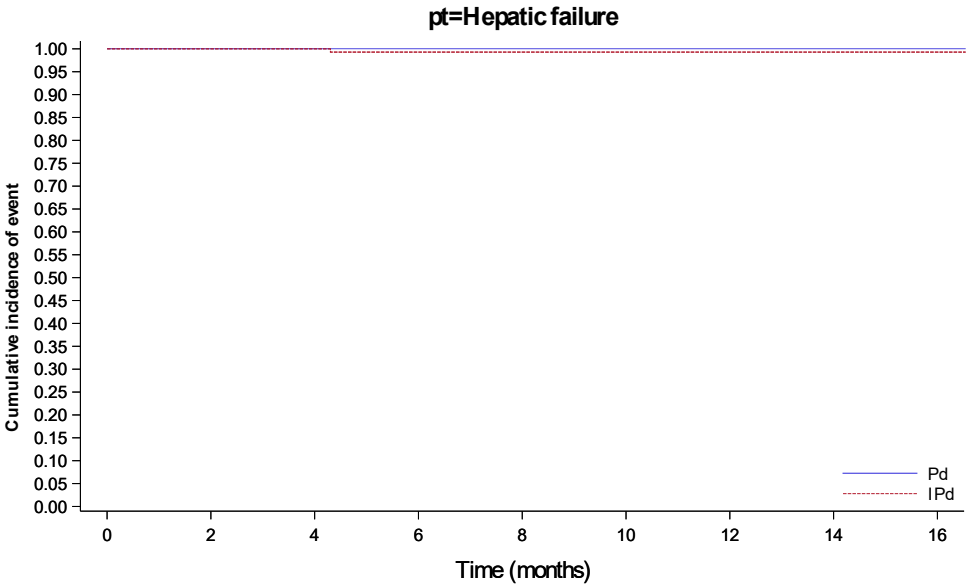
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.12 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population



Number at Risk

Pd	149	142	134	117	106	102	87	54	26
IPd	152	149	141	128	123	116	104	71	30

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.12 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population



Number at Risk

Pd	149	142	134	117	106	102	87	54	26
IPd	152	149	141	128	123	116	104	71	30

16.2.7.1 Safety endpoints
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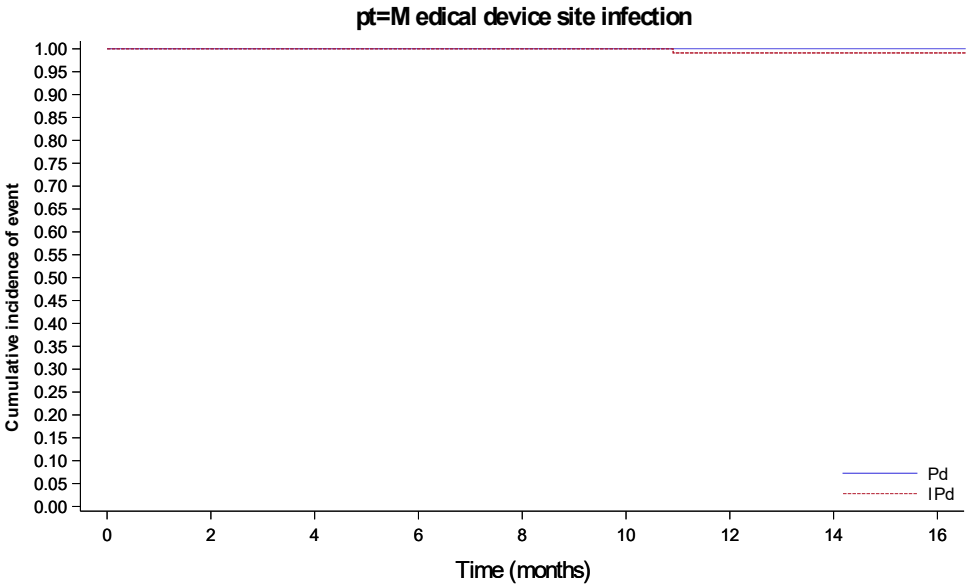
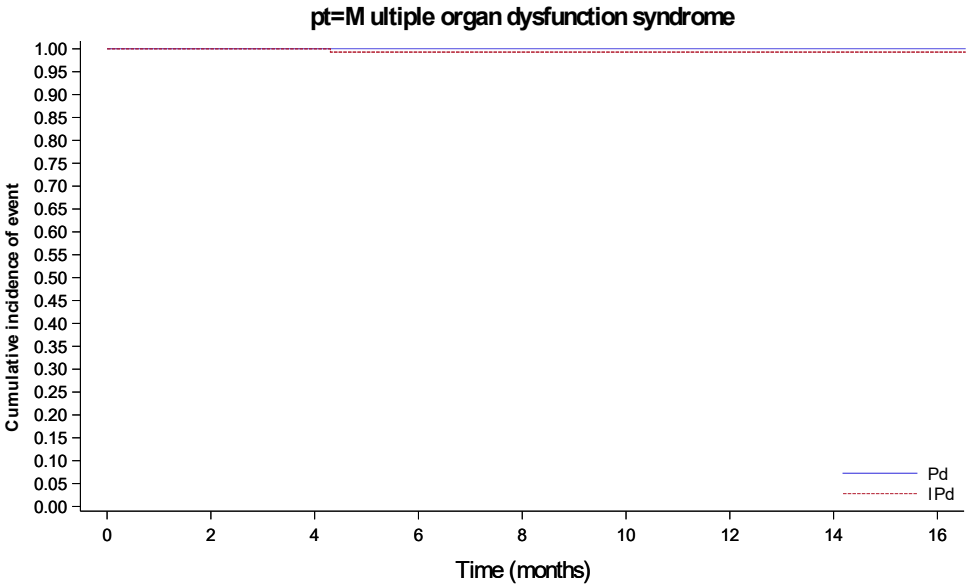


Number at Risk

Pd	149	142	134	117	106	102	87	54	26
IPd	152	149	141	128	123	116	103	71	30

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.12 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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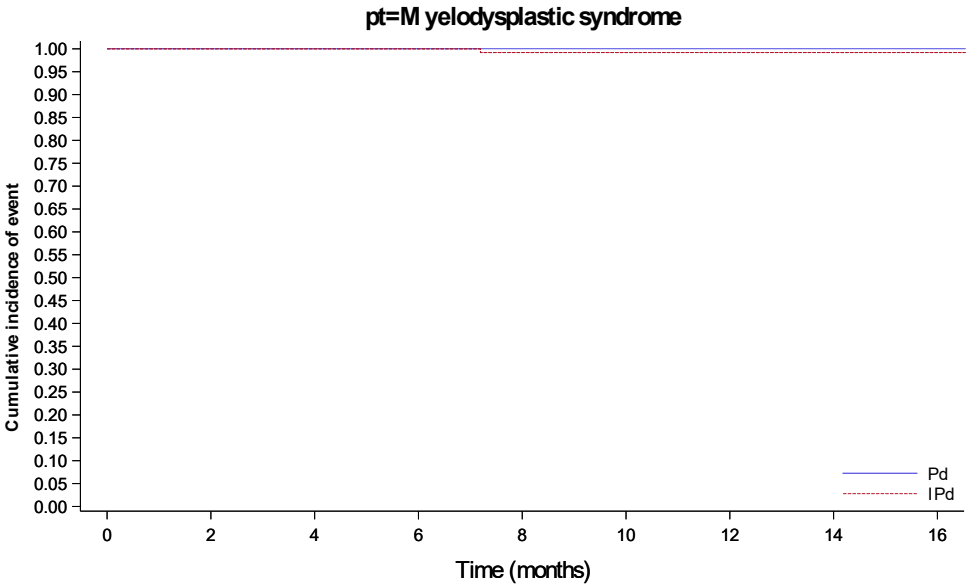
16.2.7.1.2.1.12 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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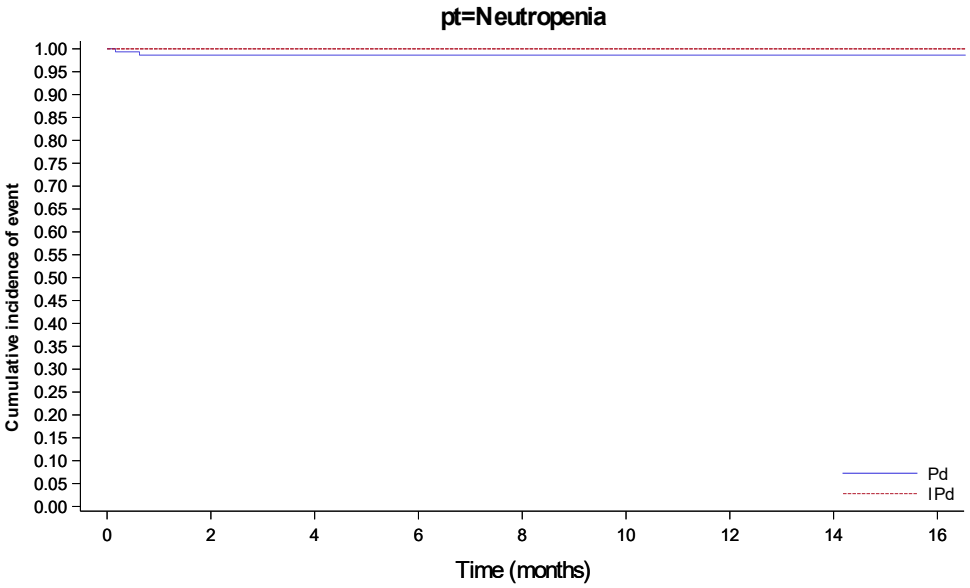
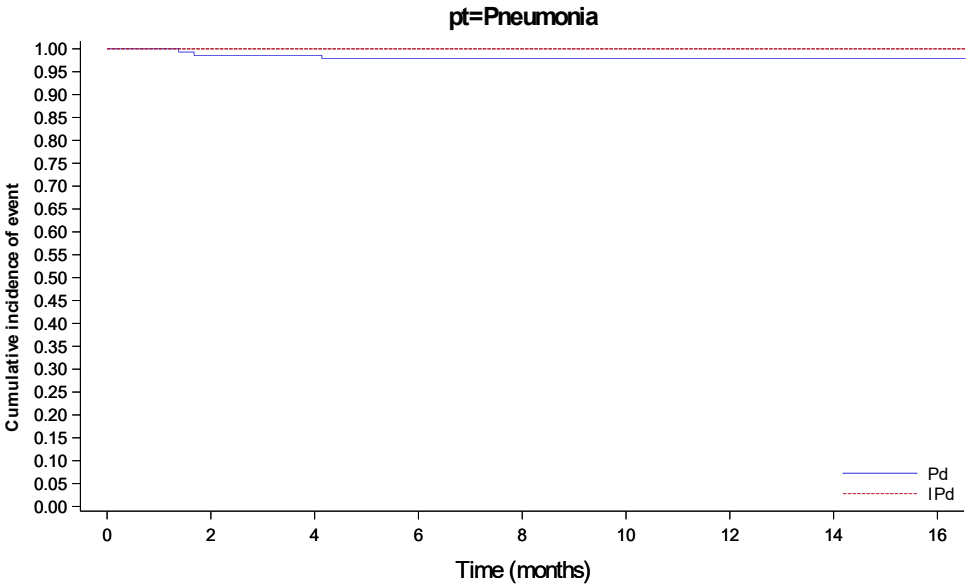
16.2.7.1.2.1.12 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population



Number at Risk

Pd	149	140	132	115	106	102	87	54	26
IPd	152	149	141	128	123	116	104	71	30

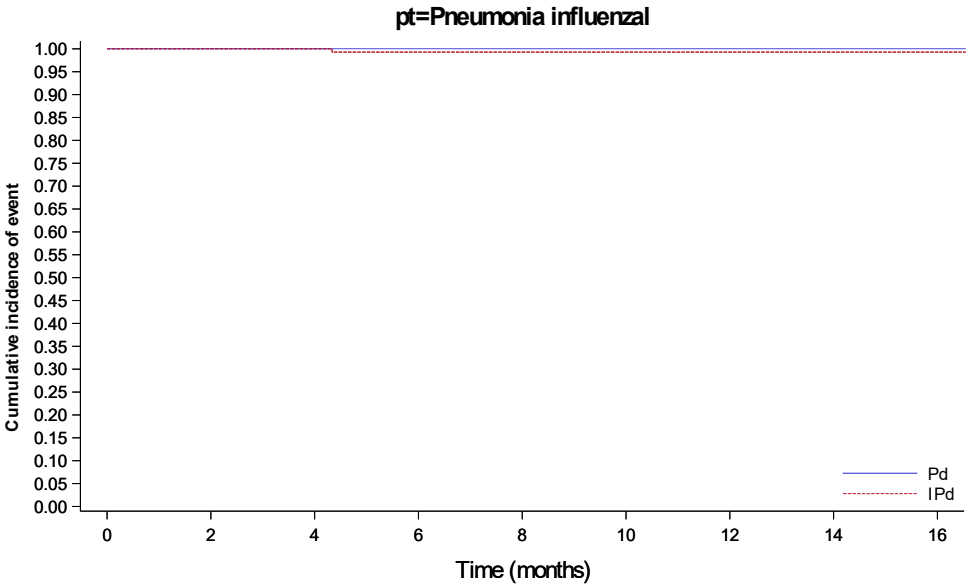
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.12 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population



Number at Risk

Pd	149	140	132	117	106	102	87	54	26
IPd	152	149	141	128	123	116	104	71	30

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.12 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population



Number at Risk

Pd	149	142	134	117	106	102	87	54	26
IPd	152	149	141	128	123	116	104	71	30

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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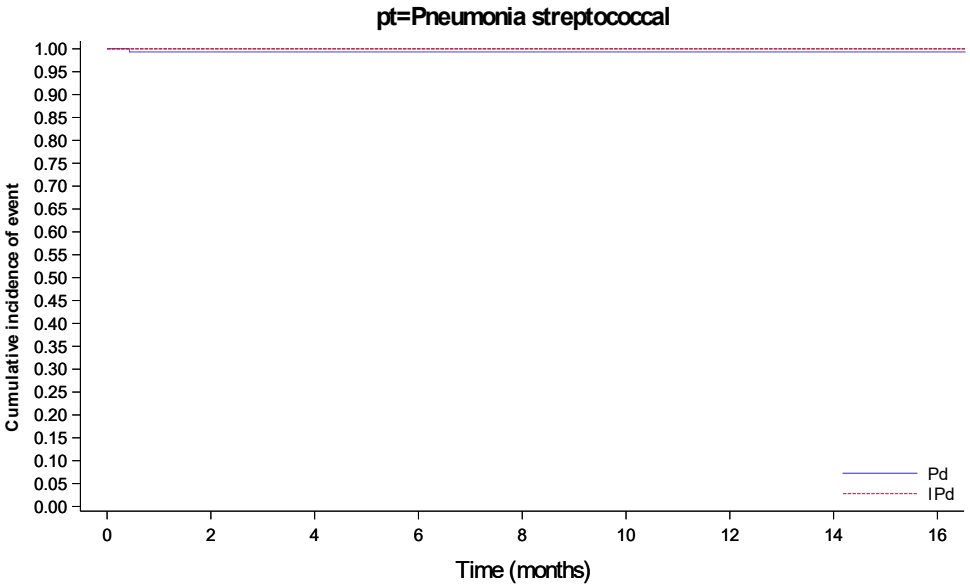

Number at Risk

Pd	149	141	133	117	106	102	87	54	26
IPd	152	149	141	128	123	116	104	71	30

16.2.7.1 Safety endpoints
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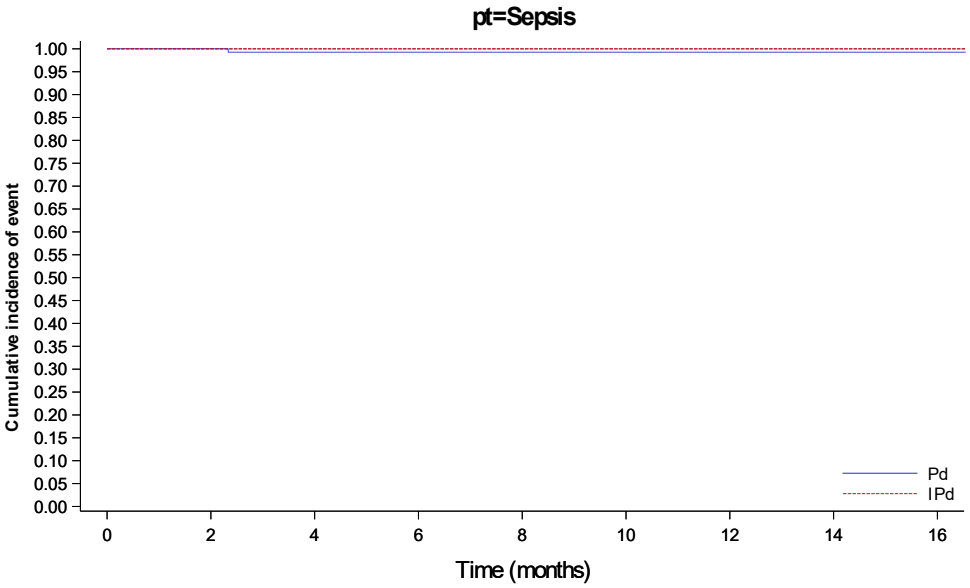

Number at Risk

Pd	149	142	134	117	106	102	87	54	26
IPd	152	149	141	128	123	116	104	71	30

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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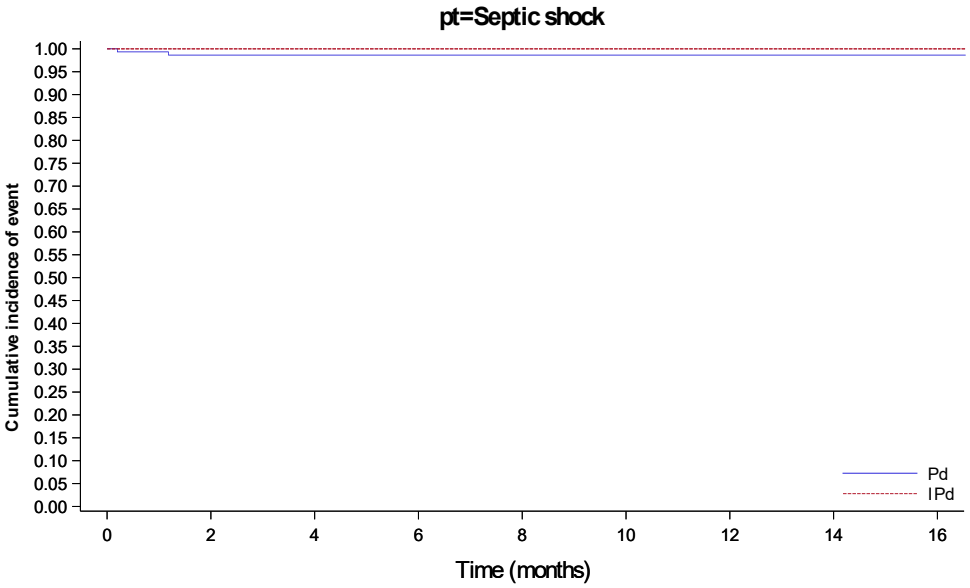
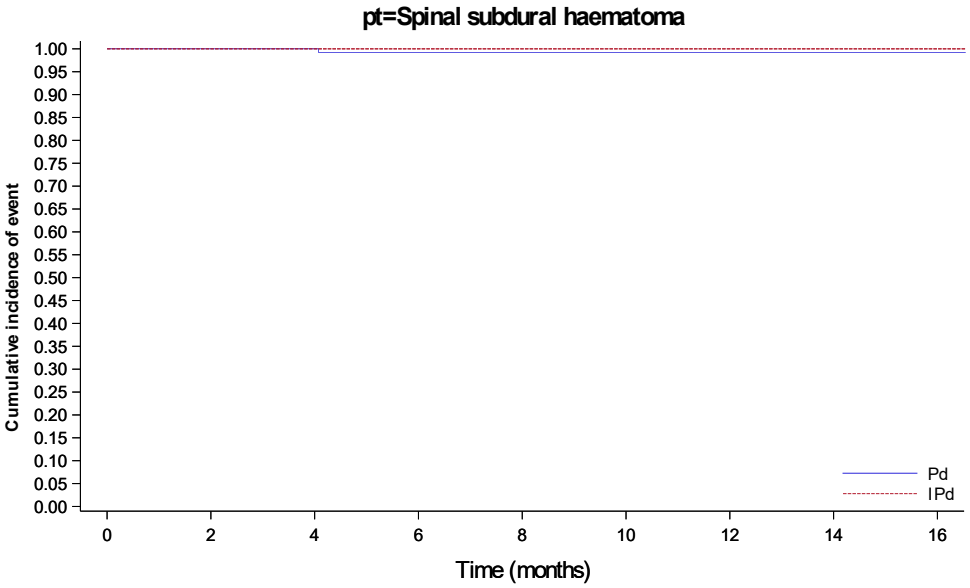


Number at Risk

Pd	149	142	134	117	106	102	87	54	26
IPd	152	149	141	128	123	116	104	71	30

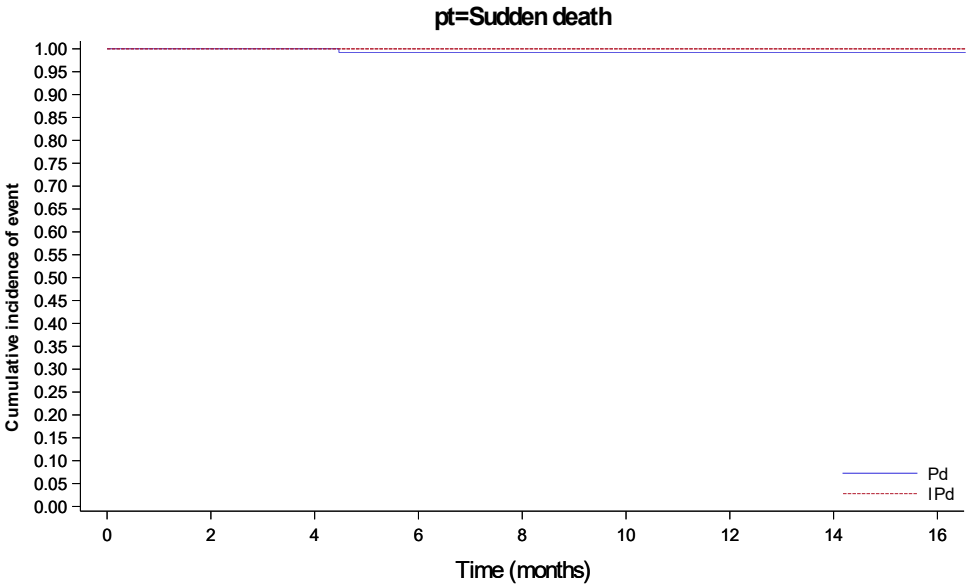
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.12 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population



Number at Risk

Pd	149	142	134	116	105	101	86	53	25
IPd	152	149	141	128	123	116	104	71	30

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.12 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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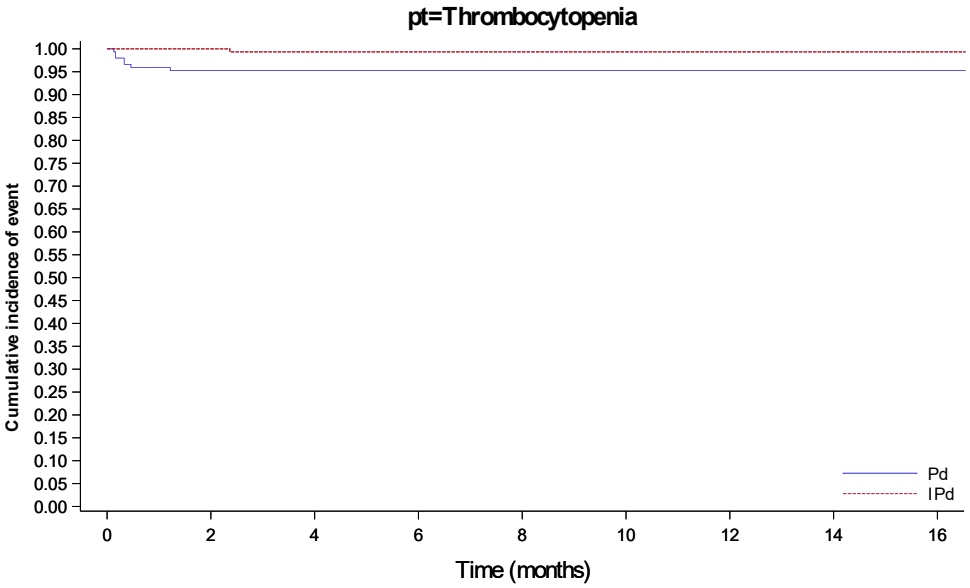
16.2.7.1.2.1.12 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population



Number at Risk

Pd	149	136	130	114	105	101	86	53	25
IPd	152	149	140	127	122	115	103	70	29

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Blood and lymphatic system disorders (days)		
Number (%) of events	10 (6.7)	10 (6.6)
Number (%) of patients censored	139 (93.3)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.8572
Hazard ratio (95% CI) vs Pd	-	0.923 (0.384 to 2.217)
P-value	-	0.8571
Events probability (95% CI)[b]		
2 Months	0.972 (0.928 to 0.990)	0.987 (0.948 to 0.997)
4 Months	0.958 (0.908 to 0.981)	0.959 (0.911 to 0.981)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	0.933 (0.875 to 0.965)	0.945 (0.893 to 0.972)
8 Months	0.933 (0.875 to 0.965)	0.937 (0.882 to 0.967)
10 Months	0.923 (0.861 to 0.958)	0.928 (0.871 to 0.961)
12 Months	0.923 (0.861 to 0.958)	0.928 (0.871 to 0.961)
14 Months	0.923 (0.861 to 0.958)	0.928 (0.871 to 0.961)
16 Months	0.923 (0.861 to 0.958)	0.928 (0.871 to 0.961)
Number of patients at risk[b]		
2 Months	138	147
4 Months	128	136
6 Months	108	121
8 Months	98	116
10 Months	93	110
12 Months	79	100
14 Months	50	68
16 Months	24	29
Cardiac disorders (days)		
Number (%) of events	4 (2.7)	19 (12.5)
Number (%) of patients censored	145 (97.3)	133 (87.5)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0019
Hazard ratio (95% CI) vs Pd	-	4.696 (1.598 to 13.804)
P-value	-	0.0049
Hazard ratio inverted (95% CI) vs IPd	0.213 (0.072 to 0.626)	-
Events probability (95% CI)[b]		
2 Months	0.993 (0.952 to 0.999)	0.934 (0.880 to 0.964)
4 Months	0.993 (0.952 to 0.999)	0.913 (0.855 to 0.949)
6 Months	0.985 (0.943 to 0.996)	0.899 (0.838 to 0.938)
8 Months	0.977 (0.928 to 0.992)	0.883 (0.819 to 0.926)
10 Months	0.967 (0.913 to 0.988)	0.867 (0.799 to 0.913)
12 Months	0.967 (0.913 to 0.988)	0.867 (0.799 to 0.913)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.967 (0.913 to 0.988)	0.867 (0.799 to 0.913)
16 Months	0.967 (0.913 to 0.988)	0.867 (0.799 to 0.913)
Number of patients at risk[b]		
2 Months	142	139
4 Months	134	130
6 Months	116	117
8 Months	104	110
10 Months	99	101
12 Months	84	89
14 Months	53	61
16 Months	26	23
Eye disorders (days)		
Number (%) of events	13 (8.7)	11 (7.2)
Number (%) of patients censored	136 (91.3)	141 (92.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.5041
Hazard ratio (95% CI) vs Pd	-	0.761 (0.341 to 1.699)
P-value	-	0.5050
Events probability (95% CI)[b]		
2 Months	0.973 (0.929 to 0.990)	0.987 (0.948 to 0.997)
4 Months	0.907 (0.846 to 0.945)	0.980 (0.939 to 0.994)
6 Months	0.907 (0.846 to 0.945)	0.980 (0.939 to 0.994)
8 Months	0.907 (0.846 to 0.945)	0.948 (0.893 to 0.975)
10 Months	0.907 (0.846 to 0.945)	0.922 (0.860 to 0.958)
12 Months	0.907 (0.846 to 0.945)	0.913 (0.849 to 0.951)
14 Months	0.907 (0.846 to 0.945)	0.913 (0.849 to 0.951)
16 Months	0.907 (0.846 to 0.945)	0.913 (0.849 to 0.951)
Number of patients at risk[b]		
2 Months	139	147

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	122	138
6 Months	106	125
8 Months	96	116
10 Months	93	106
12 Months	78	93
14 Months	48	64
16 Months	24	30
Gastrointestinal disorders (days)		
Number (%) of events	74 (49.7)	79 (52.0)
Number (%) of patients censored	75 (50.3)	73 (48.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	0.82 (0.559 to 1.971)	0.72 (0.460 to 1.248)
Median (95% CI)	7.46 (3.844 to NC)	8.57 (3.483 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.7937

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	1.043 (0.759 to 1.435)
P-value	-	0.7938
Events probability (95% CI)[b]		
2 Months	0.677 (0.594 to 0.746)	0.649 (0.568 to 0.720)
4 Months	0.573 (0.487 to 0.649)	0.567 (0.483 to 0.642)
6 Months	0.521 (0.434 to 0.601)	0.559 (0.476 to 0.635)
8 Months	0.492 (0.404 to 0.574)	0.513 (0.429 to 0.591)
10 Months	0.482 (0.393 to 0.565)	0.497 (0.412 to 0.575)
12 Months	0.471 (0.382 to 0.555)	0.470 (0.385 to 0.550)
14 Months	0.471 (0.382 to 0.555)	0.460 (0.375 to 0.541)
16 Months	0.446 (0.350 to 0.538)	0.433 (0.338 to 0.524)
Number of patients at risk[b]		
2 Months	95	96
4 Months	75	80
6 Months	58	73
8 Months	48	64
10 Months	46	56
12 Months	41	47

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	26	30
16 Months	13	12
General disorders and administration site conditions (days)		
Number (%) of events	81 (54.4)	69 (45.4)
Number (%) of patients censored	68 (45.6)	83 (54.6)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	0.99 (0.493 to 1.544)	2.07 (0.887 to 3.220)
Median (95% CI)	6.18 (3.745 to 13.010)	NC (6.538 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0483
Hazard ratio (95% CI) vs Pd	-	0.724 (0.524 to 0.999)
P-value	-	0.0493
Events probability (95% CI)[b]		
2 Months	0.649 (0.565 to 0.720)	0.769 (0.694 to 0.829)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.546 (0.460 to 0.624)	0.648 (0.565 to 0.718)
6 Months	0.514 (0.428 to 0.593)	0.605 (0.521 to 0.678)
8 Months	0.463 (0.377 to 0.544)	0.566 (0.481 to 0.642)
10 Months	0.445 (0.359 to 0.527)	0.532 (0.446 to 0.610)
12 Months	0.424 (0.337 to 0.507)	0.532 (0.446 to 0.610)
14 Months	0.410 (0.323 to 0.495)	0.532 (0.446 to 0.610)
16 Months	0.410 (0.323 to 0.495)	0.506 (0.411 to 0.594)
Number of patients at risk[b]		
2 Months	91	115
4 Months	73	94
6 Months	61	79
8 Months	52	71
10 Months	46	60
12 Months	39	52
14 Months	24	38
16 Months	12	21
Infections and infestations (days)		
Number (%) of events	82 (55.0)	99 (65.1)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	67 (45.0)	53 (34.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	1.68 (1.347 to 1.906)	0.85 (0.723 to 1.807)
Median (95% CI)	6.51 (2.595 to 9.166)	3.91 (2.793 to 5.060)
75% quantile (95% CI)	NC (NC to NC)	NC (11.269 to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1429
Hazard ratio (95% CI) vs Pd	-	1.244 (0.928 to 1.668)
P-value	-	0.1437
Events probability (95% CI)[b]		
2 Months	0.660 (0.576 to 0.731)	0.662 (0.580 to 0.731)
4 Months	0.527 (0.441 to 0.606)	0.480 (0.397 to 0.558)
6 Months	0.502 (0.415 to 0.582)	0.373 (0.294 to 0.453)
8 Months	0.428 (0.341 to 0.511)	0.349 (0.270 to 0.428)
10 Months	0.398 (0.312 to 0.483)	0.330 (0.252 to 0.410)
12 Months	0.398 (0.312 to 0.483)	0.309 (0.232 to 0.389)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.385 (0.298 to 0.471)	0.297 (0.220 to 0.378)
16 Months	0.385 (0.298 to 0.471)	0.297 (0.220 to 0.378)
Number of patients at risk[b]		
2 Months	93	98
4 Months	68	66
6 Months	57	45
8 Months	45	42
10 Months	40	35
12 Months	33	27
14 Months	20	20
16 Months	11	11
Injury, poisoning and procedural complications (days)		
Number (%) of events	15 (10.1)	65 (42.8)
Number (%) of patients censored	134 (89.9)	87 (57.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	0.13 (0.099 to 0.197)
Median (95% CI)	NC (NC to NC)	NC (8.509 to NC)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	<.0001
Hazard ratio (95% CI) vs Pd	-	5.778 (3.240 to 10.304)
P-value	-	<.0001
Hazard ratio inverted (95% CI) vs IPd	0.173 (0.097 to 0.309)	-
Events probability (95% CI)[b]		
2 Months	0.972 (0.928 to 0.989)	0.645 (0.563 to 0.715)
4 Months	0.950 (0.899 to 0.976)	0.631 (0.549 to 0.702)
6 Months	0.943 (0.889 to 0.971)	0.624 (0.541 to 0.695)
8 Months	0.908 (0.843 to 0.947)	0.592 (0.508 to 0.666)
10 Months	0.889 (0.819 to 0.933)	0.583 (0.499 to 0.658)
12 Months	0.889 (0.819 to 0.933)	0.573 (0.488 to 0.650)
14 Months	0.889 (0.819 to 0.933)	0.573 (0.488 to 0.650)
16 Months	0.889 (0.819 to 0.933)	0.516 (0.406 to 0.615)
Number of patients at risk[b]		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
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16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	137	96
4 Months	129	89
6 Months	113	79
8 Months	98	71
10 Months	93	64
12 Months	78	55
14 Months	48	33
16 Months	23	12
Investigations (days)		
Number (%) of events	8 (5.4)	14 (9.2)
Number (%) of patients censored	141 (94.6)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1726

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	1.861 (0.751 to 4.612)
P-value	-	0.1796
Events probability (95% CI)[b]		
2 Months	0.979 (0.937 to 0.993)	0.967 (0.923 to 0.986)
4 Months	0.965 (0.918 to 0.985)	0.940 (0.888 to 0.968)
6 Months	0.956 (0.905 to 0.980)	0.933 (0.879 to 0.963)
8 Months	0.956 (0.905 to 0.980)	0.933 (0.879 to 0.963)
10 Months	0.956 (0.905 to 0.980)	0.916 (0.857 to 0.952)
12 Months	0.956 (0.905 to 0.980)	0.907 (0.845 to 0.945)
14 Months	0.944 (0.884 to 0.973)	0.897 (0.832 to 0.938)
16 Months	0.944 (0.884 to 0.973)	0.897 (0.832 to 0.938)
Number of patients at risk[b]		
2 Months	138	145
4 Months	128	133
6 Months	111	120
8 Months	100	115
10 Months	97	106

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
12 Months	83	94
14 Months	51	64
16 Months	24	29
Metabolism and nutrition disorders (days)		
Number (%) of events	13 (8.7)	21 (13.8)
Number (%) of patients censored	136 (91.3)	131 (86.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2081
Hazard ratio (95% CI) vs Pd	-	1.554 (0.778 to 3.103)
P-value	-	0.2118
Events probability (95% CI)[b]		

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CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	0.945 (0.893 to 0.972)	0.934 (0.880 to 0.964)
4 Months	0.923 (0.865 to 0.957)	0.886 (0.823 to 0.927)
6 Months	0.907 (0.845 to 0.945)	0.886 (0.823 to 0.927)
8 Months	0.907 (0.845 to 0.945)	0.870 (0.804 to 0.915)
10 Months	0.907 (0.845 to 0.945)	0.862 (0.794 to 0.909)
12 Months	0.907 (0.845 to 0.945)	0.862 (0.794 to 0.909)
14 Months	0.907 (0.845 to 0.945)	0.852 (0.782 to 0.901)
16 Months	0.907 (0.845 to 0.945)	0.852 (0.782 to 0.901)
Number of patients at risk[b]		
2 Months	134	139
4 Months	124	126
6 Months	107	116
8 Months	97	110
10 Months	93	103
12 Months	79	92
14 Months	50	62
16 Months	24	28
Musculoskeletal and connective tissue disorders (days)		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

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	Pd (N=149)	**IPd (N=152)**
Number (%) of events	69 (46.3)	81 (53.3)
Number (%) of patients censored	80 (53.7)	71 (46.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	2.50 (1.051 to 3.910)	2.10 (1.314 to 3.450)
Median (95% CI)	10.38 (5.618 to NC)	9.76 (6.604 to 15.737)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.7574
Hazard ratio (95% CI) vs Pd	-	1.052 (0.762 to 1.453)
P-value	-	0.7579
Events probability (95% CI)[b]		
2 Months	0.786 (0.709 to 0.844)	0.775 (0.700 to 0.834)
4 Months	0.674 (0.589 to 0.745)	0.638 (0.555 to 0.710)
6 Months	0.571 (0.482 to 0.651)	0.609 (0.525 to 0.683)
8 Months	0.533 (0.443 to 0.616)	0.523 (0.438 to 0.602)
10 Months	0.511 (0.419 to 0.596)	0.483 (0.398 to 0.563)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
12 Months	0.474 (0.380 to 0.562)	0.442 (0.358 to 0.524)
14 Months	0.460 (0.366 to 0.550)	0.430 (0.345 to 0.513)
16 Months	0.460 (0.366 to 0.550)	0.405 (0.312 to 0.496)
Number of patients at risk[b]		
2 Months	110	115
4 Months	88	91
6 Months	62	79
8 Months	50	67
10 Months	46	60
12 Months	35	50
14 Months	19	35
16 Months	8	14
Nervous system disorders (days)		
Number (%) of events	38 (25.5)	53 (34.9)
Number (%) of patients censored	111 (74.5)	99 (65.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	7.66 (3.844 to NC)	5.29 (2.136 to 8.016)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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	Pd (N=149)	**IPd (N=152)**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1079
Hazard ratio (95% CI) vs Pd	-	1.413 (0.925 to 2.157)
P-value	-	0.1096
Events probability (95% CI)[b]		
2 Months	0.868 (0.800 to 0.914)	0.848 (0.780 to 0.896)
4 Months	0.822 (0.748 to 0.876)	0.780 (0.705 to 0.838)
6 Months	0.772 (0.690 to 0.834)	0.713 (0.631 to 0.779)
8 Months	0.744 (0.660 to 0.811)	0.681 (0.597 to 0.751)
10 Months	0.735 (0.649 to 0.803)	0.646 (0.560 to 0.720)
12 Months	0.724 (0.637 to 0.794)	0.628 (0.541 to 0.704)
14 Months	0.724 (0.637 to 0.794)	0.618 (0.529 to 0.694)
16 Months	0.724 (0.637 to 0.794)	0.618 (0.529 to 0.694)
Number of patients at risk[b]		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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	Pd (N=149)	**IPd (N=152)**
2 Months	121	126
4 Months	108	111
6 Months	89	92
8 Months	79	83
10 Months	74	73
12 Months	64	64
14 Months	36	44
16 Months	17	20
Psychiatric disorders (days)		
Number (%) of events	26 (17.4)	25 (16.4)
Number (%) of patients censored	123 (82.6)	127 (83.6)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (7.984 to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.6811

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	0.891 (0.515 to 1.543)
P-value	-	0.6809
Events probability (95% CI)[b]		
2 Months	0.912 (0.853 to 0.948)	0.914 (0.857 to 0.949)
4 Months	0.875 (0.809 to 0.919)	0.880 (0.816 to 0.923)
6 Months	0.850 (0.778 to 0.900)	0.836 (0.765 to 0.887)
8 Months	0.823 (0.746 to 0.878)	0.836 (0.765 to 0.887)
10 Months	0.823 (0.746 to 0.878)	0.827 (0.755 to 0.880)
12 Months	0.812 (0.733 to 0.870)	0.827 (0.755 to 0.880)
14 Months	0.800 (0.719 to 0.861)	0.827 (0.755 to 0.880)
16 Months	0.800 (0.719 to 0.861)	0.827 (0.755 to 0.880)
Number of patients at risk[b]		
2 Months	129	136
4 Months	116	125
6 Months	98	109
8 Months	87	104
10 Months	84	96

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

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16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	70	87
14 Months	43	61
16 Months	19	25
Renal and urinary disorders (days)		
Number (%) of events	13 (8.7)	12 (7.9)
Number (%) of patients censored	136 (91.3)	140 (92.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.7351
Hazard ratio (95% CI) vs Pd	-	0.873 (0.398 to 1.914)
P-value	-	0.7352
Events probability (95% CI)[b]		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	0.945 (0.893 to 0.972)	0.947 (0.897 to 0.973)
4 Months	0.931 (0.875 to 0.962)	0.927 (0.872 to 0.959)
6 Months	0.931 (0.875 to 0.962)	0.927 (0.872 to 0.959)
8 Months	0.904 (0.839 to 0.943)	0.919 (0.862 to 0.953)
10 Months	0.904 (0.839 to 0.943)	0.919 (0.862 to 0.953)
12 Months	0.904 (0.839 to 0.943)	0.919 (0.862 to 0.953)
14 Months	0.904 (0.839 to 0.943)	0.919 (0.862 to 0.953)
16 Months	0.904 (0.839 to 0.943)	0.919 (0.862 to 0.953)
Number of patients at risk[b]		
2 Months	134	141
4 Months	125	132
6 Months	109	119
8 Months	96	114
10 Months	92	108
12 Months	81	96
14 Months	50	65
16 Months	24	28
Respiratory, thoracic and mediastinal disorders (days)		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of events	40 (26.8)	59 (38.8)
Number (%) of patients censored	109 (73.2)	93 (61.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	8.18 (1.873 to NC)	3.88 (1.873 to 4.567)
Median (95% CI)	NC (NC to NC)	NC (11.105 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0659
Hazard ratio (95% CI) vs Pd	-	1.454 (0.973 to 2.173)
P-value	-	0.0675
Events probability (95% CI)[b]		
2 Months	0.814 (0.741 to 0.869)	0.808 (0.735 to 0.862)
4 Months	0.778 (0.700 to 0.837)	0.738 (0.659 to 0.801)
6 Months	0.761 (0.682 to 0.823)	0.666 (0.582 to 0.736)
8 Months	0.752 (0.672 to 0.816)	0.641 (0.556 to 0.714)
10 Months	0.725 (0.641 to 0.792)	0.605 (0.518 to 0.681)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	0.716 (0.631 to 0.784)	0.586 (0.498 to 0.664)
14 Months	0.704 (0.617 to 0.775)	0.586 (0.498 to 0.664)
16 Months	0.704 (0.617 to 0.775)	0.573 (0.483 to 0.653)
Number of patients at risk[b]		
2 Months	115	120
4 Months	103	104
6 Months	90	83
8 Months	84	76
10 Months	78	66
12 Months	65	57
14 Months	41	44
16 Months	18	20
Skin and subcutaneous tissue disorders (days)		
Number (%) of events	36 (24.2)	38 (25.0)
Number (%) of patients censored	113 (75.8)	114 (75.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	9.20 (3.220 to NC)	9.76 (2.825 to NC)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.9331
Hazard ratio (95% CI) vs Pd	-	0.981 (0.622 to 1.547)
P-value	-	0.9331
Events probability (95% CI)[b]		
2 Months	0.851 (0.782 to 0.899)	0.848 (0.780 to 0.896)
4 Months	0.806 (0.732 to 0.862)	0.814 (0.742 to 0.868)
6 Months	0.780 (0.701 to 0.840)	0.807 (0.734 to 0.862)
8 Months	0.753 (0.670 to 0.817)	0.791 (0.715 to 0.848)
10 Months	0.743 (0.659 to 0.809)	0.747 (0.666 to 0.811)
12 Months	0.743 (0.659 to 0.809)	0.738 (0.655 to 0.803)
14 Months	0.729 (0.643 to 0.799)	0.738 (0.655 to 0.803)
16 Months	0.729 (0.643 to 0.799)	0.721 (0.633 to 0.791)
Number of patients at risk[b]		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	120	126
4 Months	107	115
6 Months	87	101
8 Months	76	94
10 Months	72	82
12 Months	62	73
14 Months	38	49
16 Months	17	25
Vascular disorders (days)		
Number (%) of events	13 (8.7)	19 (12.5)
Number (%) of patients censored	136 (91.3)	133 (87.5)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3613

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	1.387 (0.685 to 2.809)
P-value	-	0.3635
Events probability (95% CI)[b]		
2 Months	0.973 (0.928 to 0.990)	0.954 (0.905 to 0.978)
4 Months	0.951 (0.899 to 0.976)	0.912 (0.853 to 0.948)
6 Months	0.919 (0.858 to 0.954)	0.905 (0.845 to 0.943)
8 Months	0.901 (0.835 to 0.942)	0.897 (0.835 to 0.937)
10 Months	0.901 (0.835 to 0.942)	0.889 (0.824 to 0.930)
12 Months	0.901 (0.835 to 0.942)	0.871 (0.802 to 0.917)
14 Months	0.901 (0.835 to 0.942)	0.861 (0.789 to 0.909)
16 Months	0.901 (0.835 to 0.942)	0.861 (0.789 to 0.909)
Number of patients at risk[b]		
2 Months	138	142
4 Months	128	128
6 Months	108	115
8 Months	95	109
10 Months	91	101

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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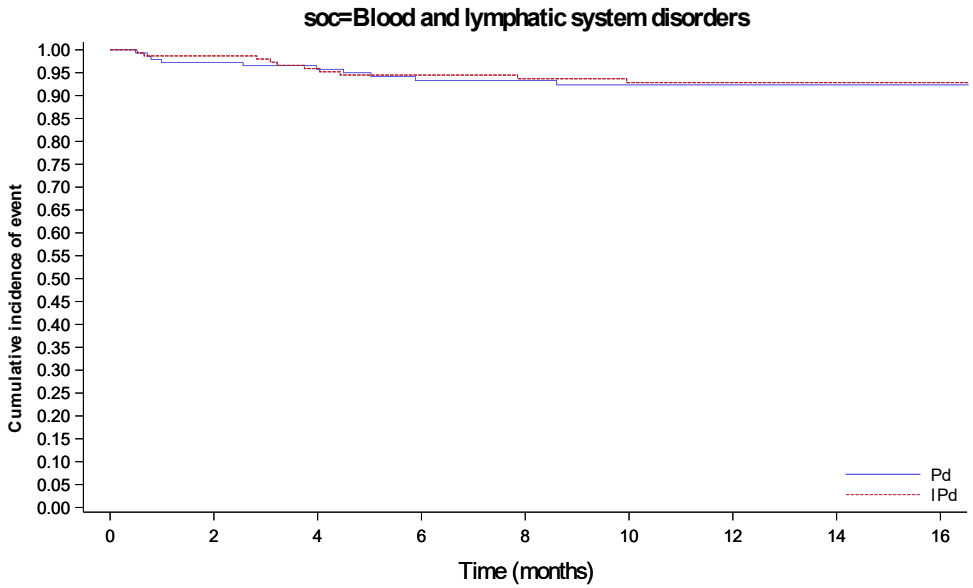
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.13 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

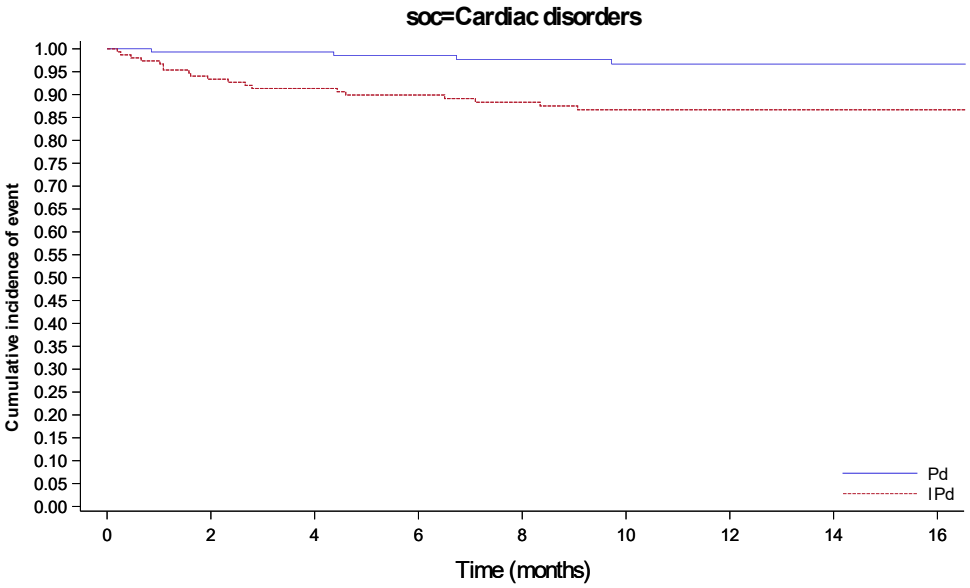
	Pd (N=149)	**IPd (N=152)**
12 Months	79	89
14 Months	49	60
16 Months	25	27

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16FEB2021 22:47)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.14 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to SOC by treatment group - Safety population



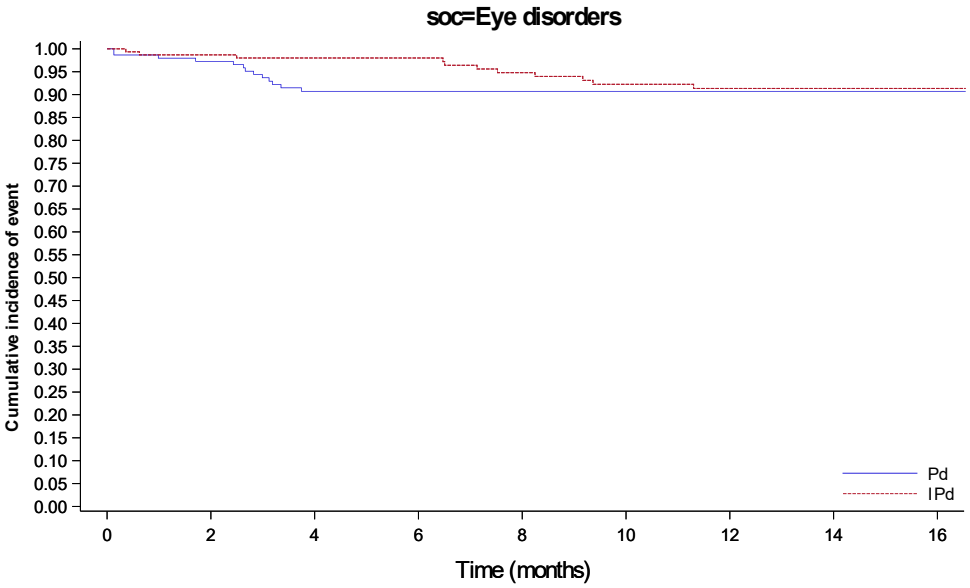
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.14 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	142	134	116	104	99	84	53	26
IPd	152	139	130	117	110	101	89	61	23

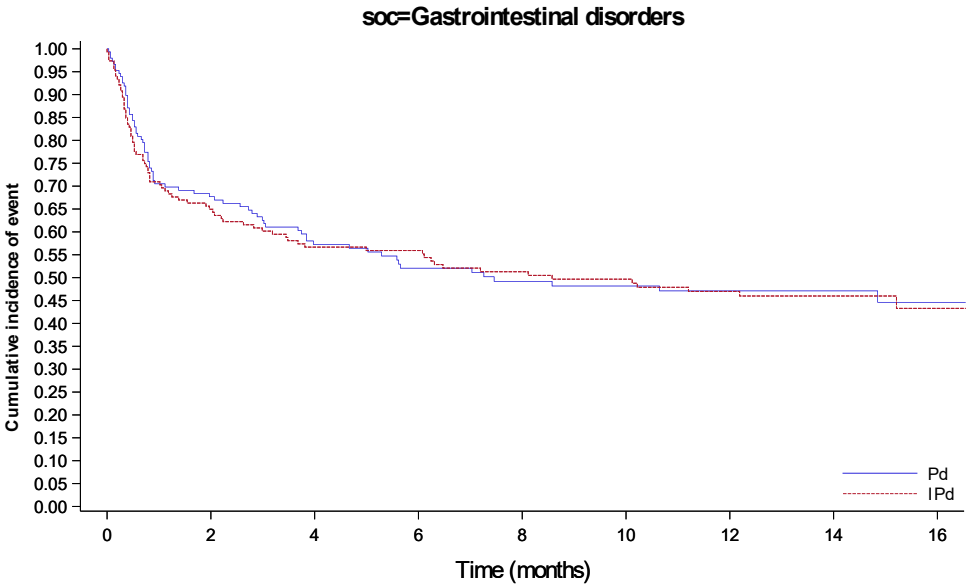
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.14 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	139	122	106	96	93	78	48	24
IPd	152	147	138	125	116	106	93	64	30

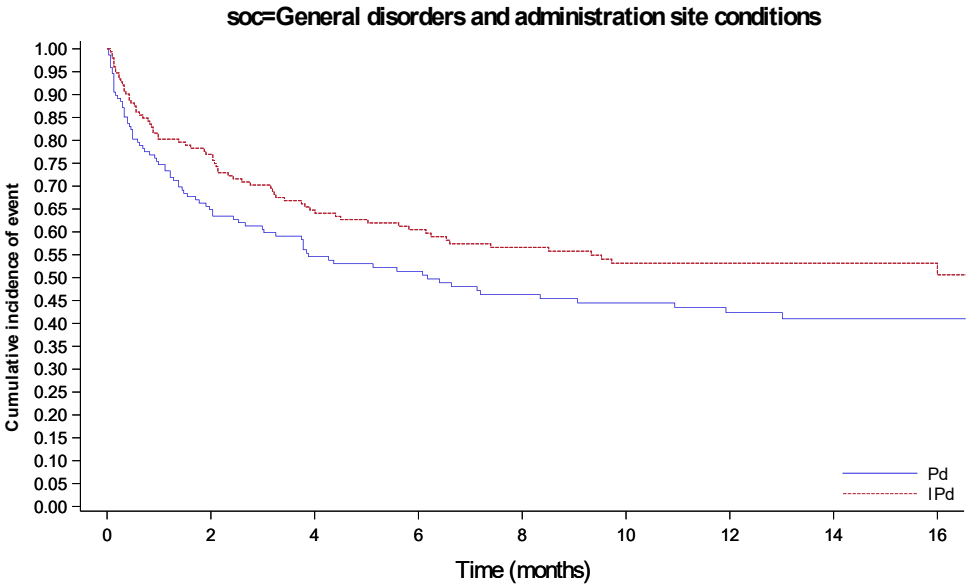
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.14 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	148	95	75	58	48	46	41	26	13
IPd	152	96	80	73	64	56	47	30	12

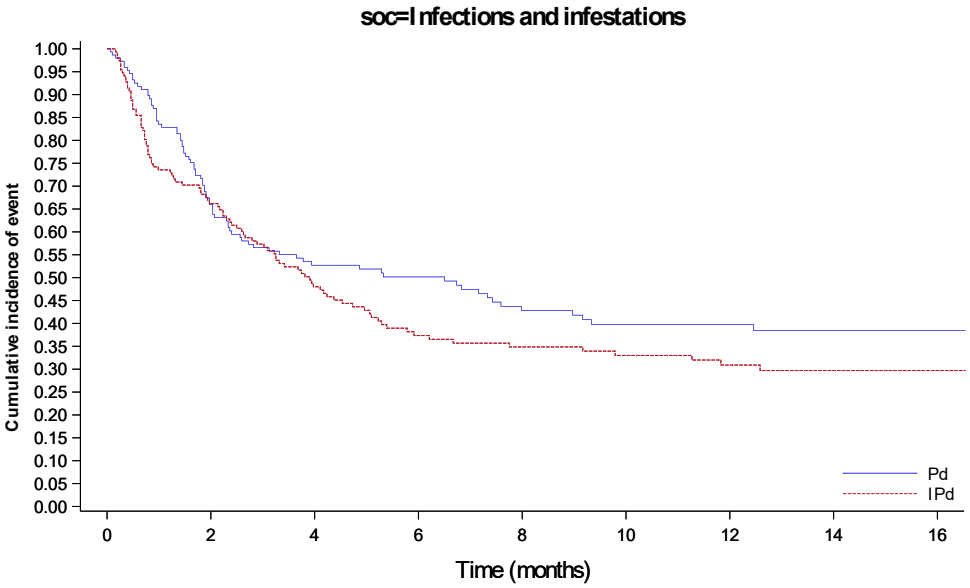
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.14 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	148	91	73	61	52	46	39	24	12
IPd	152	115	94	79	71	60	52	38	21

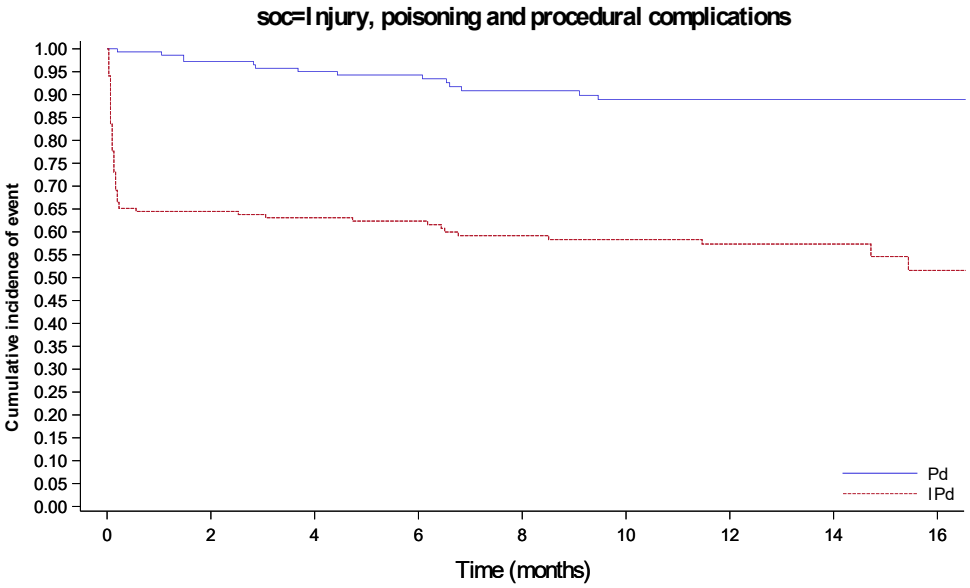
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.14 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	93	68	57	45	40	33	20	11
IPd	152	98	66	45	42	35	27	20	11

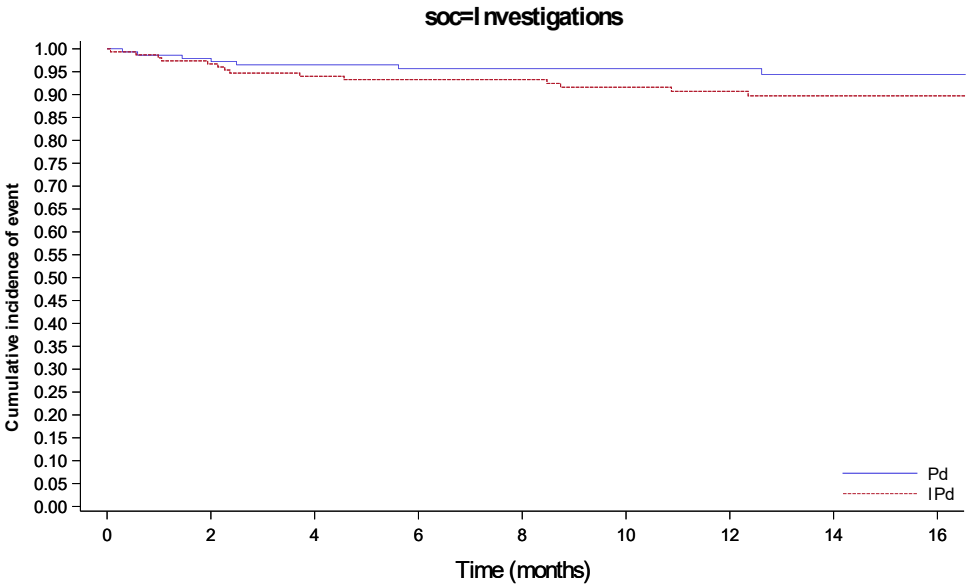
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.14 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	148	137	129	113	98	93	78	48	23
IPd	152	96	89	79	71	64	55	33	12

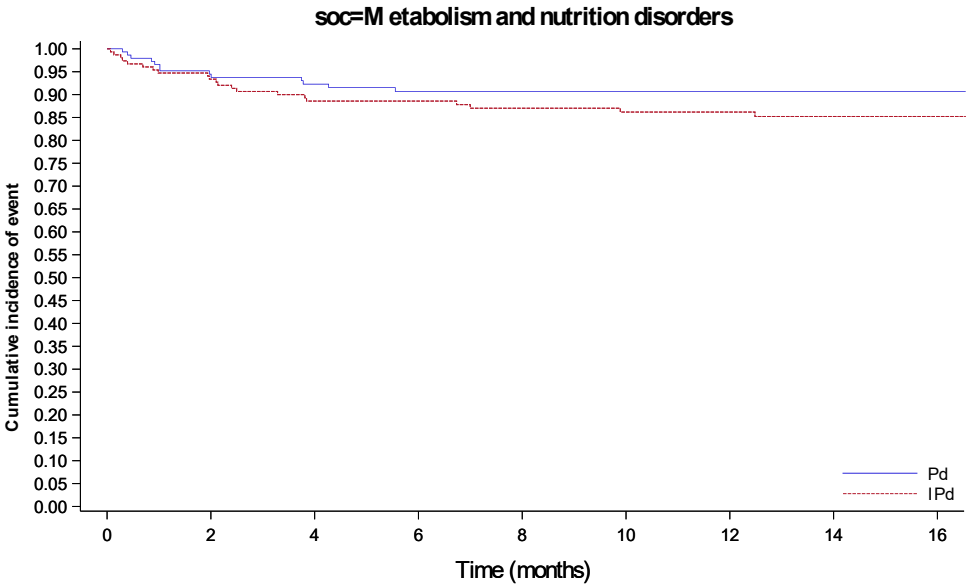
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.14 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	148	138	128	111	100	97	83	51	24
IPd	152	145	133	120	115	106	94	64	29

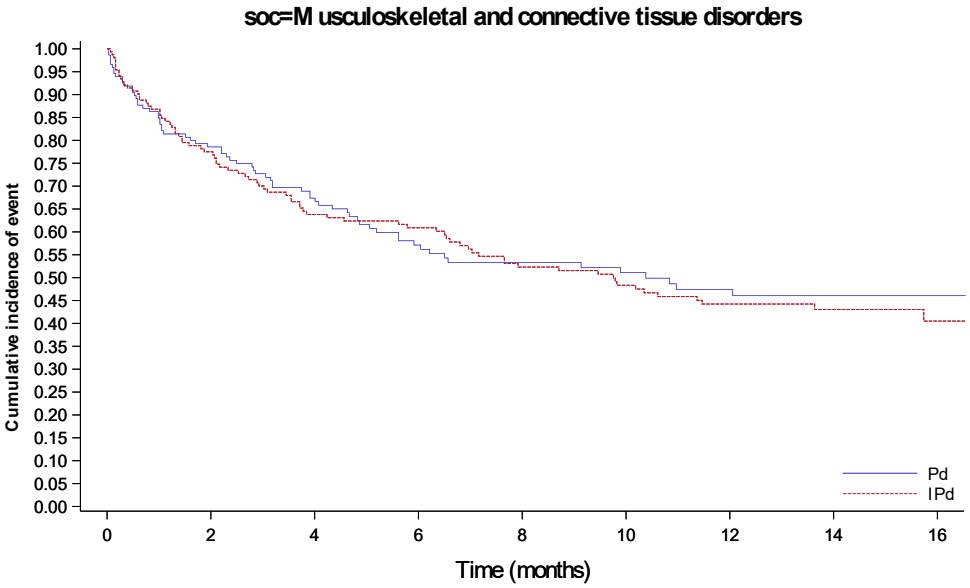
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.14 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to SOC by treatment group - Safety population



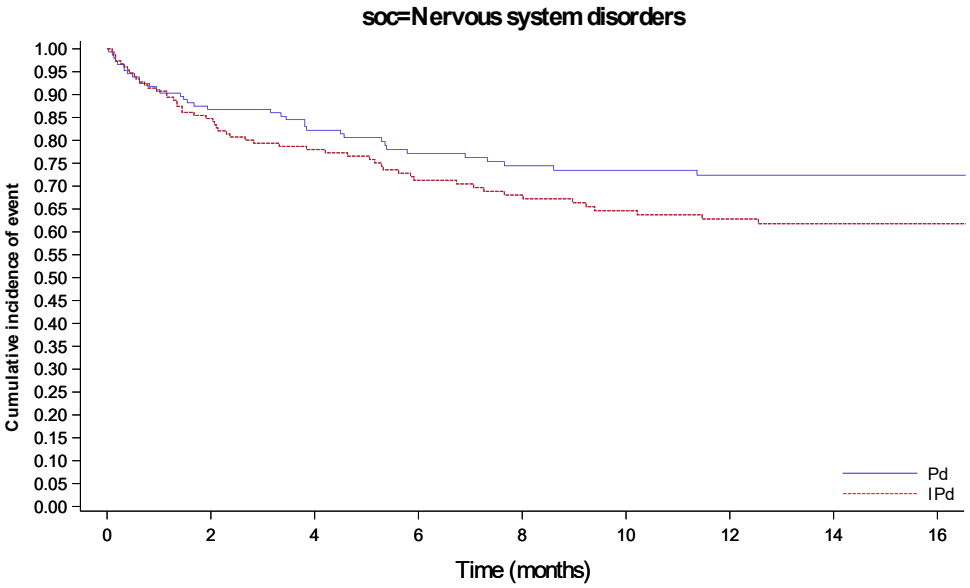
Number at Risk

Pd	149	134	124	107	97	93	79	50	24
IPd	152	139	126	116	110	103	92	62	28

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.14 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to SOC by treatment group - Safety population



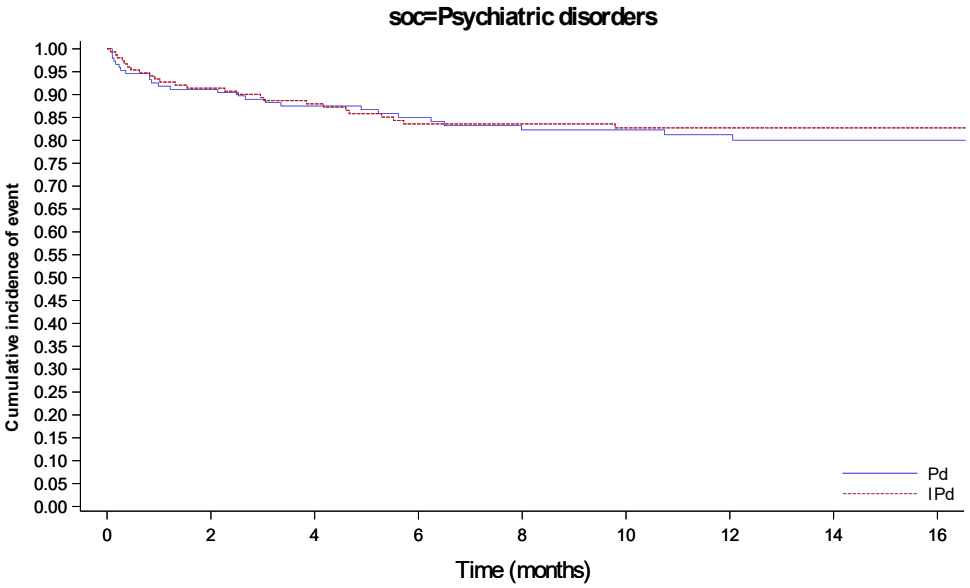
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.14 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	147	121	108	89	79	74	64	36	17
IPd	152	126	111	92	83	73	64	44	20

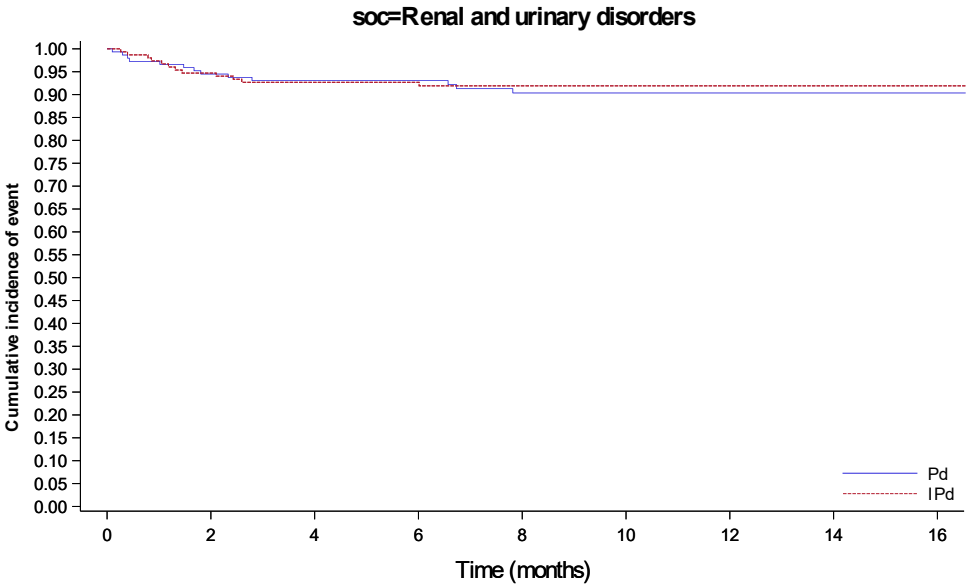
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.14 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to SOC by treatment group - Safety population



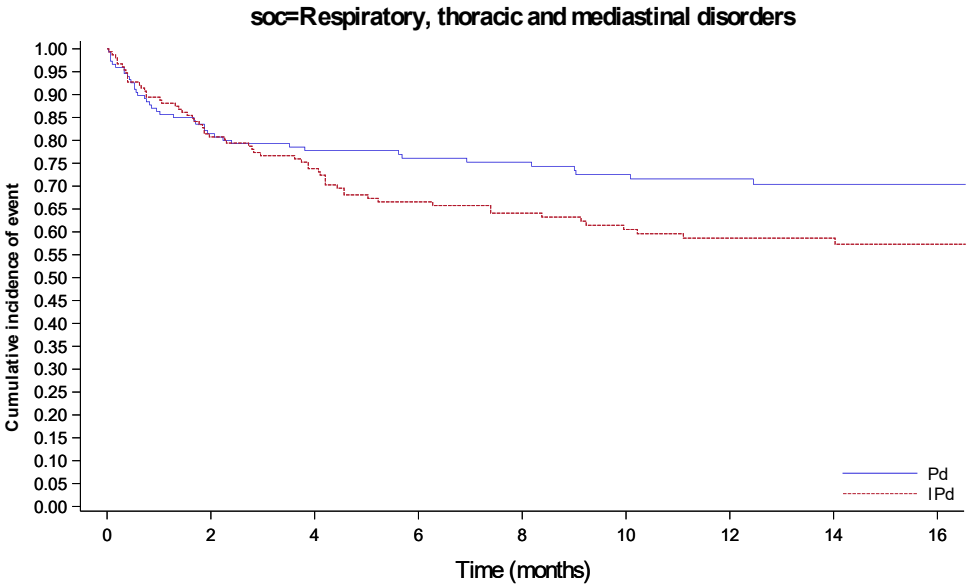
Number at Risk

Pd	149	129	116	98	87	84	70	43	19
IPd	152	136	125	109	104	96	87	61	25

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.14 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to SOC by treatment group - Safety population



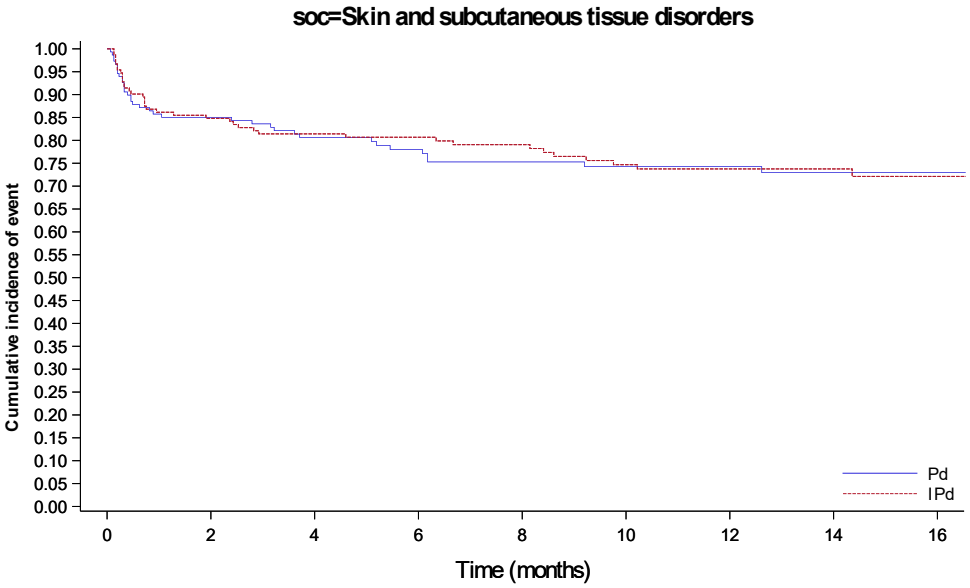
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.14 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	115	103	90	84	78	65	41	18
IPd	152	120	104	83	76	66	57	44	20

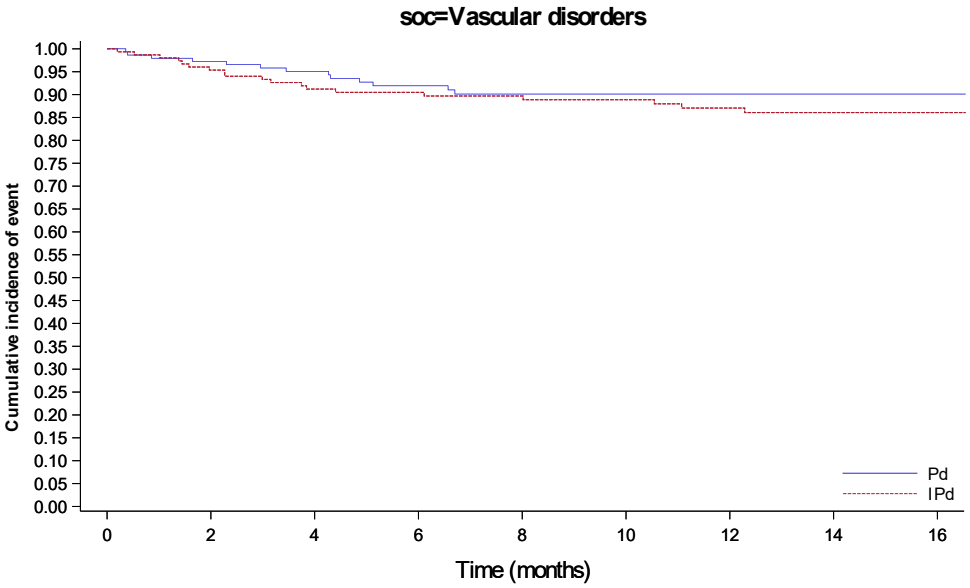
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.14 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	120	107	87	76	72	62	38	17
IPd	152	126	115	101	94	82	73	49	25

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.14 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	138	128	108	95	91	79	49	25
IPd	152	142	128	115	109	101	89	60	27

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Arthralgia (days)		
Number (%) of events	13 (8.7)	13 (8.6)
Number (%) of patients censored	136 (91.3)	139 (91.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.8200
Hazard ratio (95% CI) vs Pd	-	0.915 (0.424 to 1.973)
P-value	-	0.8198
Events probability (95% CI)[b]		
2 Months	0.966 (0.920 to 0.986)	0.967 (0.922 to 0.986)
4 Months	0.937 (0.882 to 0.967)	0.939 (0.886 to 0.968)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	0.929 (0.871 to 0.961)	0.939 (0.886 to 0.968)
8 Months	0.901 (0.835 to 0.942)	0.922 (0.864 to 0.956)
10 Months	0.901 (0.835 to 0.942)	0.922 (0.864 to 0.956)
12 Months	0.901 (0.835 to 0.942)	0.913 (0.852 to 0.950)
14 Months	0.901 (0.835 to 0.942)	0.903 (0.837 to 0.943)
16 Months	0.901 (0.835 to 0.942)	0.903 (0.837 to 0.943)
Number of patients at risk[b]		
2 Months	137	144
4 Months	125	132
6 Months	107	119
8 Months	94	112
10 Months	91	105
12 Months	76	93
14 Months	49	62
16 Months	25	25
Asthenia (days)		
Number (%) of events	25 (16.8)	20 (13.2)
Number (%) of patients censored	124 (83.2)	132 (86.8)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (11.926 to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3918
Hazard ratio (95% CI) vs Pd	-	0.772 (0.427 to 1.398)
P-value	-	0.3934
Events probability (95% CI)[b]		
2 Months	0.911 (0.851 to 0.947)	0.941 (0.889 to 0.969)
4 Months	0.888 (0.824 to 0.930)	0.893 (0.831 to 0.933)
6 Months	0.871 (0.803 to 0.917)	0.878 (0.813 to 0.922)
8 Months	0.854 (0.782 to 0.903)	0.862 (0.794 to 0.909)
10 Months	0.834 (0.758 to 0.888)	0.862 (0.794 to 0.909)
12 Months	0.823 (0.744 to 0.880)	0.862 (0.794 to 0.909)
14 Months	0.809 (0.726 to 0.870)	0.862 (0.794 to 0.909)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	0.809 (0.726 to 0.870)	0.862 (0.794 to 0.909)
Number of patients at risk[b]		
2 Months	128	140
4 Months	118	125
6 Months	102	112
8 Months	91	106
10 Months	85	99
12 Months	72	88
14 Months	46	58
16 Months	24	28
Back pain (days)		
Number (%) of events	20 (13.4)	23 (15.1)
Number (%) of patients censored	129 (86.6)	129 (84.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.8242
Hazard ratio (95% CI) vs Pd	-	1.070 (0.588 to 1.949)
P-value	-	0.8245
Events probability (95% CI)[b]		
2 Months	0.945 (0.893 to 0.972)	0.954 (0.905 to 0.978)
4 Months	0.893 (0.829 to 0.934)	0.899 (0.838 to 0.938)
6 Months	0.878 (0.811 to 0.922)	0.884 (0.820 to 0.926)
8 Months	0.869 (0.800 to 0.916)	0.852 (0.782 to 0.901)
10 Months	0.869 (0.800 to 0.916)	0.844 (0.772 to 0.895)
12 Months	0.859 (0.787 to 0.908)	0.835 (0.761 to 0.887)
14 Months	0.847 (0.772 to 0.899)	0.835 (0.761 to 0.887)
16 Months	0.847 (0.772 to 0.899)	0.835 (0.761 to 0.887)
Number of patients at risk[b]		
2 Months	134	142
4 Months	119	127

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	103	113
8 Months	93	106
10 Months	89	101
12 Months	75	89
14 Months	45	61
16 Months	20	27
Bone pain (days)		
Number (%) of events	6 (4.0)	10 (6.6)
Number (%) of patients censored	143 (96.0)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.4012
Hazard ratio (95% CI) vs Pd	-	1.538 (0.559 to 4.232)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
P-value	-	0.4048
Events probability (95% CI)[b]		
2 Months	0.980 (0.938 to 0.993)	0.980 (0.940 to 0.994)
4 Months	0.980 (0.938 to 0.993)	0.953 (0.904 to 0.977)
6 Months	0.971 (0.925 to 0.989)	0.953 (0.904 to 0.977)
8 Months	0.971 (0.925 to 0.989)	0.953 (0.904 to 0.977)
10 Months	0.952 (0.894 to 0.978)	0.953 (0.904 to 0.977)
12 Months	0.952 (0.894 to 0.978)	0.936 (0.879 to 0.966)
14 Months	0.952 (0.894 to 0.978)	0.936 (0.879 to 0.966)
16 Months	0.952 (0.894 to 0.978)	0.906 (0.808 to 0.956)
Number of patients at risk[b]		
2 Months	139	146
4 Months	132	134
6 Months	114	121
8 Months	103	116
10 Months	97	113
12 Months	84	99
14 Months	52	68

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	25	26
Bronchitis (days)		
Number (%) of events	12 (8.1)	33 (21.7)
Number (%) of patients censored	137 (91.9)	119 (78.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (4.961 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0013
Hazard ratio (95% CI) vs Pd	-	2.819 (1.456 to 5.459)
P-value	-	0.0021
Hazard ratio inverted (95% CI) vs IPd	0.355 (0.183 to 0.687)	-
Events probability (95% CI)[b]		
2 Months	0.972 (0.928 to 0.990)	0.901 (0.841 to 0.939)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.958 (0.908 to 0.981)	0.845 (0.776 to 0.894)
6 Months	0.934 (0.877 to 0.965)	0.801 (0.726 to 0.857)
8 Months	0.916 (0.853 to 0.953)	0.777 (0.699 to 0.837)
10 Months	0.916 (0.853 to 0.953)	0.777 (0.699 to 0.837)
12 Months	0.916 (0.853 to 0.953)	0.777 (0.699 to 0.837)
14 Months	0.904 (0.834 to 0.945)	0.766 (0.686 to 0.828)
16 Months	0.904 (0.834 to 0.945)	0.766 (0.686 to 0.828)
Number of patients at risk[b]		
2 Months	138	134
4 Months	128	118
6 Months	110	102
8 Months	97	94
10 Months	93	88
12 Months	78	78
14 Months	47	53
16 Months	22	22
Constipation (days)		
Number (%) of events	26 (17.4)	24 (15.8)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	123 (82.6)	128 (84.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (7.458 to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.5767
Hazard ratio (95% CI) vs Pd	-	0.854 (0.490 to 1.487)
P-value	-	0.5767
Events probability (95% CI)[b]		
2 Months	0.863 (0.796 to 0.909)	0.894 (0.833 to 0.934)
4 Months	0.841 (0.771 to 0.892)	0.867 (0.801 to 0.912)
6 Months	0.825 (0.752 to 0.878)	0.860 (0.793 to 0.906)
8 Months	0.816 (0.741 to 0.871)	0.843 (0.773 to 0.893)
10 Months	0.816 (0.741 to 0.871)	0.843 (0.773 to 0.893)
12 Months	0.816 (0.741 to 0.871)	0.843 (0.773 to 0.893)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.816 (0.741 to 0.871)	0.833 (0.760 to 0.885)
16 Months	0.816 (0.741 to 0.871)	0.833 (0.760 to 0.885)
Number of patients at risk[b]		
2 Months	122	133
4 Months	113	122
6 Months	98	108
8 Months	86	101
10 Months	82	95
12 Months	70	84
14 Months	45	57
16 Months	21	23
Cough (days)		
Number (%) of events	10 (6.7)	14 (9.2)
Number (%) of patients censored	139 (93.3)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.5111
Hazard ratio (95% CI) vs Pd	-	1.312 (0.583 to 2.953)
P-value	-	0.5124
Events probability (95% CI)[b]		
2 Months	0.959 (0.911 to 0.981)	0.973 (0.930 to 0.990)
4 Months	0.952 (0.901 to 0.977)	0.952 (0.903 to 0.977)
6 Months	0.944 (0.890 to 0.971)	0.938 (0.885 to 0.967)
8 Months	0.944 (0.890 to 0.971)	0.906 (0.843 to 0.944)
10 Months	0.934 (0.877 to 0.965)	0.897 (0.832 to 0.938)
12 Months	0.934 (0.877 to 0.965)	0.897 (0.832 to 0.938)
14 Months	0.922 (0.858 to 0.958)	0.897 (0.832 to 0.938)
16 Months	0.922 (0.858 to 0.958)	0.897 (0.832 to 0.938)
Number of patients at risk[b]		
2 Months	136	145

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	128	134
6 Months	112	120
8 Months	103	111
10 Months	98	103
12 Months	83	92
14 Months	50	63
16 Months	23	27
Decreased appetite (days)		
Number (%) of events	7 (4.7)	15 (9.9)
Number (%) of patients censored	142 (95.3)	137 (90.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1000

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	2.088 (0.851 to 5.120)
P-value	-	0.1079
Events probability (95% CI)[b]		
2 Months	0.979 (0.937 to 0.993)	0.947 (0.897 to 0.973)
4 Months	0.957 (0.908 to 0.981)	0.913 (0.854 to 0.948)
6 Months	0.949 (0.896 to 0.975)	0.913 (0.854 to 0.948)
8 Months	0.949 (0.896 to 0.975)	0.905 (0.845 to 0.943)
10 Months	0.949 (0.896 to 0.975)	0.897 (0.834 to 0.936)
12 Months	0.949 (0.896 to 0.975)	0.897 (0.834 to 0.936)
14 Months	0.949 (0.896 to 0.975)	0.897 (0.834 to 0.936)
16 Months	0.949 (0.896 to 0.975)	0.897 (0.834 to 0.936)
Number of patients at risk[b]		
2 Months	139	141
4 Months	129	130
6 Months	112	119
8 Months	101	114
10 Months	97	107
12 Months	82	96

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	51	65
16 Months	24	30
Diarrhoea (days)		
Number (%) of events	28 (18.8)	39 (25.7)
Number (%) of patients censored	121 (81.2)	113 (74.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (7.031 to NC)	10.12 (4.172 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2302
Hazard ratio (95% CI) vs Pd	-	1.345 (0.827 to 2.185)
P-value	-	0.2319
Events probability (95% CI)[b]		
2 Months	0.897 (0.835 to 0.937)	0.868 (0.803 to 0.913)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.846 (0.775 to 0.896)	0.826 (0.756 to 0.878)
6 Months	0.829 (0.755 to 0.882)	0.812 (0.739 to 0.866)
8 Months	0.820 (0.745 to 0.875)	0.773 (0.696 to 0.833)
10 Months	0.810 (0.733 to 0.867)	0.757 (0.678 to 0.819)
12 Months	0.800 (0.721 to 0.859)	0.731 (0.648 to 0.797)
14 Months	0.800 (0.721 to 0.859)	0.731 (0.648 to 0.797)
16 Months	0.775 (0.680 to 0.845)	0.710 (0.619 to 0.783)
Number of patients at risk[b]		
2 Months	127	129
4 Months	114	118
6 Months	97	106
8 Months	86	97
10 Months	83	88
12 Months	73	76
14 Months	45	51
16 Months	22	21
Dyspnoea (days)		
Number (%) of events	13 (8.7)	21 (13.8)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	136 (91.3)	131 (86.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2220
Hazard ratio (95% CI) vs Pd	-	1.534 (0.768 to 3.063)
P-value	-	0.2256
Events probability (95% CI)[b]		
2 Months	0.945 (0.893 to 0.972)	0.947 (0.897 to 0.973)
4 Months	0.930 (0.874 to 0.962)	0.927 (0.872 to 0.959)
6 Months	0.922 (0.863 to 0.956)	0.883 (0.819 to 0.926)
8 Months	0.913 (0.852 to 0.950)	0.875 (0.809 to 0.919)
10 Months	0.904 (0.840 to 0.943)	0.858 (0.787 to 0.906)
12 Months	0.904 (0.840 to 0.943)	0.849 (0.777 to 0.899)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.904 (0.840 to 0.943)	0.849 (0.777 to 0.899)
16 Months	0.904 (0.840 to 0.943)	0.849 (0.777 to 0.899)
Number of patients at risk[b]		
2 Months	134	141
4 Months	124	132
6 Months	109	113
8 Months	99	107
10 Months	94	98
12 Months	81	87
14 Months	50	61
16 Months	23	27
Fatigue (days)		
Number (%) of events	32 (21.5)	22 (14.5)
Number (%) of patients censored	117 (78.5)	130 (85.5)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (2.530 to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

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	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0776
Hazard ratio (95% CI) vs Pd	-	0.616 (0.358 to 1.061)
P-value	-	0.0805
Events probability (95% CI)[b]		
2 Months	0.842 (0.772 to 0.892)	0.921 (0.864 to 0.954)
4 Months	0.806 (0.731 to 0.862)	0.893 (0.831 to 0.933)
6 Months	0.806 (0.731 to 0.862)	0.878 (0.813 to 0.921)
8 Months	0.780 (0.701 to 0.840)	0.854 (0.784 to 0.902)
10 Months	0.771 (0.690 to 0.832)	0.845 (0.774 to 0.896)
12 Months	0.771 (0.690 to 0.832)	0.845 (0.774 to 0.896)
14 Months	0.771 (0.690 to 0.832)	0.845 (0.774 to 0.896)
16 Months	0.771 (0.690 to 0.832)	0.845 (0.774 to 0.896)
Number of patients at risk[b]		
2 Months	119	137

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

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	Pd (N=149)	**IPd (N=152)**
4 Months	107	125
6 Months	95	111
8 Months	84	104
10 Months	79	96
12 Months	68	87
14 Months	40	61
16 Months	19	27
Headache (days)		
Number (%) of events	8 (5.4)	15 (9.9)
Number (%) of patients censored	141 (94.6)	137 (90.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1316

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	1.968 (0.802 to 4.828)
P-value	-	0.1391
Events probability (95% CI)[b]		
2 Months	0.972 (0.927 to 0.989)	0.973 (0.931 to 0.990)
4 Months	0.972 (0.927 to 0.989)	0.967 (0.922 to 0.986)
6 Months	0.947 (0.892 to 0.975)	0.930 (0.873 to 0.962)
8 Months	0.947 (0.892 to 0.975)	0.922 (0.863 to 0.956)
10 Months	0.947 (0.892 to 0.975)	0.905 (0.842 to 0.944)
12 Months	0.947 (0.892 to 0.975)	0.897 (0.831 to 0.938)
14 Months	0.947 (0.892 to 0.975)	0.887 (0.819 to 0.931)
16 Months	0.947 (0.892 to 0.975)	0.887 (0.819 to 0.931)
Number of patients at risk[b]		
2 Months	137	145
4 Months	129	138
6 Months	111	121
8 Months	101	115
10 Months	97	107
12 Months	83	94

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

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	Pd (N=149)	**IPd (N=152)**
14 Months	52	65
16 Months	24	28
Infusion related reaction (days)		
Number (%) of events	2 (1.3)	53 (34.9)
Number (%) of patients censored	147 (98.7)	99 (65.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	0.13 (0.099 to 0.197)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	<.0001
Hazard ratio (95% CI) vs Pd	-	31.035 (7.560 to 127.404)
P-value	-	<.0001
Hazard ratio inverted (95% CI) vs IPd	0.032 (0.008 to 0.132)	-
Events probability (95% CI)[b]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
2 Months	0.993 (0.952 to 0.999)	0.651 (0.570 to 0.721)
4 Months	0.993 (0.952 to 0.999)	0.651 (0.570 to 0.721)
6 Months	0.993 (0.952 to 0.999)	0.651 (0.570 to 0.721)
8 Months	0.984 (0.939 to 0.996)	0.651 (0.570 to 0.721)
10 Months	0.984 (0.939 to 0.996)	0.651 (0.570 to 0.721)
12 Months	0.984 (0.939 to 0.996)	0.651 (0.570 to 0.721)
14 Months	0.984 (0.939 to 0.996)	0.651 (0.570 to 0.721)
16 Months	0.984 (0.939 to 0.996)	0.651 (0.570 to 0.721)
Number of patients at risk[b]		
2 Months	141	97
4 Months	134	91
6 Months	117	82
8 Months	105	78
10 Months	101	72
12 Months	86	64
14 Months	53	41
16 Months	26	16
Insomnia (days)		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
Number (%) of events	12 (8.1)	13 (8.6)
Number (%) of patients censored	137 (91.9)	139 (91.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.9998
Hazard ratio (95% CI) vs Pd	-	1.000 (0.456 to 2.192)
P-value	-	1.0000
Events probability (95% CI)[b]		
2 Months	0.939 (0.886 to 0.968)	0.967 (0.922 to 0.986)
4 Months	0.931 (0.876 to 0.963)	0.960 (0.913 to 0.982)
6 Months	0.931 (0.876 to 0.963)	0.930 (0.874 to 0.962)
8 Months	0.922 (0.864 to 0.956)	0.914 (0.853 to 0.950)
10 Months	0.922 (0.864 to 0.956)	0.905 (0.842 to 0.944)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

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	Pd (N=149)	**IPd (N=152)**
12 Months	0.912 (0.849 to 0.949)	0.905 (0.842 to 0.944)
14 Months	0.912 (0.849 to 0.949)	0.905 (0.842 to 0.944)
16 Months	0.912 (0.849 to 0.949)	0.905 (0.842 to 0.944)
Number of patients at risk[b]		
2 Months	133	144
4 Months	124	135
6 Months	108	118
8 Months	97	111
10 Months	93	103
12 Months	77	92
14 Months	48	63
16 Months	23	26
Muscle spasms (days)		
Number (%) of events	15 (10.1)	14 (9.2)
Number (%) of patients censored	134 (89.9)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

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	Pd (N=149)	**IPd (N=152)**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.6642
Hazard ratio (95% CI) vs Pd	-	0.851 (0.411 to 1.763)
P-value	-	0.6641
Events probability (95% CI)[b]		
2 Months	0.958 (0.910 to 0.981)	0.967 (0.922 to 0.986)
4 Months	0.929 (0.873 to 0.961)	0.939 (0.886 to 0.968)
6 Months	0.905 (0.841 to 0.944)	0.932 (0.876 to 0.963)
8 Months	0.905 (0.841 to 0.944)	0.907 (0.845 to 0.945)
10 Months	0.884 (0.814 to 0.929)	0.907 (0.845 to 0.945)
12 Months	0.884 (0.814 to 0.929)	0.907 (0.845 to 0.945)
14 Months	0.884 (0.814 to 0.929)	0.894 (0.826 to 0.937)
16 Months	0.884 (0.814 to 0.929)	0.894 (0.826 to 0.937)
Number of patients at risk[b]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

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	Pd (N=149)	**IPd (N=152)**
2 Months	136	144
4 Months	124	132
6 Months	104	118
8 Months	93	110
10 Months	87	103
12 Months	74	93
14 Months	46	65
16 Months	20	26
Muscular weakness (days)		
Number (%) of events	7 (4.7)	10 (6.6)
Number (%) of patients censored	142 (95.3)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.6072

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	1.288 (0.490 to 3.384)
P-value	-	0.6082
Events probability (95% CI)[b]		
2 Months	0.987 (0.947 to 0.997)	0.987 (0.948 to 0.997)
4 Months	0.965 (0.917 to 0.985)	0.973 (0.930 to 0.990)
6 Months	0.957 (0.907 to 0.980)	0.959 (0.910 to 0.981)
8 Months	0.957 (0.907 to 0.980)	0.951 (0.899 to 0.976)
10 Months	0.957 (0.907 to 0.980)	0.951 (0.899 to 0.976)
12 Months	0.947 (0.890 to 0.974)	0.933 (0.875 to 0.965)
14 Months	0.947 (0.890 to 0.974)	0.933 (0.875 to 0.965)
16 Months	0.947 (0.890 to 0.974)	0.904 (0.805 to 0.954)
Number of patients at risk[b]		
2 Months	140	147
4 Months	129	138
6 Months	111	124
8 Months	100	119
10 Months	96	112

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	81	98
14 Months	50	67
16 Months	24	28
Musculoskeletal chest pain (days)		
Number (%) of events	7 (4.7)	13 (8.6)
Number (%) of patients censored	142 (95.3)	139 (91.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2138
Hazard ratio (95% CI) vs Pd	-	1.777 (0.709 to 4.454)
P-value	-	0.2201
Events probability (95% CI)[b]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	0.993 (0.951 to 0.999)	0.967 (0.922 to 0.986)
4 Months	0.971 (0.926 to 0.989)	0.932 (0.877 to 0.963)
6 Months	0.963 (0.914 to 0.985)	0.925 (0.868 to 0.958)
8 Months	0.955 (0.902 to 0.979)	0.925 (0.868 to 0.958)
10 Months	0.955 (0.902 to 0.979)	0.908 (0.846 to 0.946)
12 Months	0.944 (0.885 to 0.973)	0.908 (0.846 to 0.946)
14 Months	0.944 (0.885 to 0.973)	0.908 (0.846 to 0.946)
16 Months	0.944 (0.885 to 0.973)	0.908 (0.846 to 0.946)
Number of patients at risk[b]		
2 Months	141	144
4 Months	130	131
6 Months	112	119
8 Months	100	115
10 Months	98	106
12 Months	82	95
14 Months	50	65
16 Months	25	29
Myalgia (days)		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of events	5 (3.4)	10 (6.6)
Number (%) of patients censored	144 (96.6)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1371
Hazard ratio (95% CI) vs Pd	-	2.348 (0.736 to 7.491)
P-value	-	0.1491
Events probability (95% CI)[b]		
2 Months	0.986 (0.946 to 0.997)	0.967 (0.922 to 0.986)
4 Months	0.986 (0.946 to 0.997)	0.953 (0.904 to 0.977)
6 Months	0.978 (0.932 to 0.993)	0.946 (0.895 to 0.973)
8 Months	0.969 (0.918 to 0.988)	0.946 (0.895 to 0.973)
10 Months	0.969 (0.918 to 0.988)	0.946 (0.895 to 0.973)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	0.969 (0.918 to 0.988)	0.946 (0.895 to 0.973)
14 Months	0.969 (0.918 to 0.988)	0.937 (0.881 to 0.967)
16 Months	0.969 (0.918 to 0.988)	0.922 (0.855 to 0.959)
Number of patients at risk[b]		
2 Months	139	144
4 Months	131	134
6 Months	113	120
8 Months	102	117
10 Months	98	110
12 Months	84	99
14 Months	52	67
16 Months	26	27
Nasopharyngitis (days)		
Number (%) of events	7 (4.7)	14 (9.2)
Number (%) of patients censored	142 (95.3)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1712
Hazard ratio (95% CI) vs Pd	-	1.865 (0.753 to 4.622)
P-value	-	0.1782
Events probability (95% CI)[b]		
2 Months	0.979 (0.937 to 0.993)	0.973 (0.931 to 0.990)
4 Months	0.965 (0.918 to 0.985)	0.946 (0.895 to 0.973)
6 Months	0.965 (0.918 to 0.985)	0.931 (0.876 to 0.962)
8 Months	0.956 (0.905 to 0.980)	0.923 (0.866 to 0.957)
10 Months	0.956 (0.905 to 0.980)	0.906 (0.844 to 0.945)
12 Months	0.946 (0.889 to 0.974)	0.906 (0.844 to 0.945)
14 Months	0.946 (0.889 to 0.974)	0.894 (0.825 to 0.937)
16 Months	0.946 (0.889 to 0.974)	0.894 (0.825 to 0.937)
Number of patients at risk[b]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	139	145
4 Months	129	134
6 Months	112	119
8 Months	100	114
10 Months	96	105
12 Months	80	93
14 Months	49	64
16 Months	23	28
Nausea (days)		
Number (%) of events	14 (9.4)	23 (15.1)
Number (%) of patients censored	135 (90.6)	129 (84.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.1444

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	1.632 (0.840 to 3.172)
P-value	-	0.1485
Events probability (95% CI)[b]		
2 Months	0.952 (0.902 to 0.977)	0.888 (0.826 to 0.929)
4 Months	0.923 (0.865 to 0.956)	0.874 (0.809 to 0.918)
6 Months	0.914 (0.854 to 0.951)	0.867 (0.801 to 0.912)
8 Months	0.905 (0.842 to 0.944)	0.859 (0.791 to 0.906)
10 Months	0.895 (0.829 to 0.937)	0.859 (0.791 to 0.906)
12 Months	0.895 (0.829 to 0.937)	0.841 (0.770 to 0.892)
14 Months	0.895 (0.829 to 0.937)	0.841 (0.770 to 0.892)
16 Months	0.895 (0.829 to 0.937)	0.841 (0.770 to 0.892)
Number of patients at risk[b]		
2 Months	135	132
4 Months	123	122
6 Months	105	111
8 Months	96	105
10 Months	91	98

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	77	87
14 Months	48	58
16 Months	24	25
Oedema peripheral (days)		
Number (%) of events	16 (10.7)	20 (13.2)
Number (%) of patients censored	133 (89.3)	132 (86.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.7321
Hazard ratio (95% CI) vs Pd	-	1.122 (0.581 to 2.165)
P-value	-	0.7322
Events probability (95% CI)[b]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	0.924 (0.868 to 0.957)	0.987 (0.948 to 0.997)
4 Months	0.910 (0.850 to 0.947)	0.953 (0.903 to 0.977)
6 Months	0.894 (0.830 to 0.935)	0.938 (0.885 to 0.968)
8 Months	0.894 (0.830 to 0.935)	0.906 (0.844 to 0.945)
10 Months	0.884 (0.818 to 0.928)	0.864 (0.792 to 0.913)
12 Months	0.884 (0.818 to 0.928)	0.847 (0.771 to 0.899)
14 Months	0.884 (0.818 to 0.928)	0.847 (0.771 to 0.899)
16 Months	0.884 (0.818 to 0.928)	0.847 (0.771 to 0.899)
Number of patients at risk[b]		
2 Months	132	147
4 Months	123	136
6 Months	104	121
8 Months	95	112
10 Months	90	100
12 Months	76	86
14 Months	48	60
16 Months	23	27
Peripheral sensory neuropathy (days)		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of events	9 (6.0)	11 (7.2)
Number (%) of patients censored	140 (94.0)	141 (92.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.5980
Hazard ratio (95% CI) vs Pd	-	1.277 (0.514 to 3.175)
P-value	-	0.5989
Events probability (95% CI)[b]		
2 Months	0.986 (0.946 to 0.997)	0.967 (0.922 to 0.986)
4 Months	0.972 (0.926 to 0.989)	0.960 (0.914 to 0.982)
6 Months	0.963 (0.913 to 0.984)	0.938 (0.883 to 0.967)
8 Months	0.954 (0.899 to 0.979)	0.938 (0.883 to 0.967)
10 Months	0.944 (0.885 to 0.973)	0.920 (0.860 to 0.955)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	0.933 (0.868 to 0.966)	0.920 (0.860 to 0.955)
14 Months	0.933 (0.868 to 0.966)	0.920 (0.860 to 0.955)
16 Months	0.933 (0.868 to 0.966)	0.920 (0.860 to 0.955)
Number of patients at risk[b]		
2 Months	139	144
4 Months	129	135
6 Months	111	119
8 Months	99	114
10 Months	94	105
12 Months	80	94
14 Months	47	62
16 Months	23	27
Pyrexia (days)		
Number (%) of events	19 (12.8)	20 (13.2)
Number (%) of patients censored	130 (87.2)	132 (86.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (16.000 to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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	Pd (N=149)	**IPd (N=152)**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.9093
Hazard ratio (95% CI) vs Pd	-	0.964 (0.514 to 1.807)
P-value	-	0.9092
Events probability (95% CI)[b]		
2 Months	0.924 (0.867 to 0.957)	0.954 (0.906 to 0.978)
4 Months	0.902 (0.840 to 0.941)	0.927 (0.872 to 0.959)
6 Months	0.886 (0.820 to 0.929)	0.919 (0.862 to 0.953)
8 Months	0.877 (0.810 to 0.922)	0.896 (0.833 to 0.936)
10 Months	0.868 (0.798 to 0.915)	0.879 (0.813 to 0.923)
12 Months	0.858 (0.785 to 0.907)	0.871 (0.802 to 0.917)
14 Months	0.858 (0.785 to 0.907)	0.858 (0.785 to 0.908)
16 Months	0.858 (0.785 to 0.907)	0.829 (0.728 to 0.895)
Number of patients at risk[b]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	131	143
4 Months	122	133
6 Months	105	120
8 Months	97	112
10 Months	92	103
12 Months	77	92
14 Months	49	63
16 Months	24	29
Upper respiratory tract infection (days)		
Number (%) of events	25 (16.8)	41 (27.0)
Number (%) of patients censored	124 (83.2)	111 (73.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (9.166 to NC)	7.92 (5.388 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0659

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	1.588 (0.966 to 2.612)
P-value	-	0.0684
Events probability (95% CI)[b]		
2 Months	0.910 (0.850 to 0.947)	0.914 (0.856 to 0.949)
4 Months	0.881 (0.816 to 0.924)	0.858 (0.791 to 0.905)
6 Months	0.865 (0.796 to 0.912)	0.789 (0.712 to 0.848)
8 Months	0.837 (0.762 to 0.890)	0.747 (0.664 to 0.812)
10 Months	0.818 (0.739 to 0.875)	0.729 (0.645 to 0.796)
12 Months	0.818 (0.739 to 0.875)	0.719 (0.633 to 0.788)
14 Months	0.799 (0.712 to 0.863)	0.697 (0.609 to 0.770)
16 Months	0.799 (0.712 to 0.863)	0.667 (0.561 to 0.753)
Number of patients at risk[b]		
2 Months	129	136
4 Months	117	120
6 Months	99	98
8 Months	88	88
10 Months	83	80

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	71	69
14 Months	42	48
16 Months	20	19
Urinary tract infection (days)		
Number (%) of events	13 (8.7)	10 (6.6)
Number (%) of patients censored	136 (91.3)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.4245
Hazard ratio (95% CI) vs Pd	-	0.716 (0.314 to 1.633)
P-value	-	0.4266
Events probability (95% CI)[b]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	0.958 (0.910 to 0.981)	0.974 (0.931 to 0.990)
4 Months	0.936 (0.881 to 0.966)	0.939 (0.887 to 0.968)
6 Months	0.928 (0.871 to 0.961)	0.939 (0.887 to 0.968)
8 Months	0.910 (0.846 to 0.948)	0.939 (0.887 to 0.968)
10 Months	0.900 (0.833 to 0.941)	0.939 (0.887 to 0.968)
12 Months	0.900 (0.833 to 0.941)	0.930 (0.874 to 0.962)
14 Months	0.900 (0.833 to 0.941)	0.930 (0.874 to 0.962)
16 Months	0.900 (0.833 to 0.941)	0.930 (0.874 to 0.962)
Number of patients at risk[b]		
2 Months	136	145
4 Months	126	132
6 Months	108	120
8 Months	95	115
10 Months	90	108
12 Months	78	95
14 Months	48	65
16 Months	24	27
Vomiting (days)		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of events	5 (3.4)	17 (11.2)
Number (%) of patients censored	144 (96.6)	135 (88.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0124
Hazard ratio (95% CI) vs Pd	-	3.318 (1.224 to 8.994)
P-value	-	0.0184
Hazard ratio inverted (95% CI) vs IPd	0.301 (0.111 to 0.817)	-
Events probability (95% CI)[b]		
2 Months	0.986 (0.947 to 0.997)	0.947 (0.897 to 0.973)
4 Months	0.986 (0.947 to 0.997)	0.926 (0.870 to 0.958)
6 Months	0.978 (0.934 to 0.993)	0.926 (0.870 to 0.958)
8 Months	0.960 (0.907 to 0.983)	0.902 (0.840 to 0.941)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
10 Months	0.960 (0.907 to 0.983)	0.893 (0.829 to 0.935)
12 Months	0.960 (0.907 to 0.983)	0.884 (0.818 to 0.928)
14 Months	0.960 (0.907 to 0.983)	0.871 (0.798 to 0.919)
16 Months	0.960 (0.907 to 0.983)	0.871 (0.798 to 0.919)
Number of patients at risk[b]		
2 Months	141	141
4 Months	133	130
6 Months	115	118
8 Months	102	110
10 Months	98	102
12 Months	83	90
14 Months	50	57
16 Months	23	25
Weight decreased (days)		
Number (%) of events	2 (1.3)	10 (6.6)
Number (%) of patients censored	147 (98.7)	142 (93.4)
Kaplan-Meier estimates of Events in months		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0084
Hazard ratio (95% CI) vs Pd	-	9.543 (1.222 to 74.547)
P-value	-	0.0315
Hazard ratio inverted (95% CI) vs IPd	0.105 (0.013 to 0.819)	-
Events probability (95% CI)[b]		
2 Months	0.993 (0.952 to 0.999)	0.967 (0.923 to 0.986)
4 Months	0.993 (0.952 to 0.999)	0.947 (0.896 to 0.973)
6 Months	0.993 (0.952 to 0.999)	0.939 (0.887 to 0.968)
8 Months	0.993 (0.952 to 0.999)	0.939 (0.887 to 0.968)
10 Months	0.993 (0.952 to 0.999)	0.931 (0.875 to 0.962)
12 Months	0.993 (0.952 to 0.999)	0.931 (0.875 to 0.962)
14 Months	0.993 (0.952 to 0.999)	0.931 (0.875 to 0.962)
16 Months	0.993 (0.952 to 0.999)	0.931 (0.875 to 0.962)

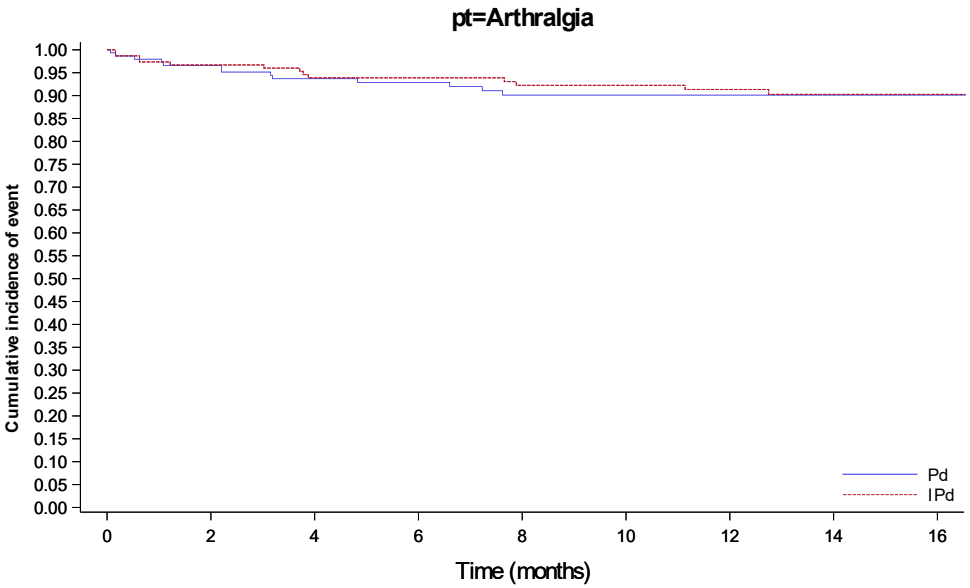
PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.15 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[b]		
2 Months	140	145
4 Months	132	134
6 Months	116	121
8 Months	105	116
10 Months	101	108
12 Months	86	97
14 Months	54	67
16 Months	26	29

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16FEB2021 22:48)

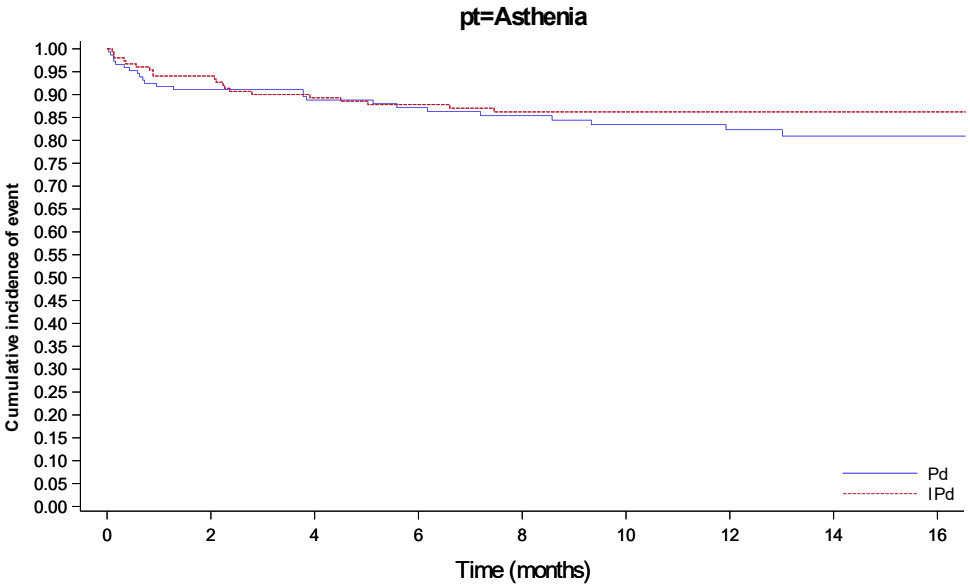
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	137	125	107	94	91	76	49	25
IPd	152	144	132	119	112	105	93	62	25

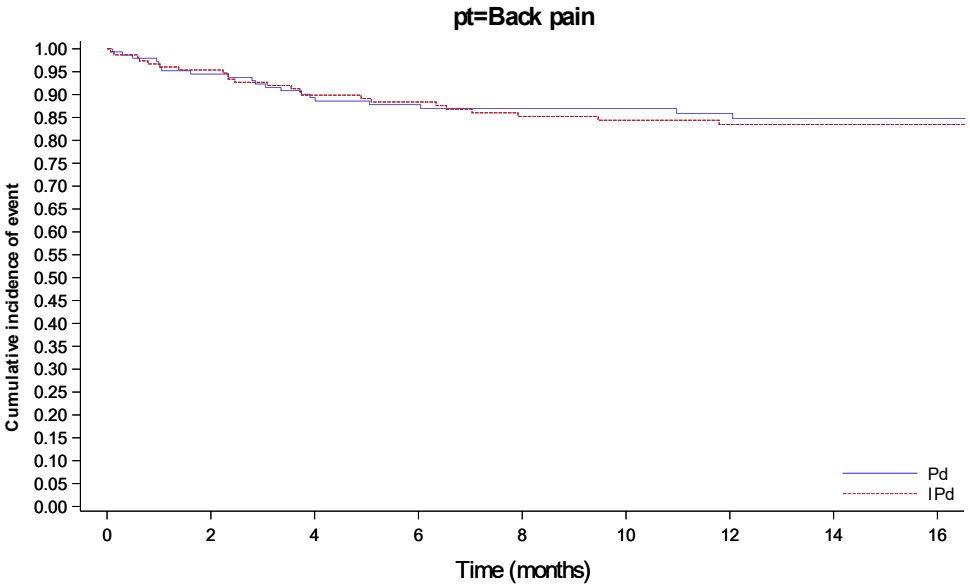
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	148	128	118	102	91	85	72	46	24
IPd	152	140	125	112	106	99	88	58	28

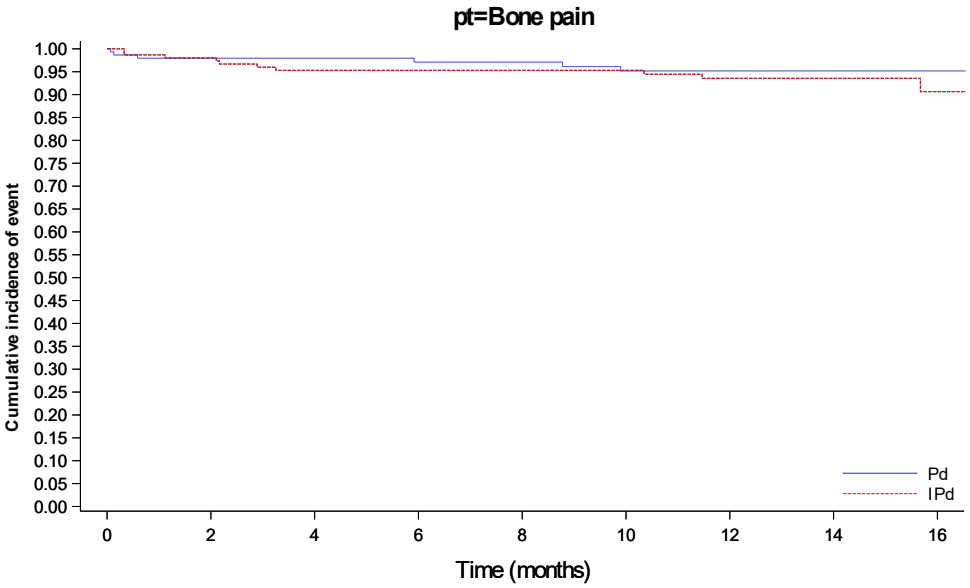
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	134	119	103	93	89	75	45	20
IPd	152	142	127	113	106	101	89	61	27

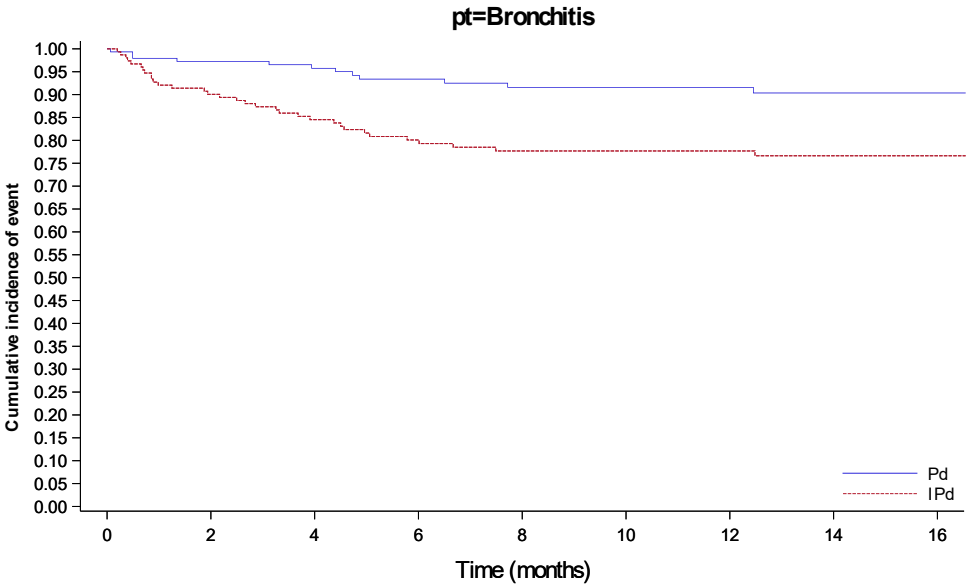
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	139	132	114	103	97	84	52	25
IPd	152	146	134	121	116	113	99	68	26

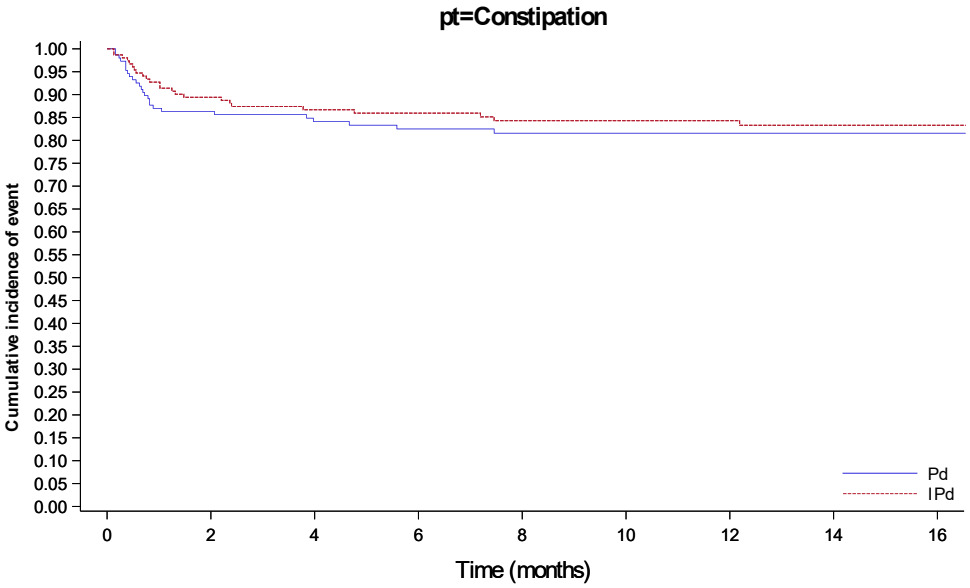
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	138	128	110	97	93	78	47	22
IPd	152	134	118	102	94	88	78	53	22

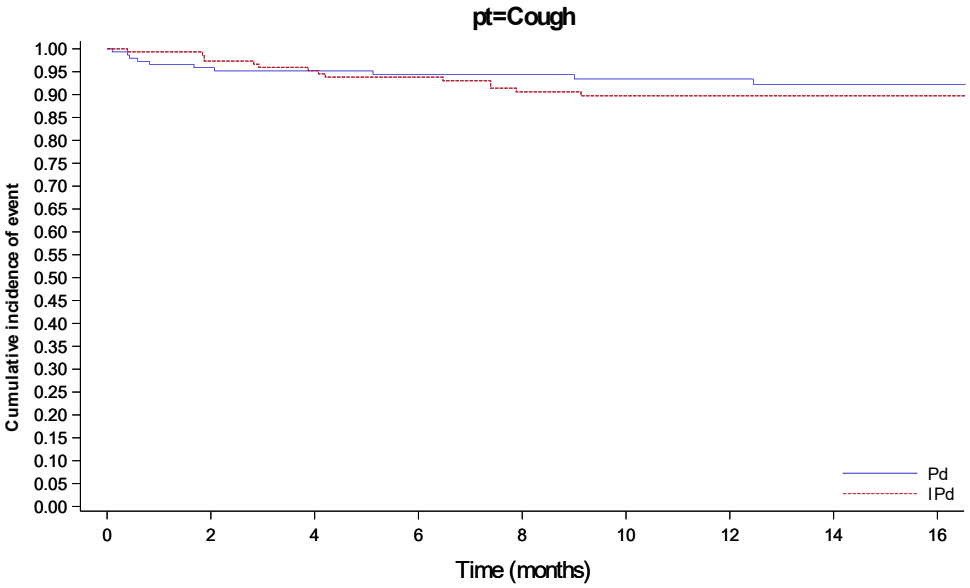
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	122	113	98	86	82	70	45	21
IPd	152	133	122	108	101	95	84	57	23

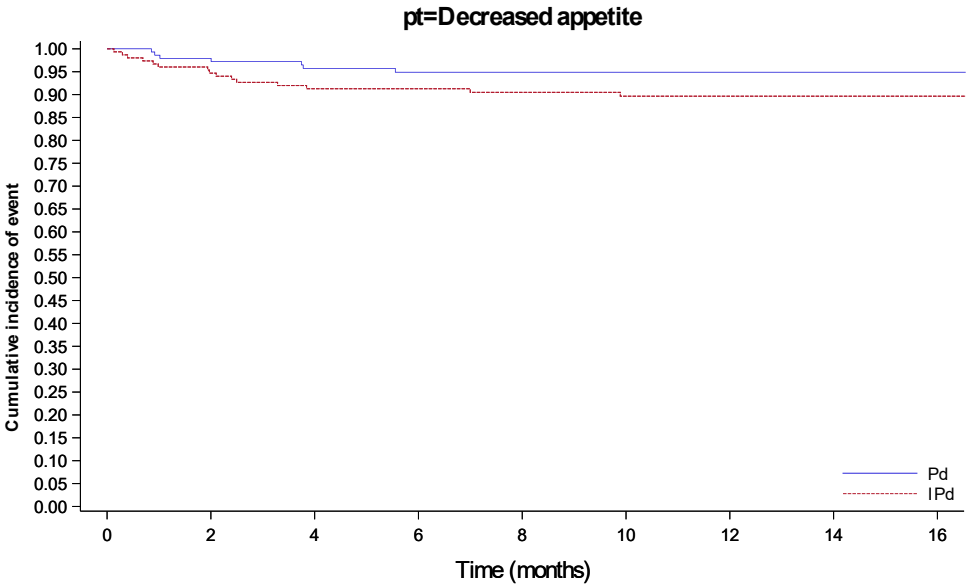
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	136	128	112	103	98	83	50	23
IPd	152	145	134	120	111	103	92	63	27

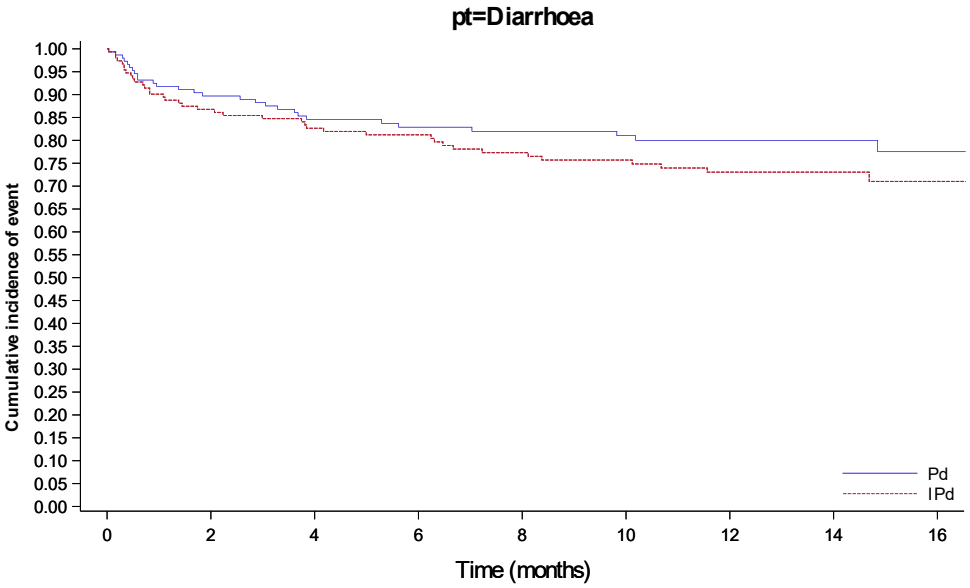
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	139	129	112	101	97	82	51	24
IPd	152	141	130	119	114	107	96	65	30

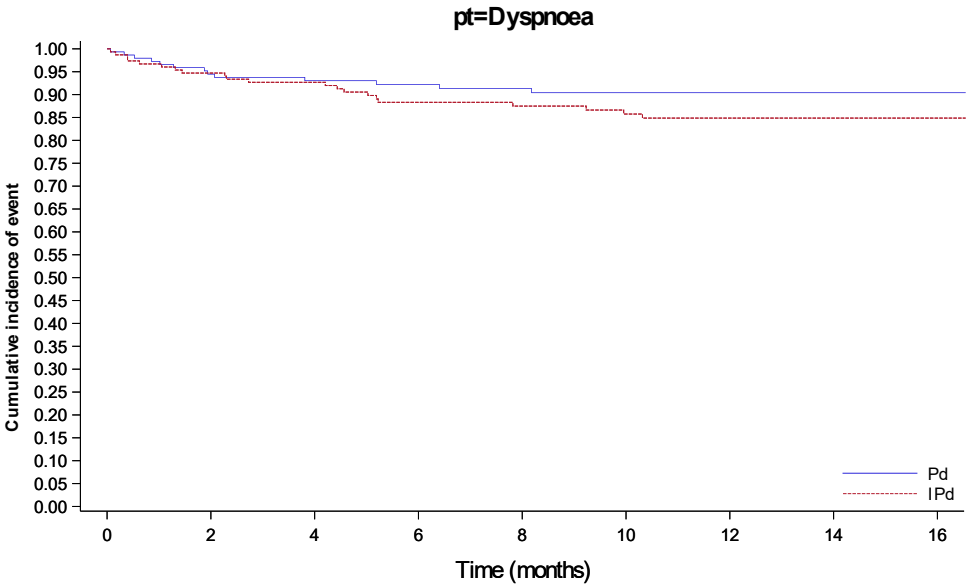
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	127	114	97	86	83	73	45	22
IPd	152	129	118	106	97	88	76	51	21

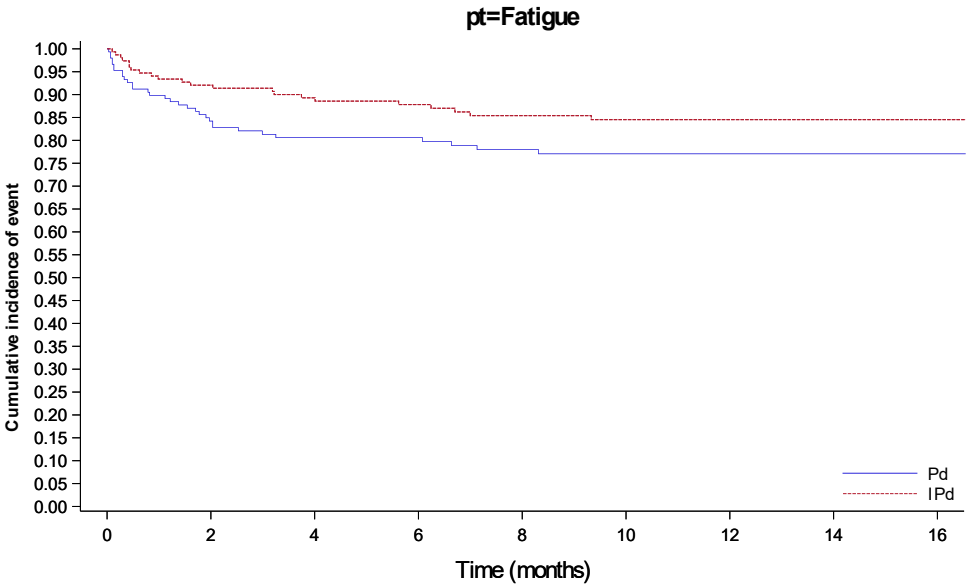
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	134	124	109	99	94	81	50	23
IPd	152	141	132	113	107	98	87	61	27

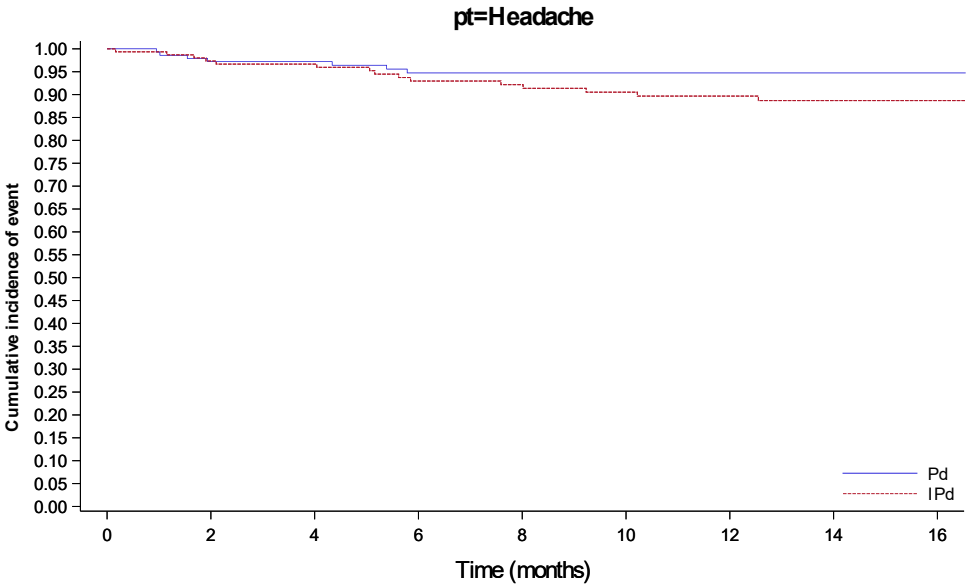
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	119	107	95	84	79	68	40	19
IPd	152	137	125	111	104	96	87	61	27

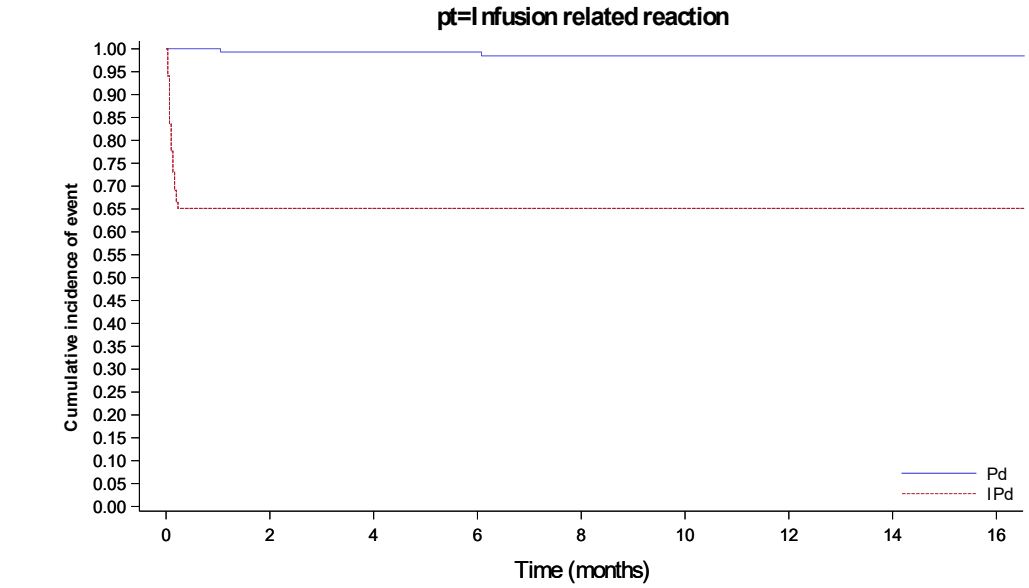
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	148	137	129	111	101	97	83	52	24
IPd	152	145	138	121	115	107	94	65	28

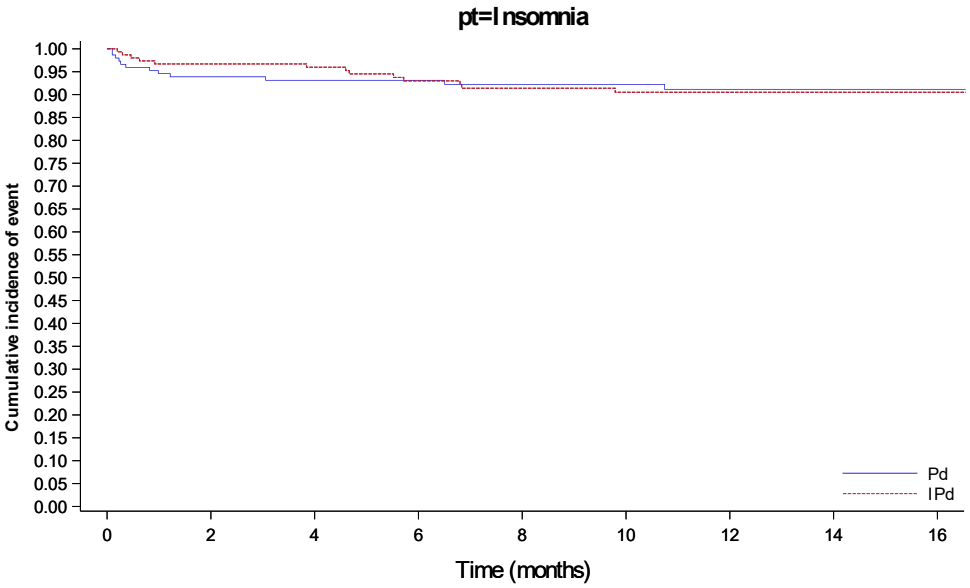
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	141	134	117	105	101	86	53	26
IPd	152	97	91	82	78	72	64	41	16

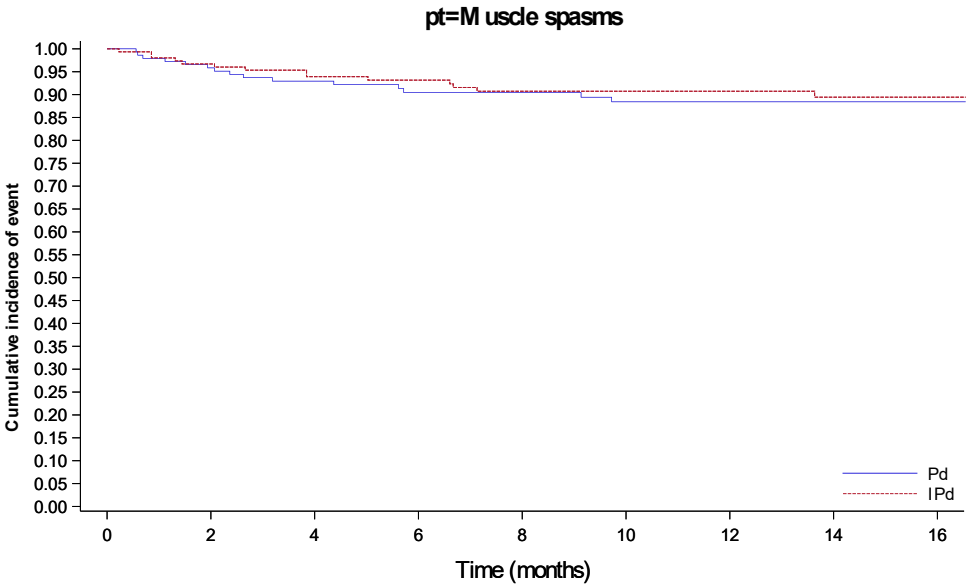
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	133	124	108	97	93	77	48	23
IPd	152	144	135	118	111	103	92	63	26

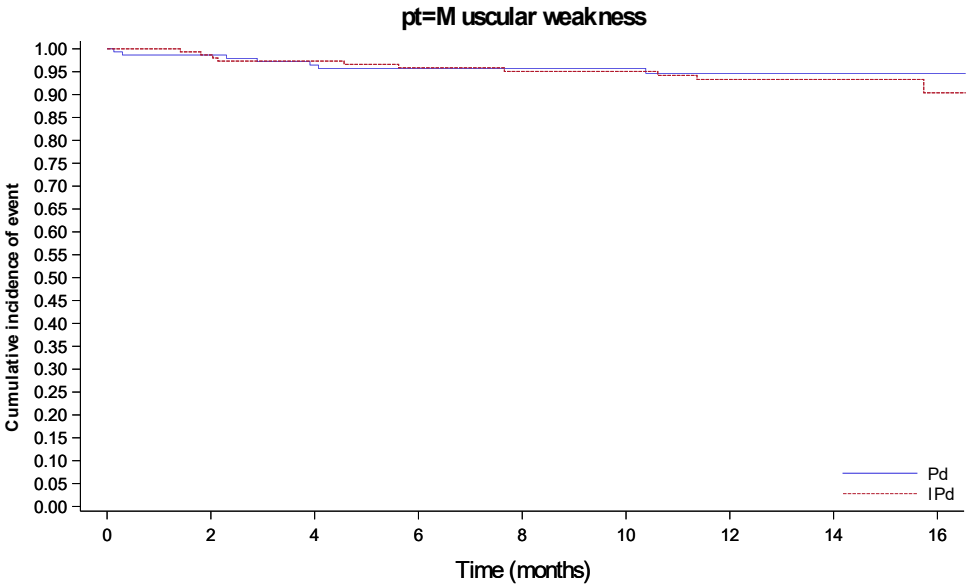
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	136	124	104	93	87	74	46	20
IPd	152	144	132	118	110	103	93	65	26

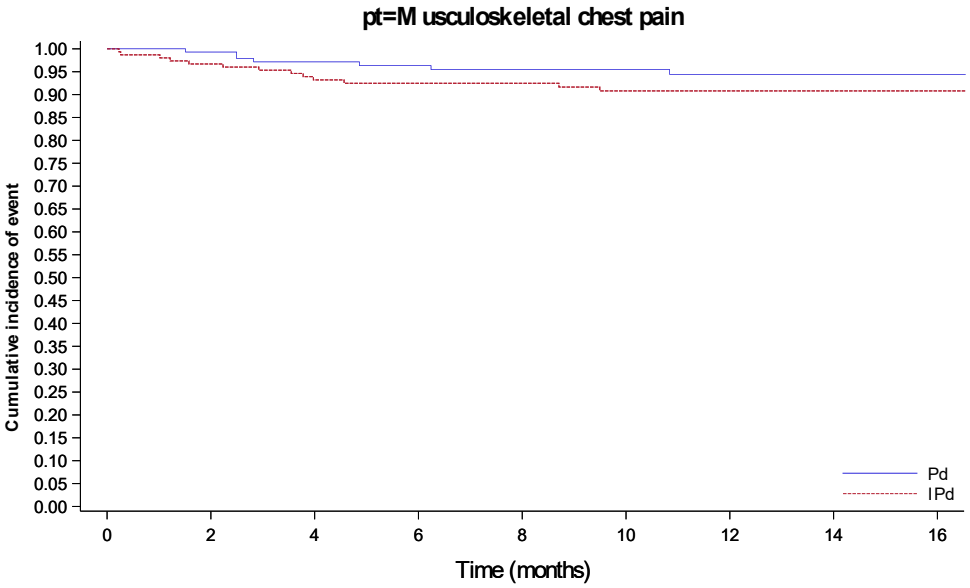
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	140	129	111	100	96	81	50	24
IPd	152	147	138	124	119	112	98	67	28

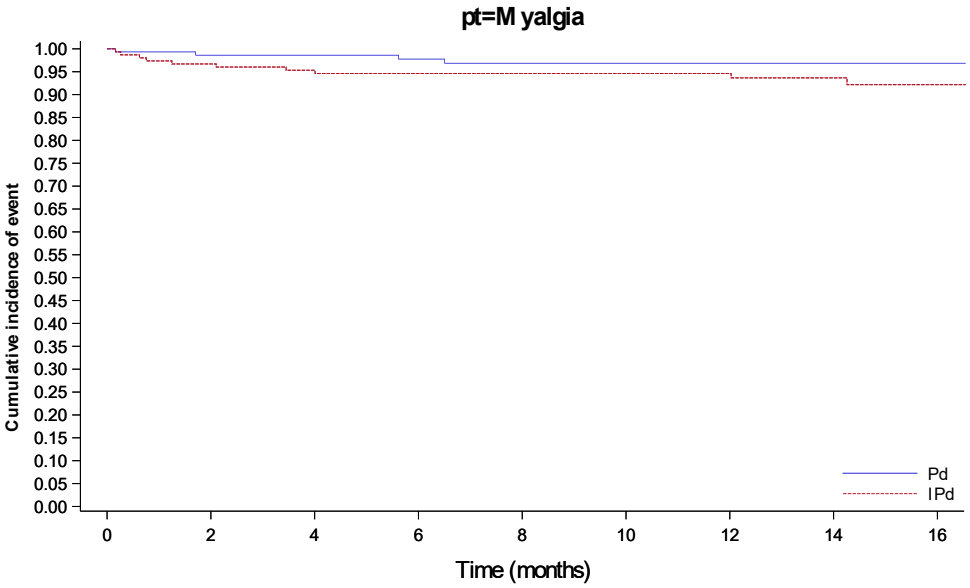
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	141	130	112	100	98	82	50	25
IPd	152	144	131	119	115	106	95	65	29

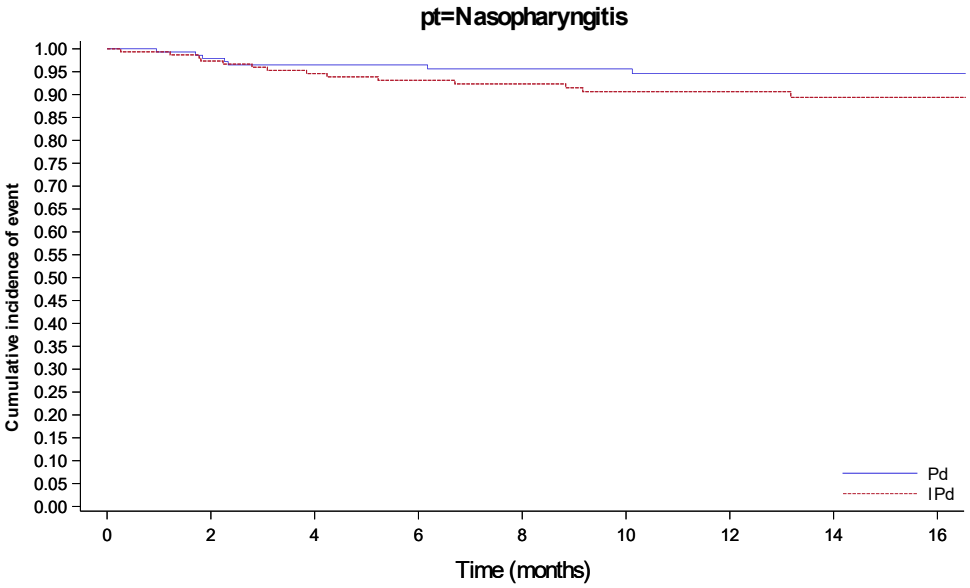
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	148	139	131	113	102	98	84	52	26
IPd	152	144	134	120	117	110	99	67	27

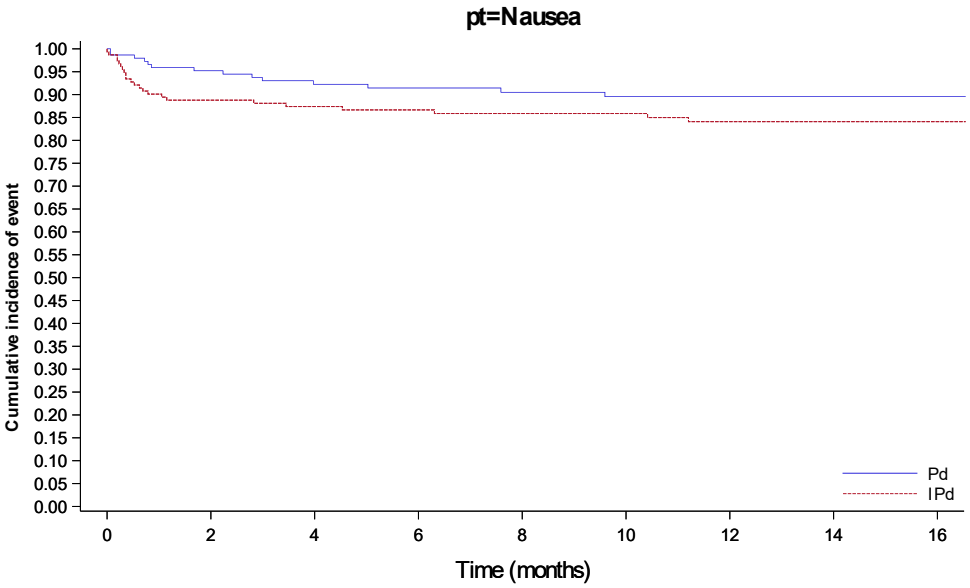
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	139	129	112	100	96	80	49	23
IPd	152	145	134	119	114	105	93	64	28

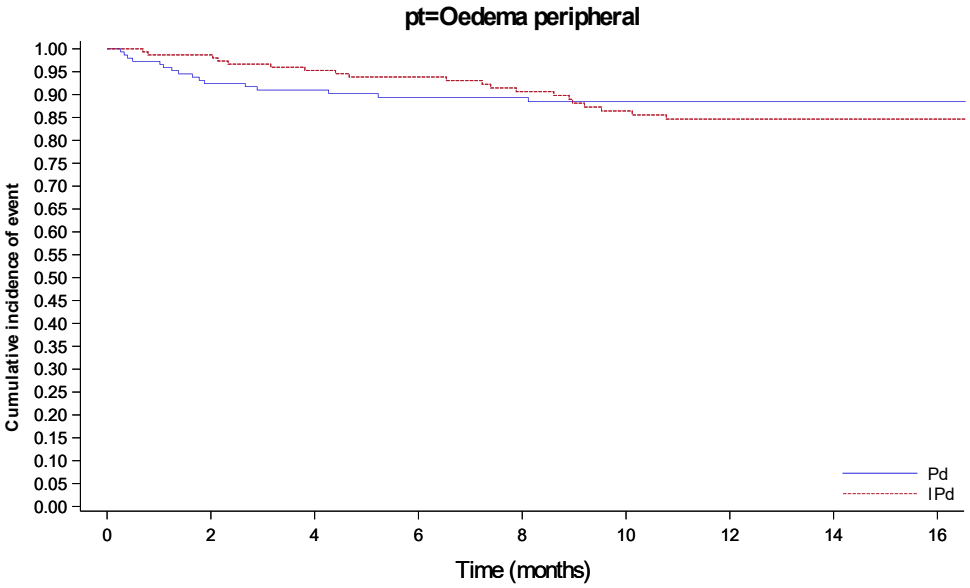
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	135	123	105	96	91	77	48	24
IPd	152	132	122	111	105	98	87	58	25

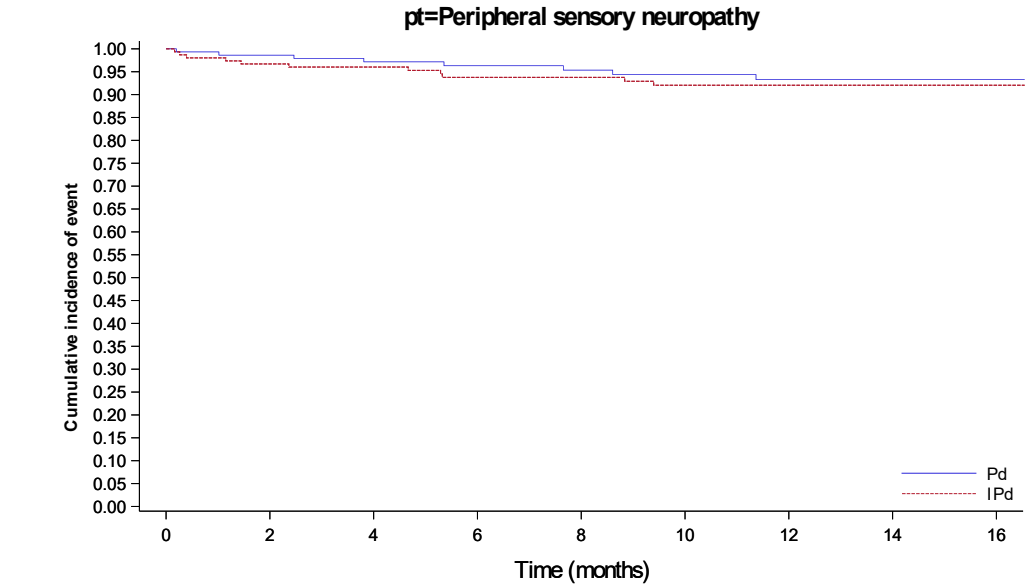
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



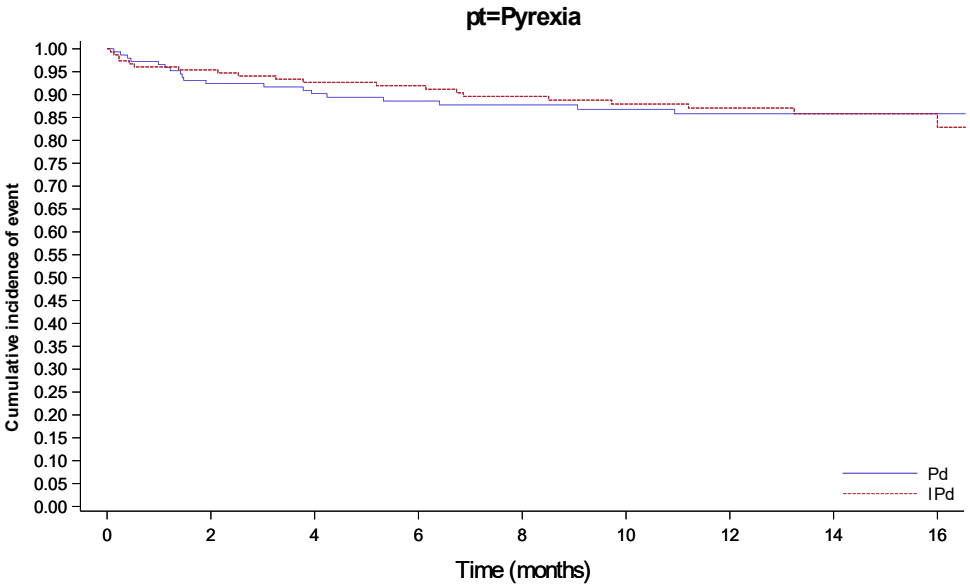
Number at Risk

Pd	149	132	123	104	95	90	76	48	23
IPd	152	147	136	121	112	100	86	60	27

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



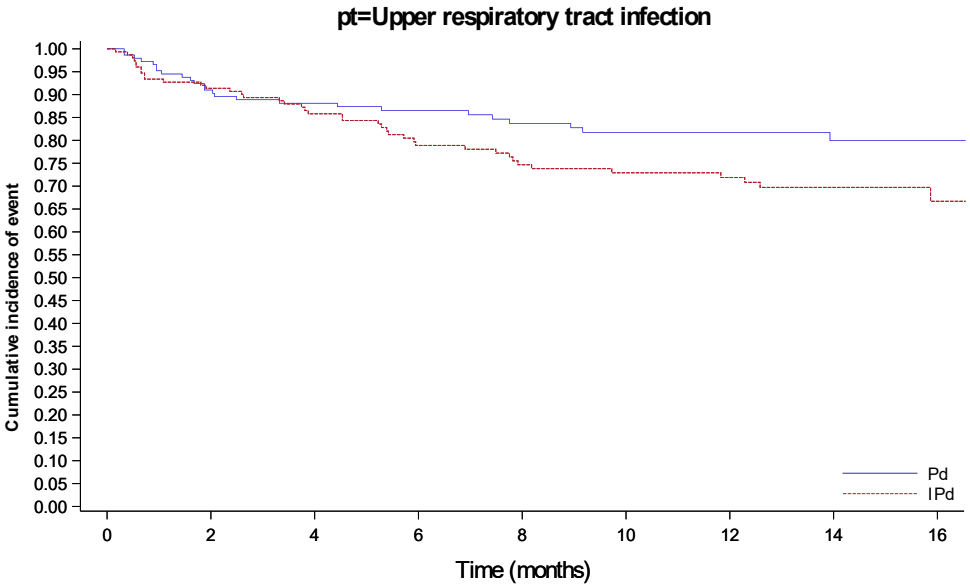
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	131	122	105	97	92	77	49	24
IPd	152	143	133	120	112	103	92	63	29

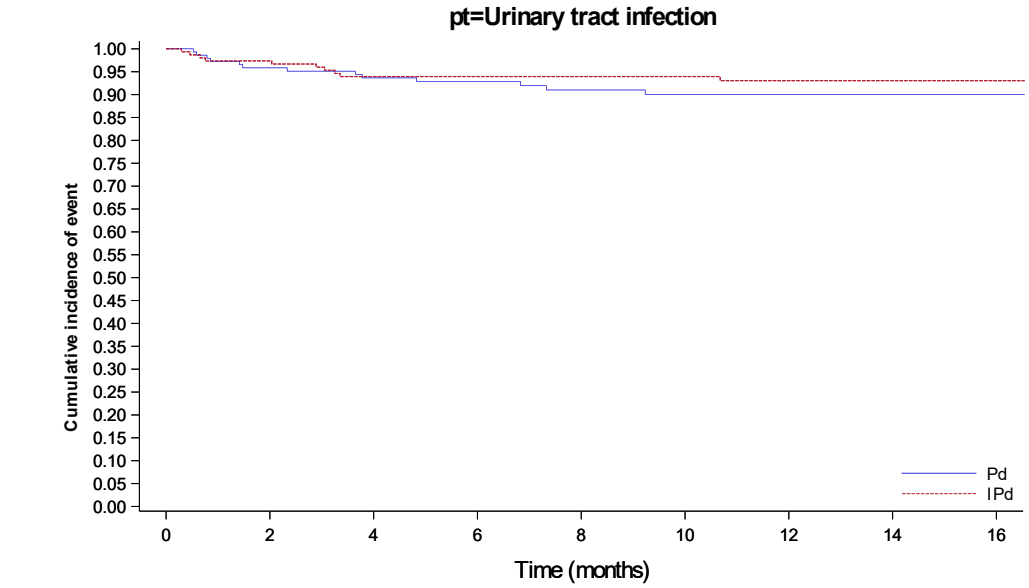
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	129	117	99	88	83	71	42	20
IPd	152	136	120	98	88	80	69	48	19

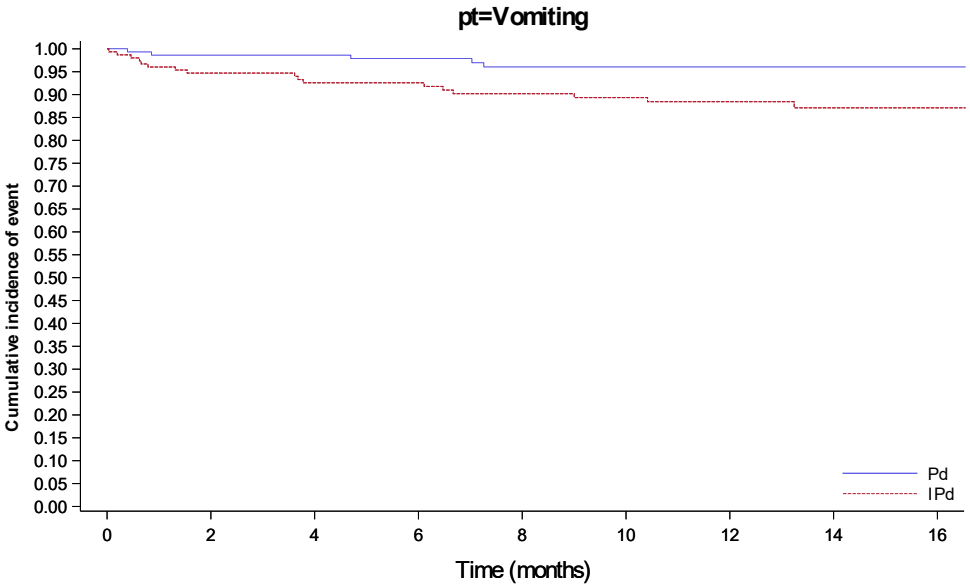
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	136	126	108	95	90	78	48	24
IPd	152	145	132	120	115	108	95	65	27

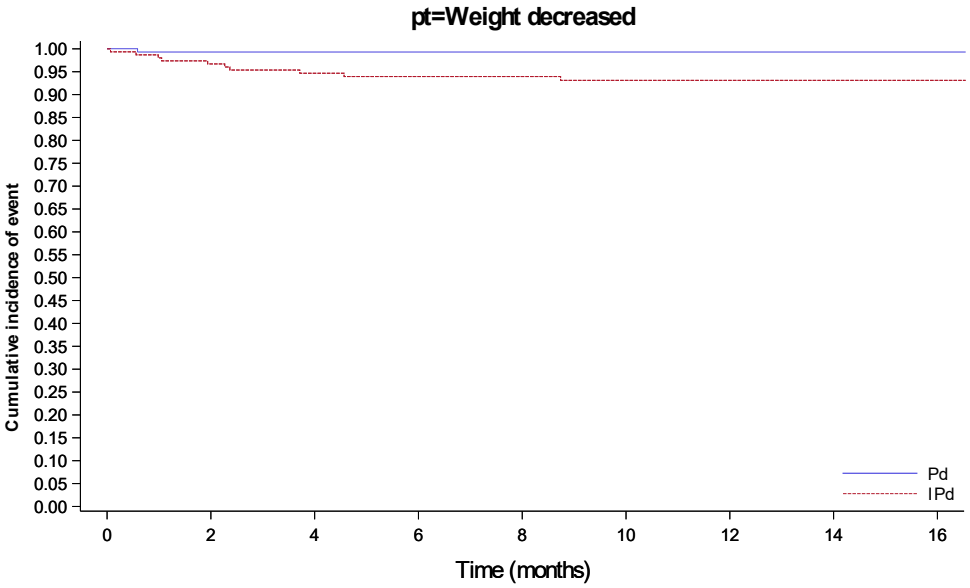
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	141	133	115	102	98	83	50	23
IPd	152	141	130	118	110	102	90	57	25

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.16 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	148	140	132	116	105	101	86	54	26
IPd	152	145	134	121	116	108	97	67	29

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.17 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Blood and lymphatic system disorders (days)		
Number (%) of events	60 (40.3)	87 (57.2)
Number (%) of patients censored	89 (59.7)	65 (42.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	0.95 (0.756 to 2.037)	0.66 (0.559 to 0.789)
Median (95% CI)	NC (7.622 to NC)	2.79 (0.953 to 10.448)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0034
Hazard ratio (95% CI) vs Pd	-	1.629 (1.171 to 2.264)
P-value	-	0.0037
Hazard ratio inverted (95% CI) vs IPd	0.614 (0.442 to 0.854)	-
Events probability (95% CI)[b]		
2 Months	0.685 (0.603 to 0.754)	0.523 (0.441 to 0.599)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.17 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.621 (0.537 to 0.695)	0.462 (0.381 to 0.539)
6 Months	0.591 (0.506 to 0.666)	0.455 (0.374 to 0.532)
8 Months	0.582 (0.497 to 0.659)	0.446 (0.365 to 0.524)
10 Months	0.582 (0.497 to 0.659)	0.428 (0.347 to 0.507)
12 Months	0.582 (0.497 to 0.659)	0.419 (0.337 to 0.498)
14 Months	0.582 (0.497 to 0.659)	0.405 (0.323 to 0.486)
16 Months	0.582 (0.497 to 0.659)	0.405 (0.323 to 0.486)
Number of patients at risk[b]		
2 Months	99	78
4 Months	86	65
6 Months	76	54
8 Months	67	51
10 Months	65	46
12 Months	56	41
14 Months	35	27
16 Months	21	9
Gastrointestinal disorders (days)		
Number (%) of events	3 (2.0)	9 (5.9)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.17 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	146 (98.0)	143 (94.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0988
Hazard ratio (95% CI) vs Pd	-	2.862 (0.775 to 10.572)
P-value	-	0.1148
Events probability (95% CI)[b]		
2 Months	0.993 (0.952 to 0.999)	0.973 (0.931 to 0.990)
4 Months	0.979 (0.936 to 0.993)	0.953 (0.903 to 0.977)
6 Months	0.979 (0.936 to 0.993)	0.945 (0.893 to 0.972)
8 Months	0.979 (0.936 to 0.993)	0.945 (0.893 to 0.972)
10 Months	0.979 (0.936 to 0.993)	0.937 (0.882 to 0.967)
12 Months	0.979 (0.936 to 0.993)	0.937 (0.882 to 0.967)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.17 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.979 (0.936 to 0.993)	0.937 (0.882 to 0.967)
16 Months	0.979 (0.936 to 0.993)	0.937 (0.882 to 0.967)
Number of patients at risk[b]		
2 Months	141	145
4 Months	131	134
6 Months	114	120
8 Months	103	116
10 Months	100	108
12 Months	86	97
14 Months	54	67
16 Months	26	27
General disorders and administration site conditions (days)		
Number (%) of events	13 (8.7)	17 (11.2)
Number (%) of patients censored	136 (91.3)	135 (88.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (15.967 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.17 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.5645
Hazard ratio (95% CI) vs Pd	-	1.236 (0.600 to 2.545)
P-value	-	0.5652
Events probability (95% CI)[b]		
2 Months	0.959 (0.910 to 0.981)	0.947 (0.897 to 0.973)
4 Months	0.937 (0.882 to 0.967)	0.933 (0.880 to 0.964)
6 Months	0.921 (0.862 to 0.956)	0.919 (0.862 to 0.953)
8 Months	0.912 (0.850 to 0.949)	0.904 (0.843 to 0.942)
10 Months	0.903 (0.838 to 0.943)	0.896 (0.832 to 0.936)
12 Months	0.903 (0.838 to 0.943)	0.896 (0.832 to 0.936)
14 Months	0.903 (0.838 to 0.943)	0.896 (0.832 to 0.936)
16 Months	0.903 (0.838 to 0.943)	0.843 (0.733 to 0.910)
Number of patients at risk[b]		
2 Months	137	142

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.17 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	127	133
6 Months	113	120
8 Months	101	116
10 Months	96	108
12 Months	81	96
14 Months	50	65
16 Months	26	26
Infections and infestations (days)		
Number (%) of events	43 (28.9)	63 (41.4)
Number (%) of patients censored	106 (71.1)	89 (58.6)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	4.37 (2.267 to NC)	4.04 (2.004 to 6.275)
Median (95% CI)	NC (NC to NC)	NC (11.269 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0847

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.17 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	1.406 (0.953 to 2.074)
P-value	-	0.0862
Events probability (95% CI)[b]		
2 Months	0.842 (0.772 to 0.892)	0.827 (0.756 to 0.879)
4 Months	0.756 (0.677 to 0.818)	0.752 (0.675 to 0.814)
6 Months	0.725 (0.643 to 0.791)	0.688 (0.606 to 0.756)
8 Months	0.709 (0.626 to 0.777)	0.642 (0.558 to 0.714)
10 Months	0.709 (0.626 to 0.777)	0.603 (0.517 to 0.678)
12 Months	0.699 (0.614 to 0.768)	0.570 (0.484 to 0.648)
14 Months	0.699 (0.614 to 0.768)	0.559 (0.471 to 0.638)
16 Months	0.678 (0.585 to 0.755)	0.559 (0.471 to 0.638)
Number of patients at risk[b]		
2 Months	120	123
4 Months	103	109
6 Months	91	91
8 Months	80	84
10 Months	79	76
12 Months	65	66

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.17 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	40	44
16 Months	20	19
Injury, poisoning and procedural complications (days)		
Number (%) of events	0 (0.0)	8 (5.3)
Number (%) of patients censored	149 (100.0)	144 (94.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0055
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9929
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	0.967 (0.923 to 0.986)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.17 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	1.000 (1.000 to 1.000)	0.954 (0.905 to 0.978)
6 Months	1.000 (1.000 to 1.000)	0.954 (0.905 to 0.978)
8 Months	1.000 (1.000 to 1.000)	0.954 (0.905 to 0.978)
10 Months	1.000 (1.000 to 1.000)	0.954 (0.905 to 0.978)
12 Months	1.000 (1.000 to 1.000)	0.954 (0.905 to 0.978)
14 Months	1.000 (1.000 to 1.000)	0.944 (0.890 to 0.972)
16 Months	1.000 (1.000 to 1.000)	0.944 (0.890 to 0.972)
Number of patients at risk[b]		
2 Months	142	145
4 Months	134	137
6 Months	117	124
8 Months	106	119
10 Months	102	112
12 Months	87	100
14 Months	54	67
16 Months	26	28
Metabolism and nutrition disorders (days)		
Number (%) of events	8 (5.4)	13 (8.6)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.17 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	141 (94.6)	139 (91.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3088
Hazard ratio (95% CI) vs Pd	-	1.574 (0.652 to 3.797)
P-value	-	0.3130
Events probability (95% CI)[b]		
2 Months	0.966 (0.921 to 0.986)	0.954 (0.906 to 0.978)
4 Months	0.952 (0.902 to 0.977)	0.933 (0.880 to 0.964)
6 Months	0.944 (0.892 to 0.972)	0.926 (0.870 to 0.958)
8 Months	0.944 (0.892 to 0.972)	0.926 (0.870 to 0.958)
10 Months	0.944 (0.892 to 0.972)	0.909 (0.848 to 0.946)
12 Months	0.944 (0.892 to 0.972)	0.909 (0.848 to 0.946)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.17 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.944 (0.892 to 0.972)	0.909 (0.848 to 0.946)
16 Months	0.944 (0.892 to 0.972)	0.909 (0.848 to 0.946)
Number of patients at risk[b]		
2 Months	138	143
4 Months	130	133
6 Months	112	120
8 Months	102	115
10 Months	99	106
12 Months	84	96
14 Months	52	64
16 Months	26	26
Musculoskeletal and connective tissue disorders (days)		
Number (%) of events	8 (5.4)	12 (7.9)
Number (%) of patients censored	141 (94.6)	140 (92.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.17 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.4761
Hazard ratio (95% CI) vs Pd	-	1.383 (0.565 to 3.384)
P-value	-	0.4780
Events probability (95% CI)[b]		
2 Months	0.952 (0.902 to 0.977)	0.967 (0.922 to 0.986)
4 Months	0.952 (0.902 to 0.977)	0.960 (0.914 to 0.982)
6 Months	0.952 (0.902 to 0.977)	0.946 (0.895 to 0.973)
8 Months	0.943 (0.890 to 0.971)	0.946 (0.895 to 0.973)
10 Months	0.943 (0.890 to 0.971)	0.938 (0.883 to 0.967)
12 Months	0.943 (0.890 to 0.971)	0.929 (0.872 to 0.961)
14 Months	0.943 (0.890 to 0.971)	0.929 (0.872 to 0.961)
16 Months	0.943 (0.890 to 0.971)	0.889 (0.798 to 0.941)
Number of patients at risk[b]		
2 Months	137	145

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.17 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	129	136
6 Months	113	123
8 Months	101	122
10 Months	97	114
12 Months	84	101
14 Months	52	69
16 Months	25	28
Nervous system disorders (days)		
Number (%) of events	7 (4.7)	12 (7.9)
Number (%) of patients censored	142 (95.3)	140 (92.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2929

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.17 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	1.641 (0.646 to 4.168)
P-value	-	0.2978
Events probability (95% CI)[b]		
2 Months	0.959 (0.911 to 0.981)	0.960 (0.914 to 0.982)
4 Months	0.959 (0.911 to 0.981)	0.940 (0.887 to 0.968)
6 Months	0.952 (0.901 to 0.977)	0.940 (0.887 to 0.968)
8 Months	0.952 (0.901 to 0.977)	0.924 (0.866 to 0.957)
10 Months	0.952 (0.901 to 0.977)	0.924 (0.866 to 0.957)
12 Months	0.952 (0.901 to 0.977)	0.915 (0.854 to 0.951)
14 Months	0.952 (0.901 to 0.977)	0.915 (0.854 to 0.951)
16 Months	0.952 (0.901 to 0.977)	0.915 (0.854 to 0.951)
Number of patients at risk[b]		
2 Months	137	143
4 Months	129	132
6 Months	113	119
8 Months	102	113
10 Months	98	107
12 Months	83	94

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.17 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	51	64
16 Months	25	27
Renal and urinary disorders (days)		
Number (%) of events	10 (6.7)	8 (5.3)
Number (%) of patients censored	139 (93.3)	144 (94.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.4913
Hazard ratio (95% CI) vs Pd	-	0.723 (0.285 to 1.832)
P-value	-	0.4935
Events probability (95% CI)[b]		
2 Months	0.951 (0.901 to 0.977)	0.987 (0.948 to 0.997)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.17 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.944 (0.892 to 0.972)	0.980 (0.939 to 0.994)
6 Months	0.936 (0.881 to 0.966)	0.972 (0.928 to 0.990)
8 Months	0.936 (0.881 to 0.966)	0.972 (0.928 to 0.990)
10 Months	0.936 (0.881 to 0.966)	0.956 (0.904 to 0.980)
12 Months	0.926 (0.866 to 0.960)	0.947 (0.892 to 0.975)
14 Months	0.926 (0.866 to 0.960)	0.947 (0.892 to 0.975)
16 Months	0.926 (0.866 to 0.960)	0.947 (0.892 to 0.975)
Number of patients at risk[b]		
2 Months	135	147
4 Months	127	138
6 Months	113	126
8 Months	102	121
10 Months	99	112
12 Months	84	100
14 Months	52	68
16 Months	25	29
Respiratory, thoracic and mediastinal disorders (days)		
Number (%) of events	10 (6.7)	14 (9.2)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.17 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	139 (93.3)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.5152
Hazard ratio (95% CI) vs Pd	-	1.308 (0.581 to 2.946)
P-value	-	0.5165
Events probability (95% CI)[b]		
2 Months	0.980 (0.938 to 0.993)	0.960 (0.914 to 0.982)
4 Months	0.980 (0.938 to 0.993)	0.946 (0.896 to 0.973)
6 Months	0.964 (0.914 to 0.985)	0.939 (0.886 to 0.968)
8 Months	0.955 (0.901 to 0.979)	0.915 (0.854 to 0.951)
10 Months	0.936 (0.874 to 0.968)	0.907 (0.844 to 0.945)
12 Months	0.936 (0.874 to 0.968)	0.898 (0.832 to 0.938)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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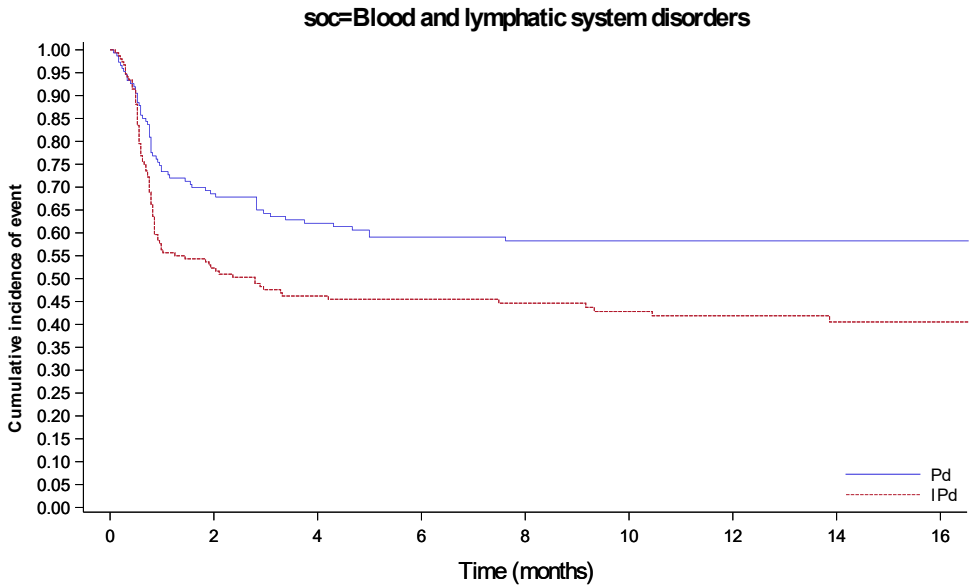
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.17 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.912 (0.841 to 0.953)	0.898 (0.832 to 0.938)
16 Months	0.912 (0.841 to 0.953)	0.898 (0.832 to 0.938)
Number of patients at risk[b]		
2 Months	140	143
4 Months	132	133
6 Months	113	121
8 Months	102	113
10 Months	96	105
12 Months	82	94
14 Months	48	64
16 Months	24	28

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16FEB2021 22:48)

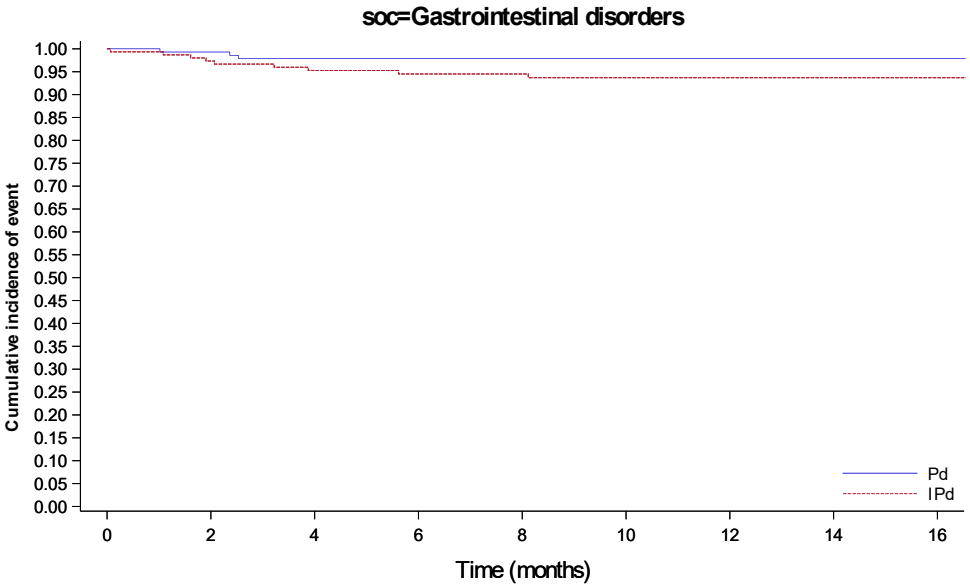
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	99	86	76	67	65	56	35	21
IPd	152	78	65	54	51	46	41	27	9

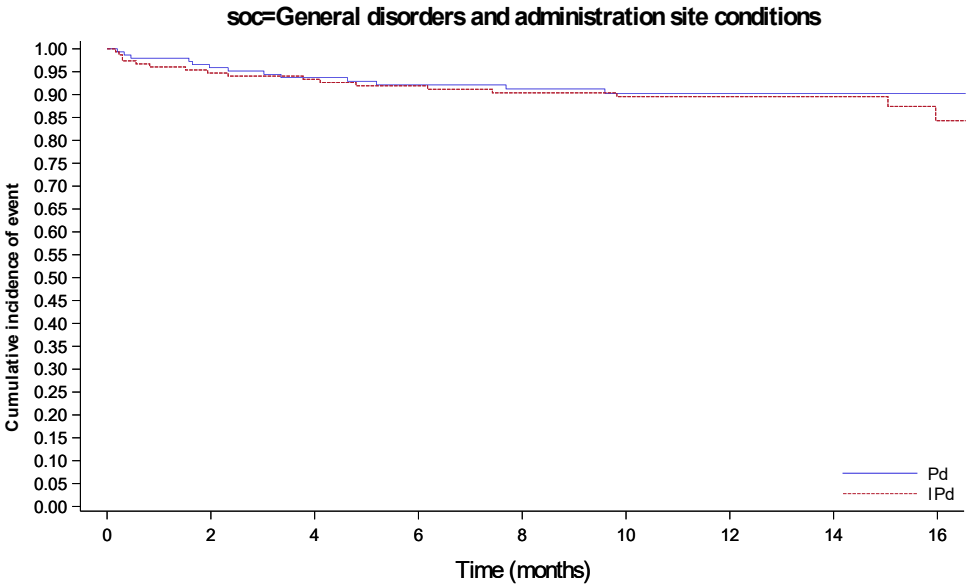
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	141	131	114	103	100	86	54	26
IPd	152	145	134	120	116	108	97	67	27

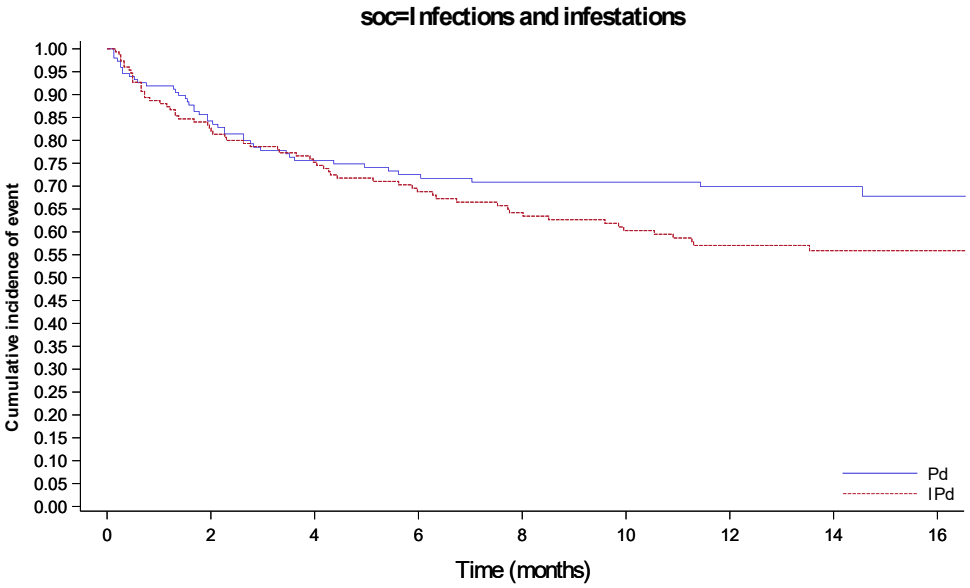
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	137	127	113	101	96	81	50	26
IPd	152	142	133	120	116	108	96	65	26

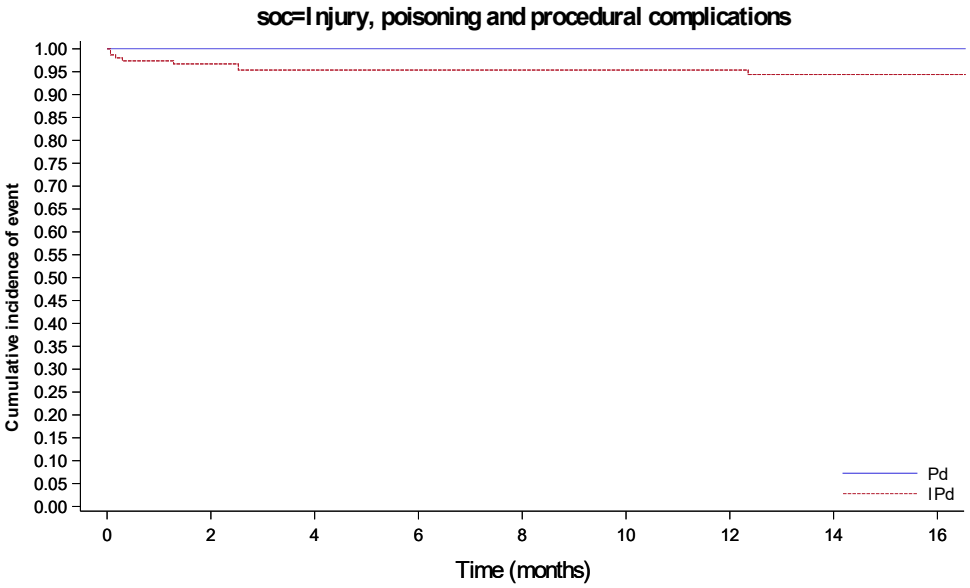
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	120	103	91	80	79	65	40	20
IPd	151	123	109	91	84	76	66	44	19

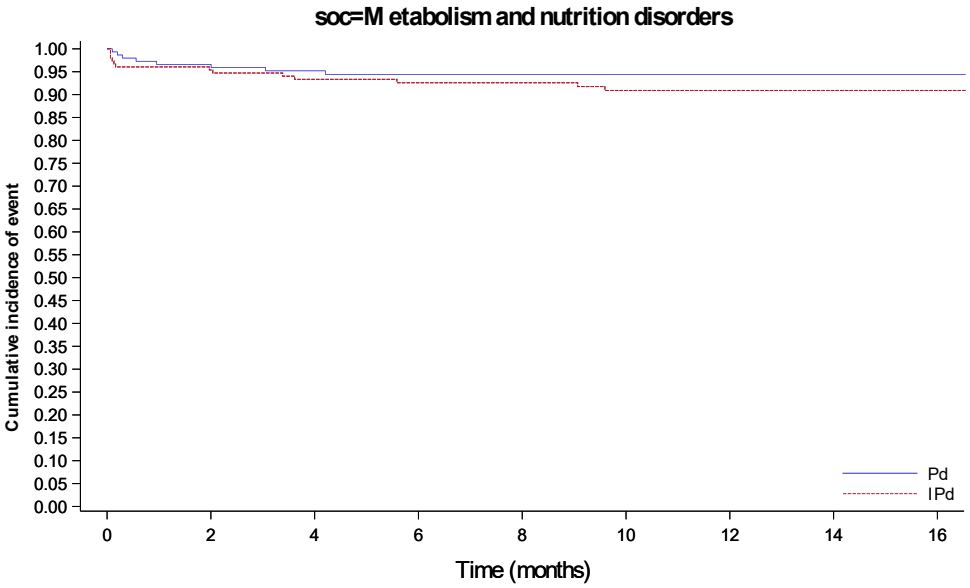
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	142	134	117	106	102	87	54	26
IPd	152	145	137	124	119	112	100	67	28

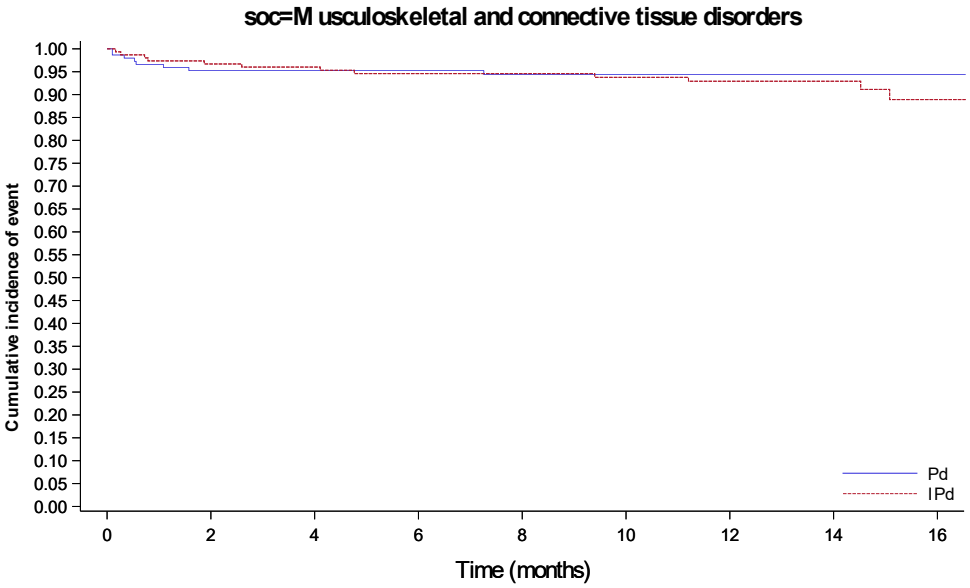
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	138	130	112	102	99	84	52	26
IPd	152	143	133	120	115	106	96	64	26

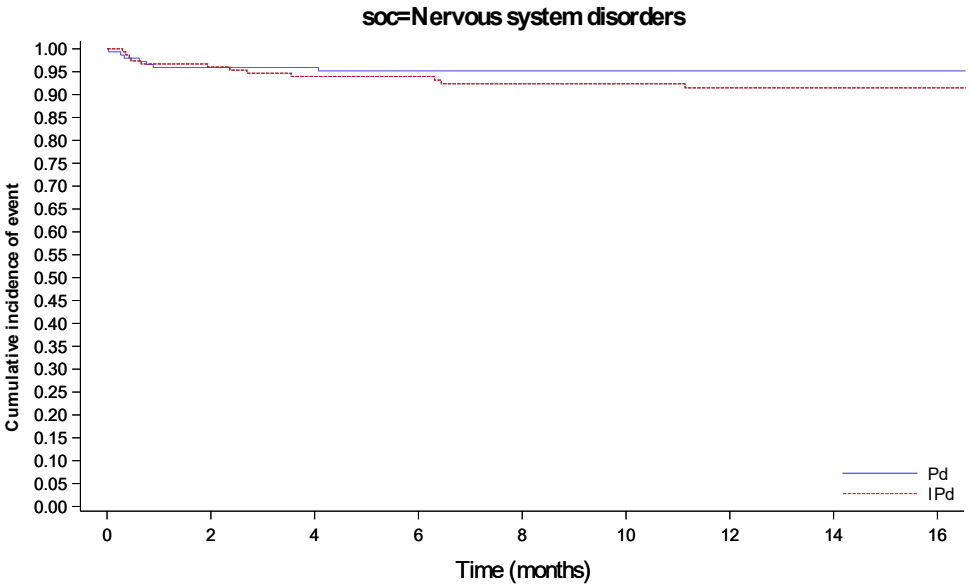
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	137	129	113	101	97	84	52	25
IPd	152	145	136	123	122	114	101	69	28

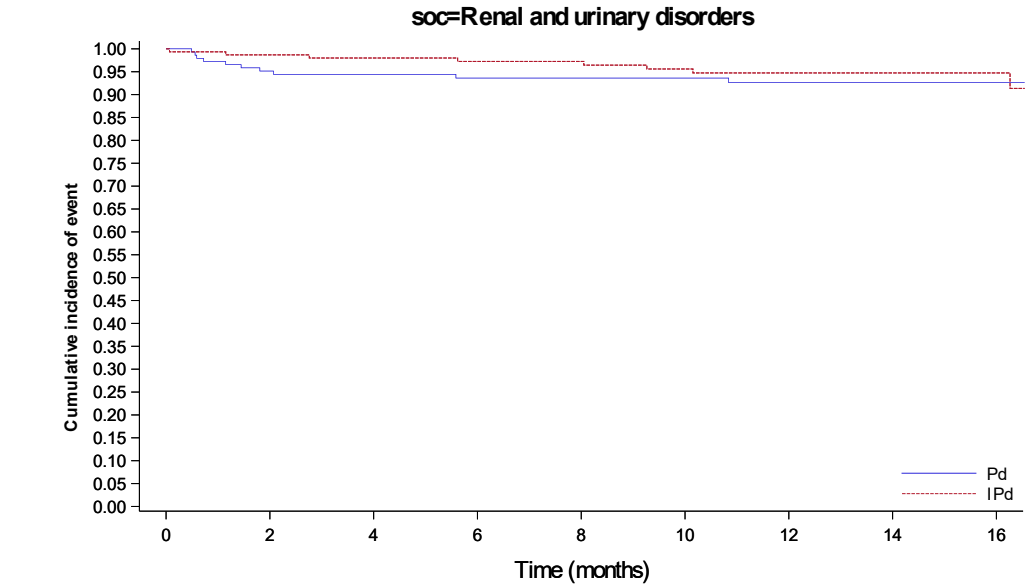
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



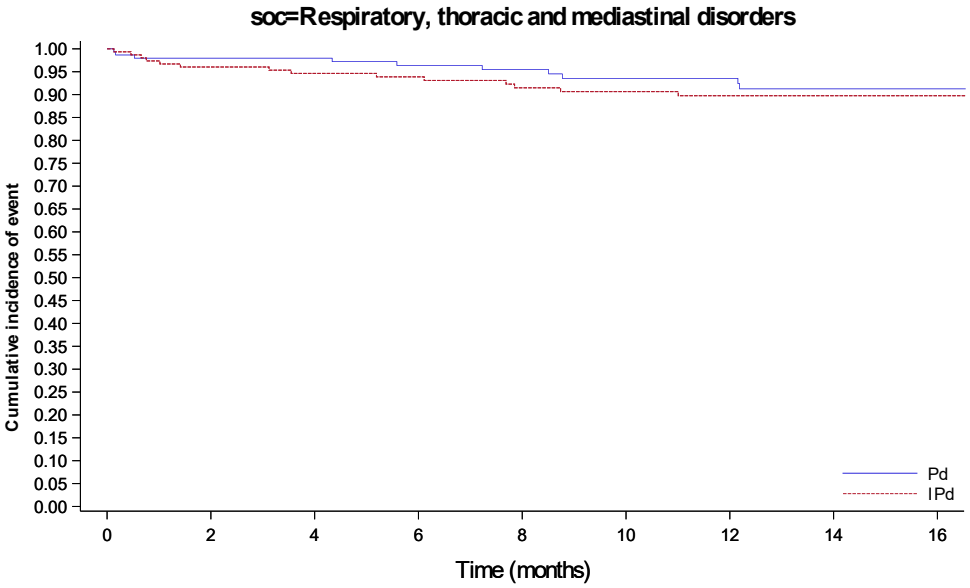
Number at Risk

Pd	149	137	129	113	102	98	83	51	25
IPd	152	143	132	119	113	107	94	64	27

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Pd	149	140	132	113	102	96	82	48	24
IPd	152	143	133	121	113	105	94	64	28

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.19 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Febrile neutropenia (days)		
Number (%) of events	3 (2.0)	18 (11.8)
Number (%) of patients censored	146 (98.0)	134 (88.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0011
Hazard ratio (95% CI) vs Pd	-	6.001 (1.768 to 20.370)
P-value	-	0.0041
Hazard ratio inverted (95% CI) vs IPd	0.167 (0.049 to 0.566)	-
Events probability (95% CI)[b]		
2 Months	0.986 (0.945 to 0.996)	0.907 (0.848 to 0.944)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.19 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.986 (0.945 to 0.996)	0.900 (0.840 to 0.939)
6 Months	0.986 (0.945 to 0.996)	0.887 (0.824 to 0.928)
8 Months	0.986 (0.945 to 0.996)	0.887 (0.824 to 0.928)
10 Months	0.976 (0.927 to 0.992)	0.887 (0.824 to 0.928)
12 Months	0.976 (0.927 to 0.992)	0.878 (0.812 to 0.921)
14 Months	0.976 (0.927 to 0.992)	0.878 (0.812 to 0.921)
16 Months	0.976 (0.927 to 0.992)	0.878 (0.812 to 0.921)
Number of patients at risk[b]		
2 Months	140	135
4 Months	132	129
6 Months	116	114
8 Months	105	110
10 Months	100	107
12 Months	86	94
14 Months	54	64
16 Months	26	26
Neutropenia (days)		
Number (%) of events	48 (32.2)	69 (45.4)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.19 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	101 (67.8)	83 (54.6)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	2.04 (0.986 to 4.994)	0.85 (0.756 to 1.018)
Median (95% CI)	NC (NC to NC)	NC (3.055 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0201
Hazard ratio (95% CI) vs Pd	-	1.543 (1.067 to 2.231)
P-value	-	0.0211
Hazard ratio inverted (95% CI) vs IPd	0.648 (0.448 to 0.937)	-
Events probability (95% CI)[b]		
2 Months	0.753 (0.675 to 0.815)	0.622 (0.540 to 0.694)
4 Months	0.703 (0.621 to 0.770)	0.581 (0.498 to 0.655)
6 Months	0.671 (0.586 to 0.741)	0.581 (0.498 to 0.655)
8 Months	0.661 (0.576 to 0.733)	0.564 (0.480 to 0.640)
10 Months	0.661 (0.576 to 0.733)	0.545 (0.460 to 0.623)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.19 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	0.661 (0.576 to 0.733)	0.536 (0.450 to 0.614)
14 Months	0.661 (0.576 to 0.733)	0.522 (0.434 to 0.602)
16 Months	0.661 (0.576 to 0.733)	0.522 (0.434 to 0.602)
Number of patients at risk[b]		
2 Months	109	92
4 Months	94	81
6 Months	80	71
8 Months	71	66
10 Months	69	57
12 Months	60	51
14 Months	38	34
16 Months	23	14
Pneumonia (days)		
Number (%) of events	22 (14.8)	25 (16.4)
Number (%) of patients censored	127 (85.2)	127 (83.6)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.19 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.7909
Hazard ratio (95% CI) vs Pd	-	1.080 (0.609 to 1.916)
P-value	-	0.7913
Events probability (95% CI)[b]		
2 Months	0.918 (0.860 to 0.952)	0.921 (0.865 to 0.954)
4 Months	0.867 (0.800 to 0.913)	0.887 (0.824 to 0.928)
6 Months	0.843 (0.772 to 0.894)	0.857 (0.788 to 0.904)
8 Months	0.843 (0.772 to 0.894)	0.833 (0.761 to 0.885)
10 Months	0.843 (0.772 to 0.894)	0.833 (0.761 to 0.885)
12 Months	0.843 (0.772 to 0.894)	0.825 (0.751 to 0.878)
14 Months	0.843 (0.772 to 0.894)	0.825 (0.751 to 0.878)
16 Months	0.843 (0.772 to 0.894)	0.825 (0.751 to 0.878)
Number of patients at risk[b]		

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.19 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	131	137
4 Months	117	126
6 Months	103	111
8 Months	94	105
10 Months	92	101
12 Months	79	91
14 Months	49	60
16 Months	24	26
Thrombocytopenia (days)		
Number (%) of events	18 (12.1)	18 (11.8)
Number (%) of patients censored	131 (87.9)	134 (88.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.8875

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.19 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	0.954 (0.496 to 1.833)
P-value	-	0.8875
Events probability (95% CI)[b]		
2 Months	0.897 (0.836 to 0.937)	0.901 (0.841 to 0.939)
4 Months	0.890 (0.827 to 0.931)	0.887 (0.825 to 0.928)
6 Months	0.875 (0.809 to 0.920)	0.887 (0.825 to 0.928)
8 Months	0.875 (0.809 to 0.920)	0.880 (0.815 to 0.922)
10 Months	0.875 (0.809 to 0.920)	0.880 (0.815 to 0.922)
12 Months	0.875 (0.809 to 0.920)	0.880 (0.815 to 0.922)
14 Months	0.875 (0.809 to 0.920)	0.880 (0.815 to 0.922)
16 Months	0.875 (0.809 to 0.920)	0.880 (0.815 to 0.922)
Number of patients at risk[b]		
2 Months	128	135
4 Months	121	126
6 Months	109	115
8 Months	100	110
10 Months	96	103

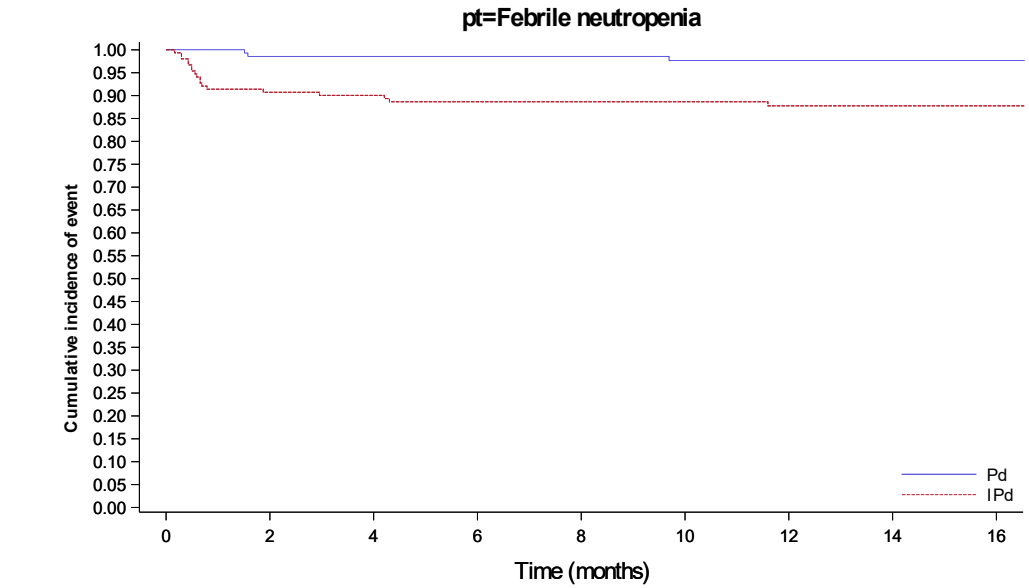
PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.19 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	82	93
14 Months	51	63
16 Months	24	27

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16FEB2021 22:48)

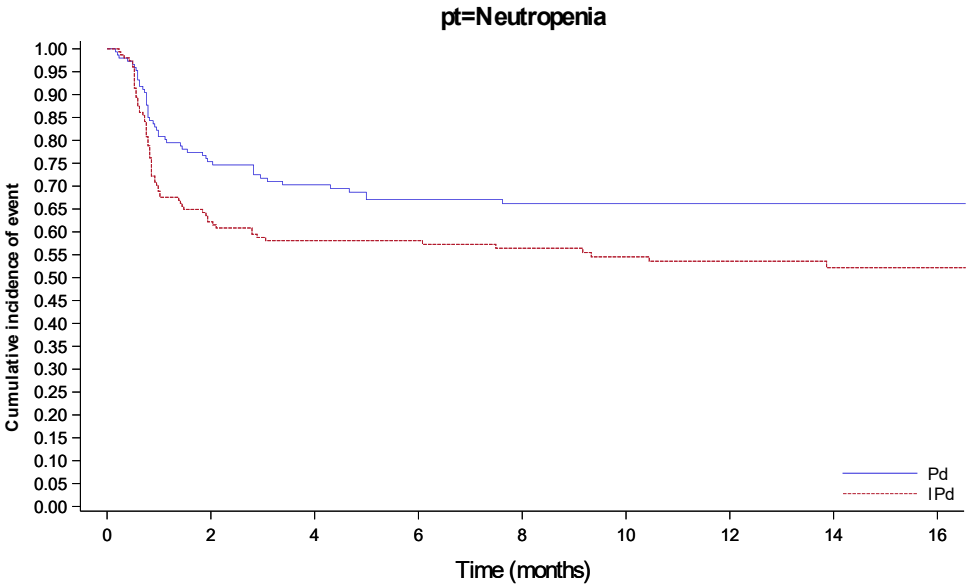
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.20 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	140	132	116	105	100	86	54	26
IPd	152	135	129	114	110	107	94	64	26

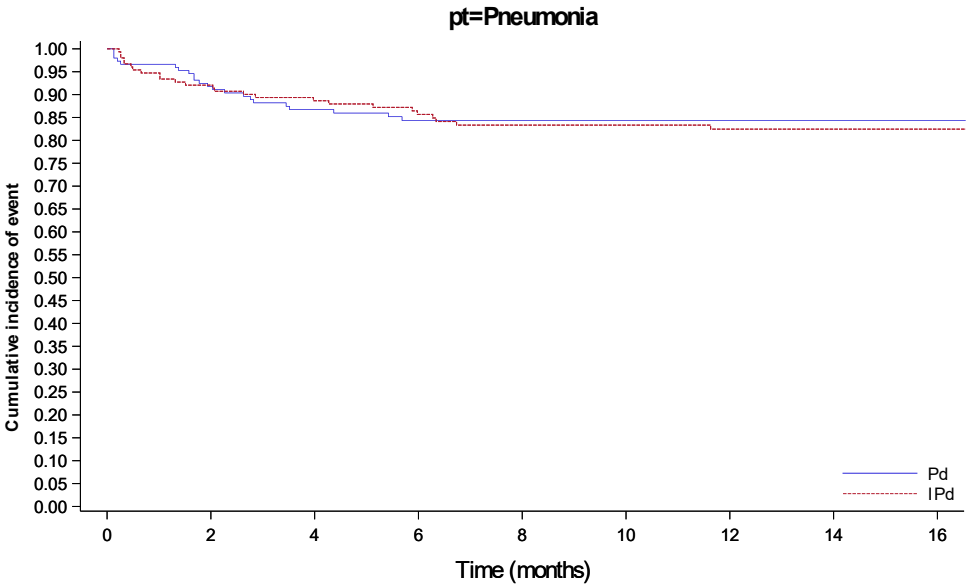
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.20 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	109	94	80	71	69	60	38	23
IPd	152	92	81	71	66	57	51	34	14

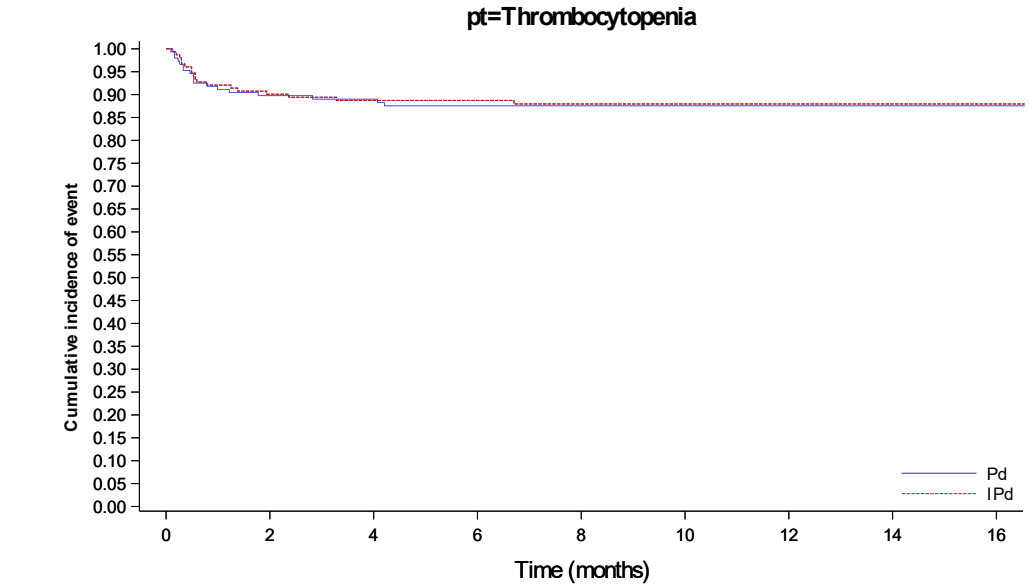
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.20 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	131	117	103	94	92	79	49	24
IPd	152	137	126	111	105	101	91	60	26

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.20 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to PT by treatment group - Safety population



Number at Risk

Pd	149	128	121	109	100	96	82	51	24
IPd	152	135	126	115	110	103	93	63	27

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.21 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Blood and lymphatic system disorders (days)		
Number (%) of events	60 (40.3)	87 (57.2)
Number (%) of patients censored	89 (59.7)	65 (42.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	0.95 (0.756 to 2.037)	0.66 (0.559 to 0.789)
Median (95% CI)	NC (7.622 to NC)	2.79 (0.953 to 10.448)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0034
Hazard ratio (95% CI) vs Pd	-	1.629 (1.171 to 2.264)
P-value	-	0.0037
Hazard ratio inverted (95% CI) vs IPd	0.614 (0.442 to 0.854)	-
Events probability (95% CI)[b]		
2 Months	0.685 (0.603 to 0.754)	0.523 (0.441 to 0.599)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.21 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.621 (0.537 to 0.695)	0.462 (0.381 to 0.539)
6 Months	0.591 (0.506 to 0.666)	0.455 (0.374 to 0.532)
8 Months	0.582 (0.497 to 0.659)	0.446 (0.365 to 0.524)
10 Months	0.582 (0.497 to 0.659)	0.428 (0.347 to 0.507)
12 Months	0.582 (0.497 to 0.659)	0.419 (0.337 to 0.498)
14 Months	0.582 (0.497 to 0.659)	0.405 (0.323 to 0.486)
16 Months	0.582 (0.497 to 0.659)	0.405 (0.323 to 0.486)
Number of patients at risk[b]		
2 Months	99	78
4 Months	86	65
6 Months	76	54
8 Months	67	51
10 Months	65	46
12 Months	56	41
14 Months	35	27
16 Months	21	9
Gastrointestinal disorders (days)		
Number (%) of events	3 (2.0)	9 (5.9)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.21 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	146 (98.0)	143 (94.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0988
Hazard ratio (95% CI) vs Pd	-	2.862 (0.775 to 10.572)
P-value	-	0.1148
Events probability (95% CI)[b]		
2 Months	0.993 (0.952 to 0.999)	0.973 (0.931 to 0.990)
4 Months	0.979 (0.936 to 0.993)	0.953 (0.903 to 0.977)
6 Months	0.979 (0.936 to 0.993)	0.945 (0.893 to 0.972)
8 Months	0.979 (0.936 to 0.993)	0.945 (0.893 to 0.972)
10 Months	0.979 (0.936 to 0.993)	0.937 (0.882 to 0.967)
12 Months	0.979 (0.936 to 0.993)	0.937 (0.882 to 0.967)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.21 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.979 (0.936 to 0.993)	0.937 (0.882 to 0.967)
16 Months	0.979 (0.936 to 0.993)	0.937 (0.882 to 0.967)
Number of patients at risk[b]		
2 Months	141	145
4 Months	131	134
6 Months	114	120
8 Months	103	116
10 Months	100	108
12 Months	86	97
14 Months	54	67
16 Months	26	27
General disorders and administration site conditions (days)		
Number (%) of events	18 (12.1)	23 (15.1)
Number (%) of patients censored	131 (87.9)	129 (84.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (15.967 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.21 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.5417
Hazard ratio (95% CI) vs Pd	-	1.211 (0.654 to 2.245)
P-value	-	0.5423
Events probability (95% CI)[b]		
2 Months	0.945 (0.894 to 0.972)	0.934 (0.881 to 0.964)
4 Months	0.917 (0.858 to 0.952)	0.914 (0.856 to 0.949)
6 Months	0.887 (0.822 to 0.929)	0.886 (0.823 to 0.928)
8 Months	0.879 (0.812 to 0.923)	0.871 (0.805 to 0.916)
10 Months	0.869 (0.800 to 0.916)	0.855 (0.786 to 0.903)
12 Months	0.869 (0.800 to 0.916)	0.855 (0.786 to 0.903)
14 Months	0.869 (0.800 to 0.916)	0.855 (0.786 to 0.903)
16 Months	0.869 (0.800 to 0.916)	0.805 (0.699 to 0.877)
Number of patients at risk[b]		
2 Months	137	140

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.21 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	126	133
6 Months	113	120
8 Months	101	116
10 Months	96	108
12 Months	81	96
14 Months	50	65
16 Months	26	26
Infections and infestations (days)		
Number (%) of events	45 (30.2)	65 (42.8)
Number (%) of patients censored	104 (69.8)	87 (57.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	3.61 (2.136 to 14.554)	4.04 (2.004 to 5.979)
Median (95% CI)	NC (NC to NC)	NC (10.546 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0911

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.21 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	1.387 (0.947 to 2.031)
P-value	-	0.0925
Events probability (95% CI)[b]		
2 Months	0.836 (0.765 to 0.887)	0.827 (0.756 to 0.879)
4 Months	0.744 (0.664 to 0.807)	0.752 (0.675 to 0.814)
6 Months	0.713 (0.631 to 0.780)	0.675 (0.592 to 0.744)
8 Months	0.697 (0.614 to 0.766)	0.630 (0.545 to 0.703)
10 Months	0.697 (0.614 to 0.766)	0.591 (0.506 to 0.667)
12 Months	0.687 (0.603 to 0.758)	0.559 (0.473 to 0.637)
14 Months	0.687 (0.603 to 0.758)	0.548 (0.461 to 0.627)
16 Months	0.667 (0.575 to 0.744)	0.548 (0.461 to 0.627)
Number of patients at risk[b]		
2 Months	120	123
4 Months	103	109
6 Months	91	91
8 Months	80	84
10 Months	79	76
12 Months	65	66

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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16.2.7.1.2.1.21 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	40	44
16 Months	20	19
Injury, poisoning and procedural complications (days)		
Number (%) of events	0 (0.0)	8 (5.3)
Number (%) of patients censored	149 (100.0)	144 (94.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0055
Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9929
Events probability (95% CI)[b]		
2 Months	1.000 (1.000 to 1.000)	0.967 (0.923 to 0.986)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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	Pd (N=149)	**IPd (N=152)**
4 Months	1.000 (1.000 to 1.000)	0.954 (0.905 to 0.978)
6 Months	1.000 (1.000 to 1.000)	0.954 (0.905 to 0.978)
8 Months	1.000 (1.000 to 1.000)	0.954 (0.905 to 0.978)
10 Months	1.000 (1.000 to 1.000)	0.954 (0.905 to 0.978)
12 Months	1.000 (1.000 to 1.000)	0.954 (0.905 to 0.978)
14 Months	1.000 (1.000 to 1.000)	0.944 (0.890 to 0.972)
16 Months	1.000 (1.000 to 1.000)	0.944 (0.890 to 0.972)
Number of patients at risk[b]		
2 Months	142	145
4 Months	134	137
6 Months	117	124
8 Months	106	119
10 Months	102	112
12 Months	87	100
14 Months	54	67
16 Months	26	28
Metabolism and nutrition disorders (days)		
Number (%) of events	8 (5.4)	13 (8.6)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
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	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	141 (94.6)	139 (91.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3088
Hazard ratio (95% CI) vs Pd	-	1.574 (0.652 to 3.797)
P-value	-	0.3130
Events probability (95% CI)[b]		
2 Months	0.966 (0.921 to 0.986)	0.954 (0.906 to 0.978)
4 Months	0.952 (0.902 to 0.977)	0.933 (0.880 to 0.964)
6 Months	0.944 (0.892 to 0.972)	0.926 (0.870 to 0.958)
8 Months	0.944 (0.892 to 0.972)	0.926 (0.870 to 0.958)
10 Months	0.944 (0.892 to 0.972)	0.909 (0.848 to 0.946)
12 Months	0.944 (0.892 to 0.972)	0.909 (0.848 to 0.946)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16FEB2021 22:48)

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	Pd (N=149)	**IPd (N=152)**
14 Months	0.944 (0.892 to 0.972)	0.909 (0.848 to 0.946)
16 Months	0.944 (0.892 to 0.972)	0.909 (0.848 to 0.946)
Number of patients at risk[b]		
2 Months	138	143
4 Months	130	133
6 Months	112	120
8 Months	102	115
10 Months	99	106
12 Months	84	96
14 Months	52	64
16 Months	26	26
Musculoskeletal and connective tissue disorders (days)		
Number (%) of events	8 (5.4)	12 (7.9)
Number (%) of patients censored	141 (94.6)	140 (92.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.4761
Hazard ratio (95% CI) vs Pd	-	1.383 (0.565 to 3.384)
P-value	-	0.4780
Events probability (95% CI)[b]		
2 Months	0.952 (0.902 to 0.977)	0.967 (0.922 to 0.986)
4 Months	0.952 (0.902 to 0.977)	0.960 (0.914 to 0.982)
6 Months	0.952 (0.902 to 0.977)	0.946 (0.895 to 0.973)
8 Months	0.943 (0.890 to 0.971)	0.946 (0.895 to 0.973)
10 Months	0.943 (0.890 to 0.971)	0.938 (0.883 to 0.967)
12 Months	0.943 (0.890 to 0.971)	0.929 (0.872 to 0.961)
14 Months	0.943 (0.890 to 0.971)	0.929 (0.872 to 0.961)
16 Months	0.943 (0.890 to 0.971)	0.889 (0.798 to 0.941)
Number of patients at risk[b]		
2 Months	137	145

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
4 Months	129	136
6 Months	113	123
8 Months	101	122
10 Months	97	114
12 Months	84	101
14 Months	52	69
16 Months	25	28
Nervous system disorders (days)		
Number (%) of events	7 (4.7)	12 (7.9)
Number (%) of patients censored	142 (95.3)	140 (92.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.2929

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	1.641 (0.646 to 4.168)
P-value	-	0.2978
Events probability (95% CI)[b]		
2 Months	0.959 (0.911 to 0.981)	0.960 (0.914 to 0.982)
4 Months	0.959 (0.911 to 0.981)	0.940 (0.887 to 0.968)
6 Months	0.952 (0.901 to 0.977)	0.940 (0.887 to 0.968)
8 Months	0.952 (0.901 to 0.977)	0.924 (0.866 to 0.957)
10 Months	0.952 (0.901 to 0.977)	0.924 (0.866 to 0.957)
12 Months	0.952 (0.901 to 0.977)	0.915 (0.854 to 0.951)
14 Months	0.952 (0.901 to 0.977)	0.915 (0.854 to 0.951)
16 Months	0.952 (0.901 to 0.977)	0.915 (0.854 to 0.951)
Number of patients at risk[b]		
2 Months	137	143
4 Months	129	132
6 Months	113	119
8 Months	102	113
10 Months	98	107
12 Months	83	94

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
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16.2.7.1.2.1.21 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	51	64
16 Months	25	27
Renal and urinary disorders (days)		
Number (%) of events	12 (8.1)	9 (5.9)
Number (%) of patients censored	137 (91.9)	143 (94.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.3826
Hazard ratio (95% CI) vs Pd	-	0.682 (0.287 to 1.619)
P-value	-	0.3855
Events probability (95% CI)[b]		
2 Months	0.938 (0.884 to 0.967)	0.980 (0.940 to 0.994)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
4 Months	0.931 (0.876 to 0.962)	0.973 (0.931 to 0.990)
6 Months	0.923 (0.865 to 0.957)	0.966 (0.920 to 0.986)
8 Months	0.923 (0.865 to 0.957)	0.966 (0.920 to 0.986)
10 Months	0.923 (0.865 to 0.957)	0.950 (0.897 to 0.976)
12 Months	0.913 (0.851 to 0.950)	0.941 (0.885 to 0.970)
14 Months	0.913 (0.851 to 0.950)	0.941 (0.885 to 0.970)
16 Months	0.913 (0.851 to 0.950)	0.941 (0.885 to 0.970)
Number of patients at risk[b]		
2 Months	134	147
4 Months	127	138
6 Months	113	126
8 Months	102	121
10 Months	99	112
12 Months	84	100
14 Months	52	68
16 Months	25	29
Respiratory, thoracic and mediastinal disorders (days)		
Number (%) of events	10 (6.7)	14 (9.2)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	139 (93.3)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.5152
Hazard ratio (95% CI) vs Pd	-	1.308 (0.581 to 2.946)
P-value	-	0.5165
Events probability (95% CI)[b]		
2 Months	0.980 (0.938 to 0.993)	0.960 (0.914 to 0.982)
4 Months	0.980 (0.938 to 0.993)	0.946 (0.896 to 0.973)
6 Months	0.964 (0.914 to 0.985)	0.939 (0.886 to 0.968)
8 Months	0.955 (0.901 to 0.979)	0.915 (0.854 to 0.951)
10 Months	0.936 (0.874 to 0.968)	0.907 (0.844 to 0.945)
12 Months	0.936 (0.874 to 0.968)	0.898 (0.832 to 0.938)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16FEB2021 22:48)

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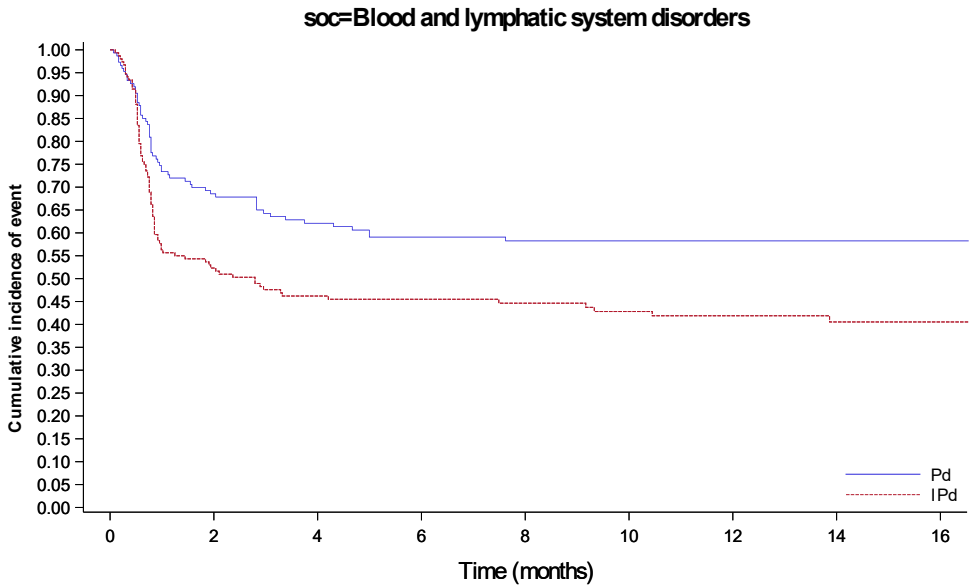
16.2.7.1.2.1.21 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.912 (0.841 to 0.953)	0.898 (0.832 to 0.938)
16 Months	0.912 (0.841 to 0.953)	0.898 (0.832 to 0.938)
Number of patients at risk[b]		
2 Months	140	143
4 Months	132	133
6 Months	113	121
8 Months	102	113
10 Months	96	105
12 Months	82	94
14 Months	48	64
16 Months	24	28

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16FEB2021 22:48)

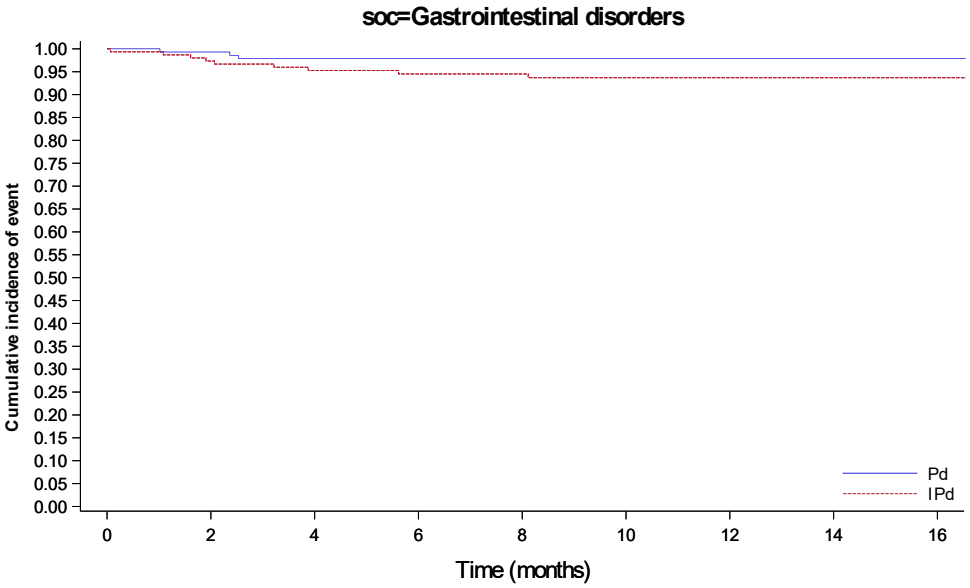
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.22 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death according to SOC by treatment group - Safety population



Number at Risk

Pd	149	99	86	76	67	65	56	35	21
IPd	152	78	65	54	51	46	41	27	9

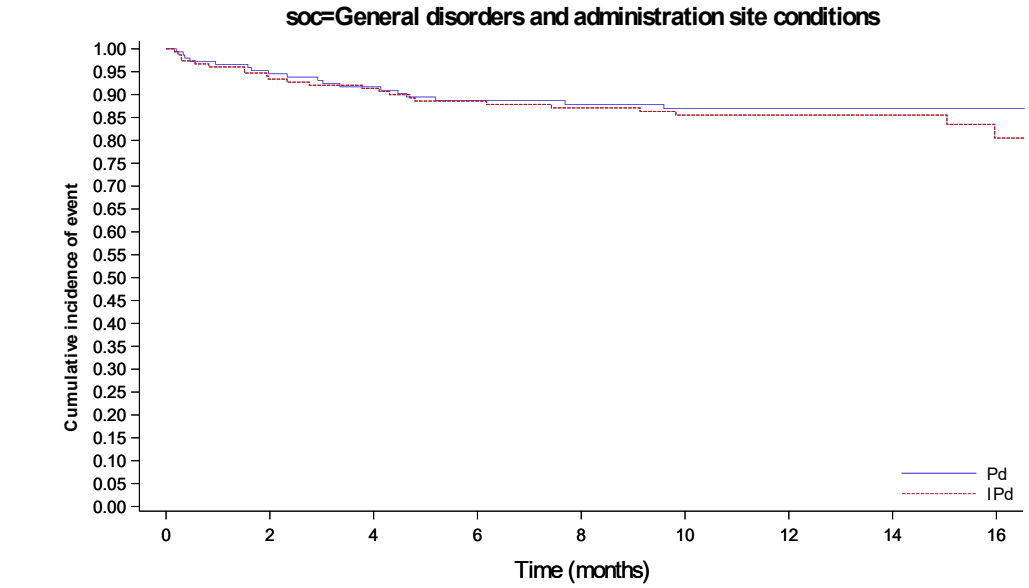
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.22 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death according to SOC by treatment group - Safety population



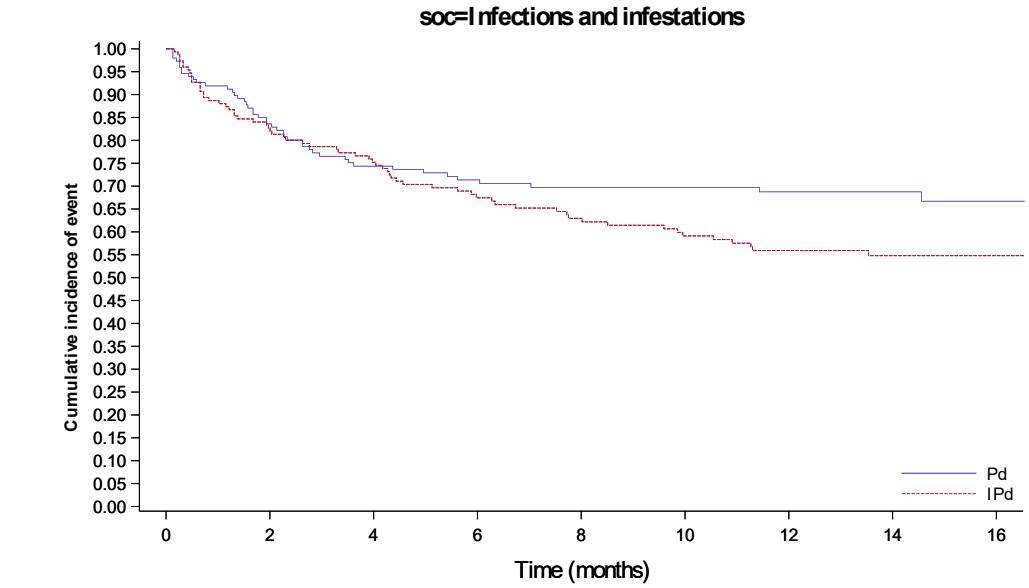
Number at Risk

Pd	149	141	131	114	103	100	86	54	26
IPd	152	145	134	120	116	108	97	67	27

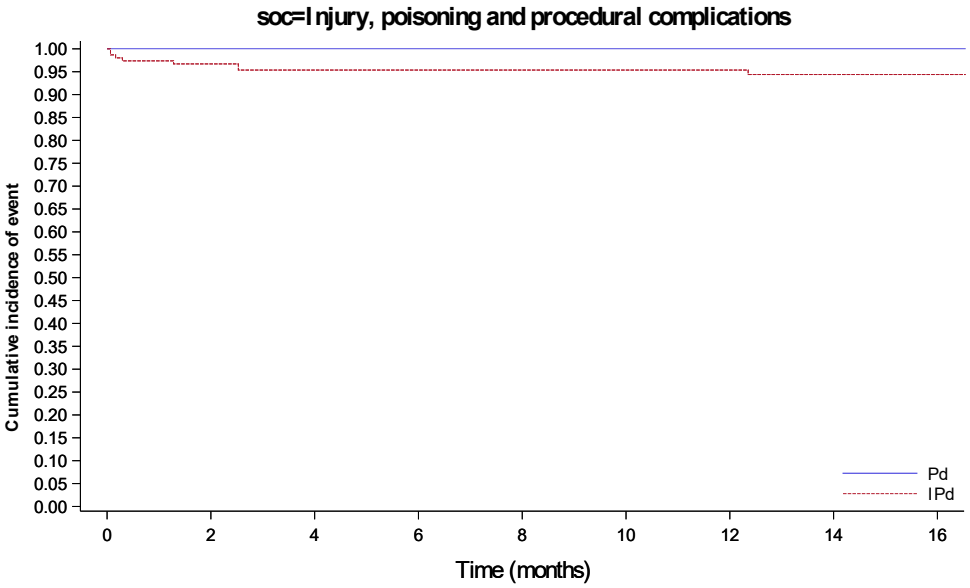
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.22 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death according to SOC by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.22 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death according to SOC by treatment group - Safety population



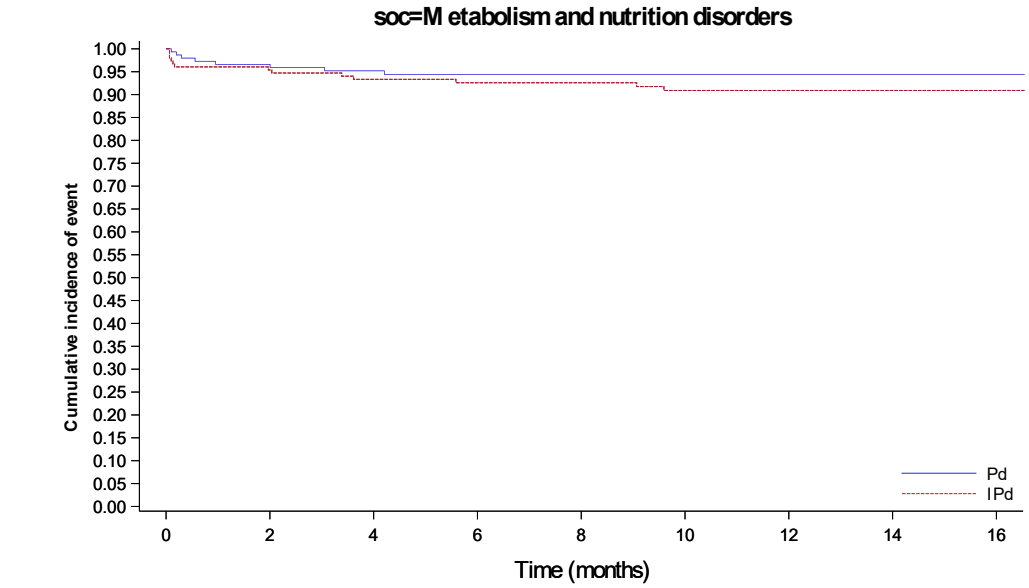
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.22 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death according to SOC by treatment group - Safety population



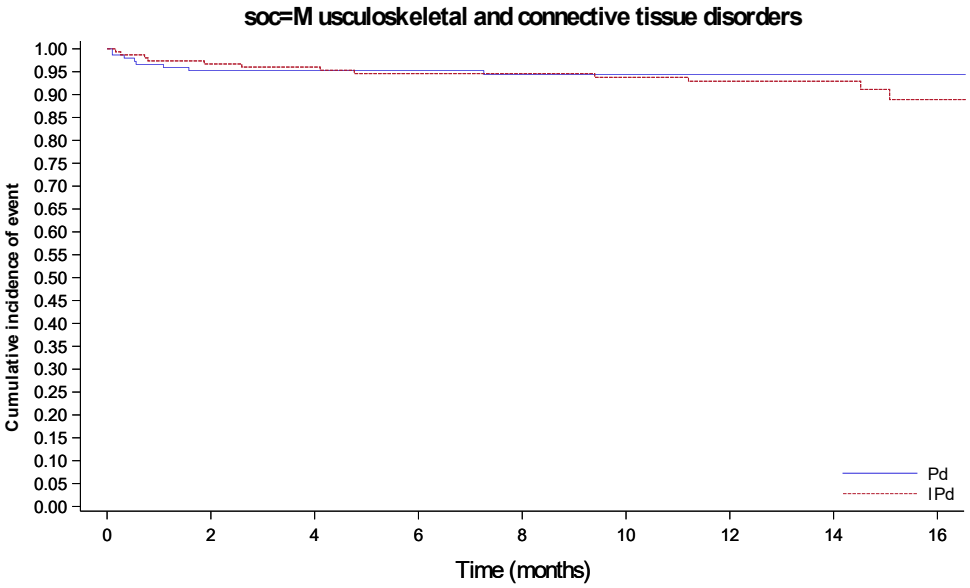
Number at Risk

Pd	149	142	134	117	106	102	87	54	26
IPd	152	145	137	124	119	112	100	67	28

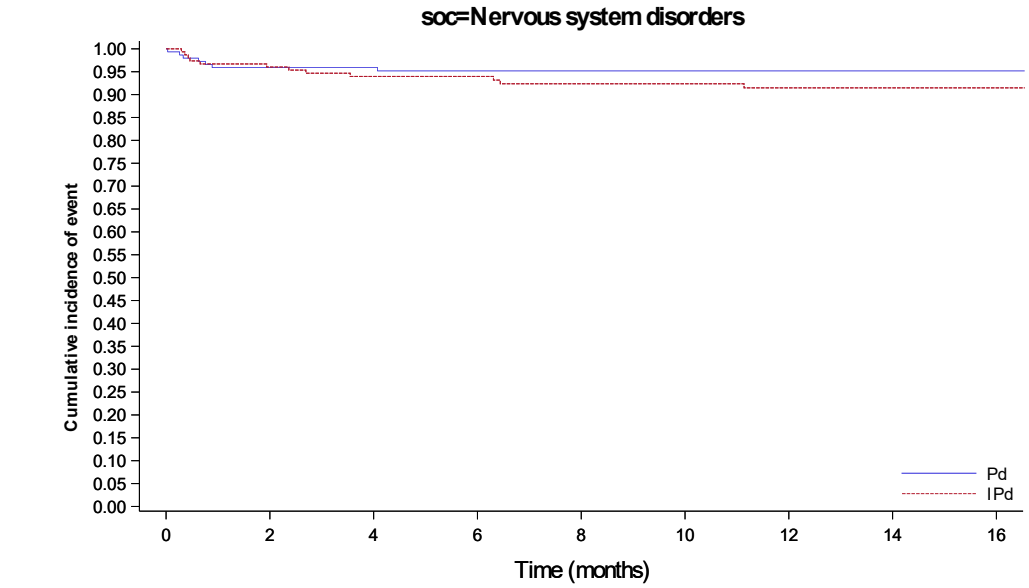
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.22 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death according to SOC by treatment group - Safety population



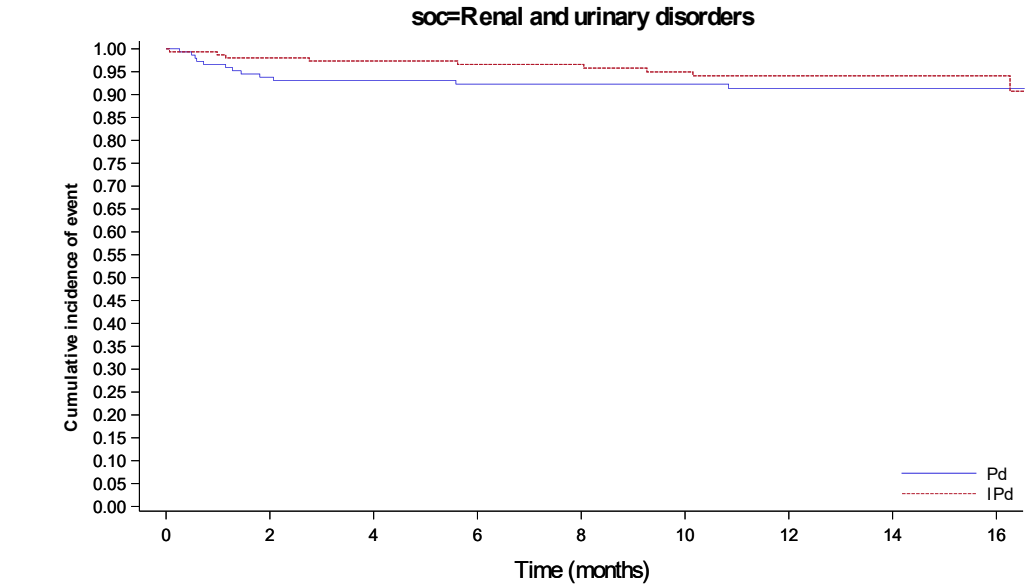
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.22 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death according to SOC by treatment group - Safety population



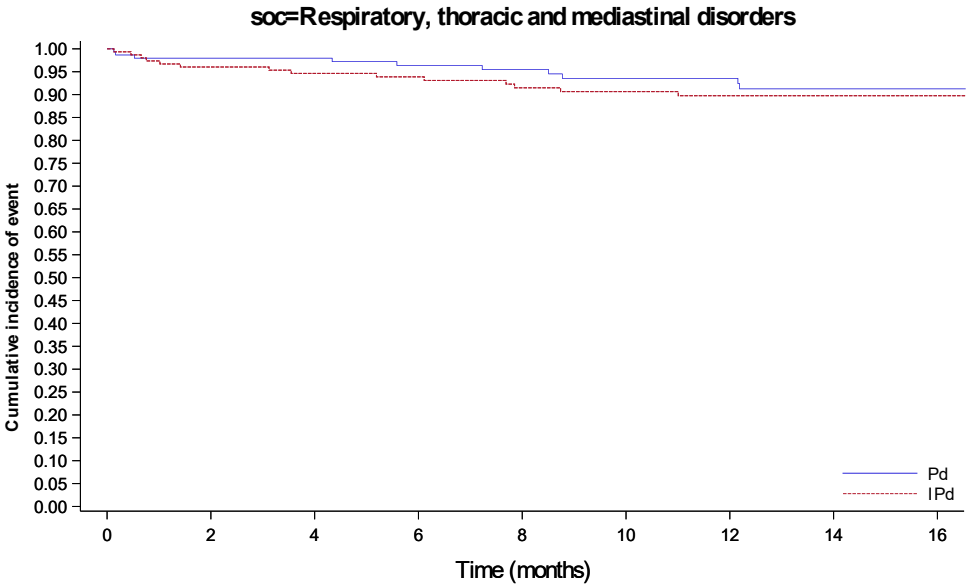
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.22 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death according to SOC by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.22 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death according to SOC by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.22 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death according to SOC by treatment group - Safety population



Number at Risk

Pd	149	140	132	113	102	96	82	48	24
IPd	152	143	133	121	113	105	94	64	28

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.23 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Disease progression (days)		
Number (%) of events	8 (5.4)	8 (5.3)
Number (%) of patients censored	141 (94.6)	144 (94.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.8964
Hazard ratio (95% CI) vs Pd	-	0.937 (0.352 to 2.497)
P-value	-	0.8963
Events probability (95% CI)[b]		
2 Months	0.979 (0.937 to 0.993)	0.973 (0.931 to 0.990)
4 Months	0.951 (0.899 to 0.976)	0.967 (0.922 to 0.986)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.23 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	0.943 (0.889 to 0.971)	0.953 (0.903 to 0.977)
8 Months	0.943 (0.889 to 0.971)	0.945 (0.893 to 0.972)
10 Months	0.943 (0.889 to 0.971)	0.945 (0.893 to 0.972)
12 Months	0.943 (0.889 to 0.971)	0.945 (0.893 to 0.972)
14 Months	0.943 (0.889 to 0.971)	0.945 (0.893 to 0.972)
16 Months	0.943 (0.889 to 0.971)	0.945 (0.893 to 0.972)
Number of patients at risk[b]		
2 Months	140	146
4 Months	129	140
6 Months	115	127
8 Months	104	123
10 Months	100	116
12 Months	85	104
14 Months	54	71
16 Months	26	30
Febrile neutropenia (days)		
Number (%) of events	3 (2.0)	18 (11.8)
Number (%) of patients censored	146 (98.0)	134 (88.2)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.23 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0011
Hazard ratio (95% CI) vs Pd	-	6.001 (1.768 to 20.370)
P-value	-	0.0041
Hazard ratio inverted (95% CI) vs IPd	0.167 (0.049 to 0.566)	-
Events probability (95% CI)[b]		
2 Months	0.986 (0.945 to 0.996)	0.907 (0.848 to 0.944)
4 Months	0.986 (0.945 to 0.996)	0.900 (0.840 to 0.939)
6 Months	0.986 (0.945 to 0.996)	0.887 (0.824 to 0.928)
8 Months	0.986 (0.945 to 0.996)	0.887 (0.824 to 0.928)
10 Months	0.976 (0.927 to 0.992)	0.887 (0.824 to 0.928)
12 Months	0.976 (0.927 to 0.992)	0.878 (0.812 to 0.921)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.23 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.976 (0.927 to 0.992)	0.878 (0.812 to 0.921)
16 Months	0.976 (0.927 to 0.992)	0.878 (0.812 to 0.921)
Number of patients at risk[b]		
2 Months	140	135
4 Months	132	129
6 Months	116	114
8 Months	105	110
10 Months	100	107
12 Months	86	94
14 Months	54	64
16 Months	26	26
Neutropenia (days)		
Number (%) of events	48 (32.2)	70 (46.1)
Number (%) of patients censored	101 (67.8)	82 (53.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	2.04 (0.986 to 4.994)	0.85 (0.756 to 0.986)
Median (95% CI)	NC (NC to NC)	NC (2.891 to NC)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.23 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.0156
Hazard ratio (95% CI) vs Pd	-	1.568 (1.085 to 2.264)
P-value	-	0.0165
Hazard ratio inverted (95% CI) vs IPd	0.638 (0.442 to 0.921)	-
Events probability (95% CI)[b]		
2 Months	0.753 (0.675 to 0.815)	0.616 (0.533 to 0.688)
4 Months	0.703 (0.621 to 0.770)	0.575 (0.492 to 0.649)
6 Months	0.671 (0.586 to 0.741)	0.575 (0.492 to 0.649)
8 Months	0.661 (0.576 to 0.733)	0.559 (0.475 to 0.634)
10 Months	0.661 (0.576 to 0.733)	0.540 (0.455 to 0.617)
12 Months	0.661 (0.576 to 0.733)	0.530 (0.445 to 0.608)
14 Months	0.661 (0.576 to 0.733)	0.516 (0.429 to 0.597)
16 Months	0.661 (0.576 to 0.733)	0.516 (0.429 to 0.597)
Number of patients at risk[b]		

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.23 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	109	92
4 Months	94	81
6 Months	80	71
8 Months	71	66
10 Months	69	57
12 Months	60	51
14 Months	38	34
16 Months	23	14
Pneumonia (days)		
Number (%) of events	23 (15.4)	25 (16.4)
Number (%) of patients censored	126 (84.6)	127 (83.6)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.9119

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.23 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Hazard ratio (95% CI) vs Pd	-	1.032 (0.586 to 1.819)
P-value	-	0.9119
Events probability (95% CI)[b]		
2 Months	0.918 (0.860 to 0.952)	0.921 (0.865 to 0.954)
4 Months	0.867 (0.800 to 0.913)	0.887 (0.824 to 0.928)
6 Months	0.836 (0.763 to 0.888)	0.857 (0.788 to 0.904)
8 Months	0.836 (0.763 to 0.888)	0.833 (0.761 to 0.885)
10 Months	0.836 (0.763 to 0.888)	0.833 (0.761 to 0.885)
12 Months	0.836 (0.763 to 0.888)	0.825 (0.751 to 0.878)
14 Months	0.836 (0.763 to 0.888)	0.825 (0.751 to 0.878)
16 Months	0.836 (0.763 to 0.888)	0.825 (0.751 to 0.878)
Number of patients at risk[b]		
2 Months	131	137
4 Months	117	126
6 Months	103	111
8 Months	94	105
10 Months	92	101

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.23 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	79	91
14 Months	49	60
16 Months	24	26
Thrombocytopenia (days)		
Number (%) of events	18 (12.1)	18 (11.8)
Number (%) of patients censored	131 (87.9)	134 (88.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Log-Rank test p-value[a] vs Pd	-	0.8875
Hazard ratio (95% CI) vs Pd	-	0.954 (0.496 to 1.833)
P-value	-	0.8875
Events probability (95% CI)[b]		

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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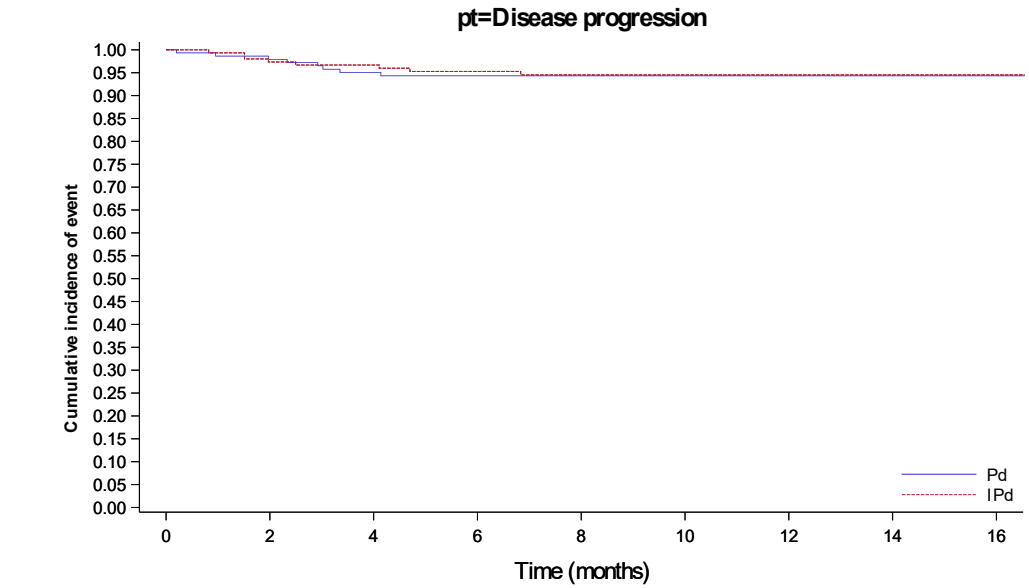
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.23 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

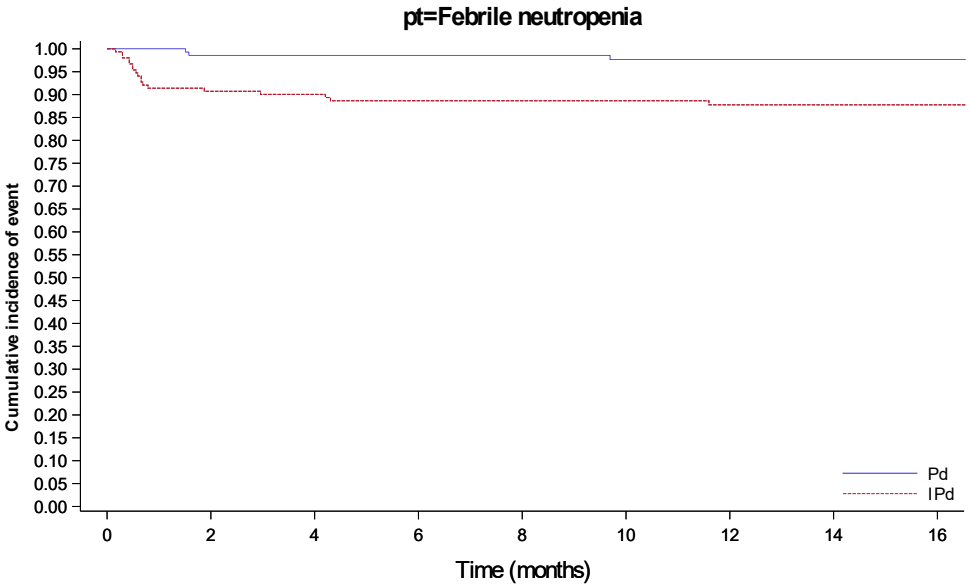
	Pd (N=149)	**IPd (N=152)**
2 Months	0.897 (0.836 to 0.937)	0.901 (0.841 to 0.939)
4 Months	0.890 (0.827 to 0.931)	0.887 (0.825 to 0.928)
6 Months	0.875 (0.809 to 0.920)	0.887 (0.825 to 0.928)
8 Months	0.875 (0.809 to 0.920)	0.880 (0.815 to 0.922)
10 Months	0.875 (0.809 to 0.920)	0.880 (0.815 to 0.922)
12 Months	0.875 (0.809 to 0.920)	0.880 (0.815 to 0.922)
14 Months	0.875 (0.809 to 0.920)	0.880 (0.815 to 0.922)
16 Months	0.875 (0.809 to 0.920)	0.880 (0.815 to 0.922)
Number of patients at risk[b]		
2 Months	128	135
4 Months	121	126
6 Months	109	115
8 Months	100	110
10 Months	96	103
12 Months	82	93
14 Months	51	63
16 Months	24	27

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.24 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death according to PT by treatment group - Safety population



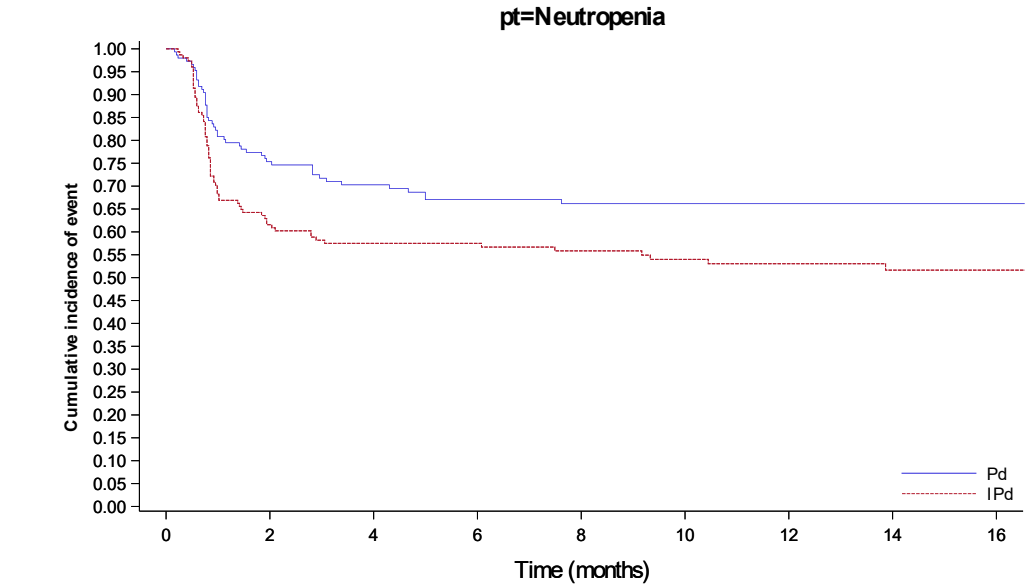
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.24 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death according to PT by treatment group - Safety population



Number at Risk

Pd	149	140	132	116	105	100	86	54	26
IPd	152	135	129	114	110	107	94	64	26

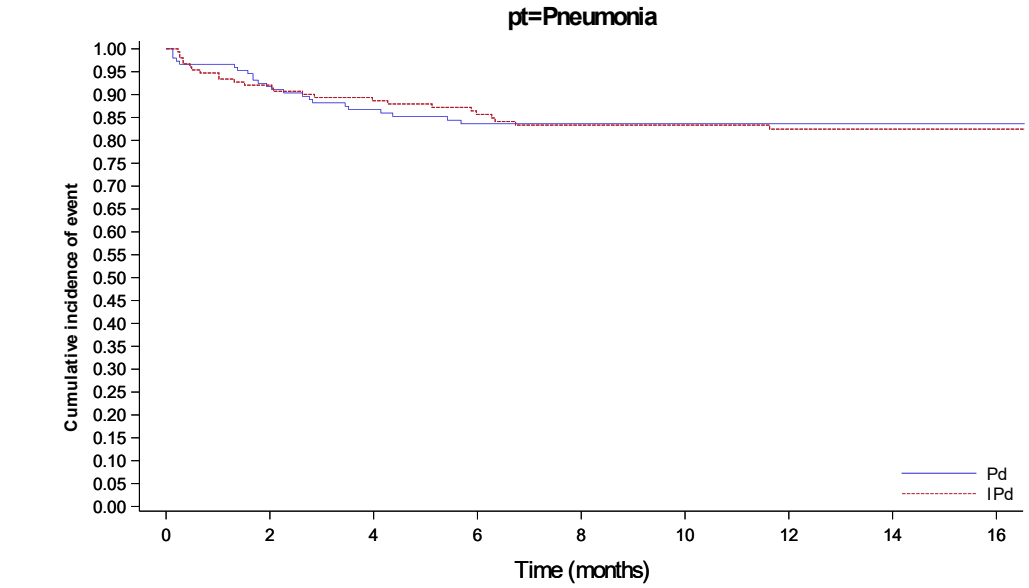
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.24 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death according to PT by treatment group - Safety population



Number at Risk

Pd	149	109	94	80	71	69	60	38	23
IPd	152	92	81	71	66	57	51	34	14

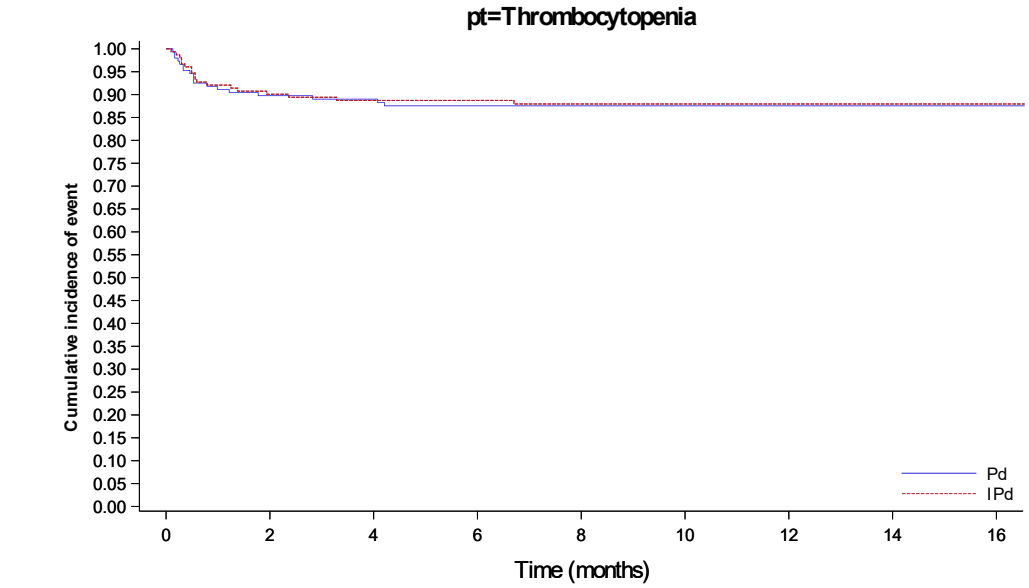
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.24 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death according to PT by treatment group - Safety population



Number at Risk

Pd	149	131	117	103	94	92	79	49	24
IPd	152	137	126	111	105	101	91	60	26

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.1 Safety population
16.2.7.1.2.1.24 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death according to PT by treatment group - Safety population



Number at Risk

Pd	149	128	121	109	100	96	82	51	24
IPd	152	135	126	115	110	103	93	63	27

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.1 Treatment emergent adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)							
Number (%) of events	25 (36.8)	29 (53.7)	25 (47.2)	38 (57.6)	15 (53.6)	22 (68.8)	0.6201
Number (%) of patients censored	43 (63.2)	25 (46.3)	28 (52.8)	28 (42.4)	13 (46.4)	10 (31.3)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	1.9384 (0.7885 to 5.0267)	0.6242 (0.5585 to 0.8214)	0.7885 (0.5257 to 2.0370)	0.7556 (0.5257 to 0.8542)	0.6078 (0.1971 to 1.1170)	0.5257 (0.3614 to 0.8214)	
Median (95% CI)	NC (7.6222 to NC)	2.1027 (0.8214 to NC)	8.6078 (1.8398 to NC)	4.0411 (0.9199 to NC)	4.3039 (0.7556 to NC)	0.8871 (0.6899 to 10.4476)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.3655 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0234		0.3472		0.2972	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_age_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.1 Treatment emergent adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	1.84 (1.08 to 3.15)		1.27 (0.77 to 2.11)		1.42 (0.73 to 2.74)	
P-value	-	0.0256		0.3484		0.2996	
Hazard ratio inverted (95% CI) vs IPd	0.54 (0.32 to 0.93)						
Events probability (95% CI)[b]							
2 Months	0.7464 (0.6242 to 0.8340)	0.5364 (0.3954 to 0.6583)	0.6469 (0.4993 to 0.7610)	0.5390 (0.4110 to 0.6508)	0.5714 (0.3706 to 0.7295)	0.4375 (0.2646 to 0.5981)	
4 Months	0.6852 (0.5590 to 0.7821)	0.4582 (0.3213 to 0.5848)	0.5416 (0.3940 to 0.6678)	0.5082 (0.3815 to 0.6216)	0.5357 (0.3381 to 0.6982)	0.3438 (0.1879 to 0.5056)	
6 Months	0.6350 (0.5060 to 0.7388)	0.4582 (0.3213 to 0.5848)	0.5199 (0.3730 to 0.6480)	0.4774 (0.3524 to 0.5920)	0.4560 (0.2656 to 0.6280)	0.3438 (0.1879 to 0.5056)	
8 Months	0.6164 (0.4860 to 0.7228)	0.4582 (0.3213 to 0.5848)	0.5199 (0.3730 to 0.6480)	0.4590 (0.3344 to 0.5749)	0.4560 (0.2656 to 0.6280)	0.3438 (0.1879 to 0.5056)	
10 Months	0.6164 (0.4860 to 0.7228)	0.4582 (0.3213 to 0.5848)	0.4963 (0.3499 to 0.6266)	0.4208 (0.2974 to 0.5391)	0.4560 (0.2656 to 0.6280)	0.3438 (0.1879 to 0.5056)	
12 Months	0.6164 (0.4860 to 0.7228)	0.4582 (0.3213 to 0.5848)	0.4963 (0.3499 to 0.6266)	0.4208 (0.2974 to 0.5391)	0.4560 (0.2656 to 0.6280)	0.3008 (0.1508 to 0.4664)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_age_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.1 Treatment emergent adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0.6164 (0.4860 to 0.7228)	0.4582 (0.3213 to 0.5848)	0.4963 (0.3499 to 0.6266)	0.3927 (0.2675 to 0.5156)	0.4560 (0.2656 to 0.6280)	0.3008 (0.1508 to 0.4664)	
16 Months	0.6164 (0.4860 to 0.7228)	0.4582 (0.3213 to 0.5848)	0.4963 (0.3499 to 0.6266)	0.3927 (0.2675 to 0.5156)	0.4560 (0.2656 to 0.6280)	0.3008 (0.1508 to 0.4664)	
Number of patients at risk[b]							
2 Months	50	28	32	35	16	14	
4 Months	44	21	25	33	15	10	
6 Months	37	18	24	26	11	8	
8 Months	33	16	22	25	9	8	
10 Months	31	15	21	22	9	8	
12 Months	29	13	18	20	6	7	
14 Months	19	10	11	12	3	5	
16 Months	13	2	4	6	2	1	
Cardiac disorders (days)							
Number (%) of events	1 (1.5)	6 (11.1)	4 (7.5)	10 (15.2)	1 (3.6)	6 (18.8)	0.5034

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.13 Treatment emergent severe adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)							
Number (%) of events	23 (33.8)	29 (53.7)	22 (41.5)	36 (54.5)	15 (53.6)	22 (68.8)	0.5874
Number (%) of patients censored	45 (66.2)	25 (46.3)	31 (58.5)	30 (45.5)	13 (46.4)	10 (31.3)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	2.8255 (0.7885 to NC)	0.6242 (0.5585 to 0.8214)	0.7885 (0.5257 to 2.0370)	0.7556 (0.5257 to 0.8542)	0.6078 (0.1971 to 1.1170)	0.5257 (0.3614 to 0.8214)	
Median (95% CI)	NC (NC to NC)	2.1027 (0.8214 to NC)	NC (1.8398 to NC)	7.4908 (0.9528 to NC)	4.3039 (0.7556 to NC)	0.8871 (0.6899 to 10.4476)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.3655 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0113		0.2531		0.2972	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.13 Treatment emergent severe adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	2.01 (1.16 to 3.48)		1.36 (0.80 to 2.31)		1.42 (0.73 to 2.74)	
P-value	-	0.0130		0.2550		0.2996	
Hazard ratio inverted (95% CI) vs IPd	0.50 (0.29 to 0.86)						
Events probability (95% CI)[b]							
2 Months	0.7614 (0.6404 to 0.8464)	0.5364 (0.3954 to 0.6583)	0.6469 (0.4993 to 0.7610)	0.5544 (0.4259 to 0.6652)	0.5714 (0.3706 to 0.7295)	0.4375 (0.2646 to 0.5981)	
4 Months	0.7001 (0.5746 to 0.7950)	0.4582 (0.3213 to 0.5848)	0.5625 (0.4143 to 0.6869)	0.5236 (0.3962 to 0.6363)	0.5357 (0.3381 to 0.6982)	0.3438 (0.1879 to 0.5056)	
6 Months	0.6668 (0.5389 to 0.7667)	0.4582 (0.3213 to 0.5848)	0.5625 (0.4143 to 0.6869)	0.5082 (0.3815 to 0.6216)	0.4560 (0.2656 to 0.6280)	0.3438 (0.1879 to 0.5056)	
8 Months	0.6483 (0.5187 to 0.7511)	0.4582 (0.3213 to 0.5848)	0.5625 (0.4143 to 0.6869)	0.4900 (0.3635 to 0.6049)	0.4560 (0.2656 to 0.6280)	0.3438 (0.1879 to 0.5056)	
10 Months	0.6483 (0.5187 to 0.7511)	0.4582 (0.3213 to 0.5848)	0.5625 (0.4143 to 0.6869)	0.4524 (0.3265 to 0.5699)	0.4560 (0.2656 to 0.6280)	0.3438 (0.1879 to 0.5056)	
12 Months	0.6483 (0.5187 to 0.7511)	0.4582 (0.3213 to 0.5848)	0.5625 (0.4143 to 0.6869)	0.4524 (0.3265 to 0.5699)	0.4560 (0.2656 to 0.6280)	0.3008 (0.1508 to 0.4664)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_age_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.13 Treatment emergent severe adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0.6483 (0.5187 to 0.7511)	0.4582 (0.3213 to 0.5848)	0.5625 (0.4143 to 0.6869)	0.4222 (0.2929 to 0.5458)	0.4560 (0.2656 to 0.6280)	0.3008 (0.1508 to 0.4664)	
16 Months	0.6483 (0.5187 to 0.7511)	0.4582 (0.3213 to 0.5848)	0.5625 (0.4143 to 0.6869)	0.4222 (0.2929 to 0.5458)	0.4560 (0.2656 to 0.6280)	0.3008 (0.1508 to 0.4664)	
Number of patients at risk[b]							
2 Months	51	28	32	36	16	14	
4 Months	45	21	26	34	15	10	
6 Months	39	18	26	28	11	8	
8 Months	35	16	23	27	9	8	
10 Months	33	15	23	23	9	8	
12 Months	30	13	20	21	6	7	
14 Months	20	10	12	12	3	5	
16 Months	14	2	5	6	2	1	
Gastrointestinal disorders (days)							
Number (%) of events	1 (1.5)	4 (7.4)	2 (3.8)	2 (3.0)	0 (0.0)	3 (9.4)	0.4489

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_age_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.1 Treatment emergent adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	45 (45.0)	55 (54.5)	20 (40.8)	34 (66.7)	0.2593
Number (%) of patients censored	55 (55.0)	46 (45.5)	29 (59.2)	17 (33.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.9199 (0.7228 to 2.5626)	0.6899 (0.5585 to 0.8214)	1.4456 (0.5914 to 4.3039)	0.5914 (0.5257 to 0.7885)	
Median (95% CI)	NC (3.3840 to NC)	2.7926 (0.9199 to NC)	NC (2.8255 to NC)	1.9384 (0.7885 to 4.2053)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.2053 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1308		0.0111	
Hazard ratio (95% CI) vs Pd	-	1.35 (0.91 to 2.01)		2.02 (1.16 to 3.52)	
P-value	-	0.1322		0.0128	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_plne_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.1 Treatment emergent adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.49 (0.28 to 0.86)		
Events probability (95% CI)[b]					
2 Months	0.6735 (0.5710 to 0.7567)	0.5303 (0.4281 to 0.6223)	0.6881 (0.5369 to 0.7988)	0.4894 (0.3470 to 0.6173)	
4 Months	0.5879 (0.4830 to 0.6786)	0.4796 (0.3790 to 0.5733)	0.6457 (0.4933 to 0.7628)	0.4078 (0.2725 to 0.5386)	
6 Months	0.5418 (0.4363 to 0.6358)	0.4796 (0.3790 to 0.5733)	0.6019 (0.4490 to 0.7248)	0.3671 (0.2368 to 0.4979)	
8 Months	0.5297 (0.4242 to 0.6245)	0.4667 (0.3658 to 0.5613)	0.6019 (0.4490 to 0.7248)	0.3671 (0.2368 to 0.4979)	
10 Months	0.5297 (0.4242 to 0.6245)	0.4392 (0.3380 to 0.5358)	0.5733 (0.4179 to 0.7013)	0.3671 (0.2368 to 0.4979)	
12 Months	0.5297 (0.4242 to 0.6245)	0.4392 (0.3380 to 0.5358)	0.5733 (0.4179 to 0.7013)	0.3388 (0.2100 to 0.4721)	
14 Months	0.5297 (0.4242 to 0.6245)	0.4392 (0.3380 to 0.5358)	0.5733 (0.4179 to 0.7013)	0.2904 (0.1572 to 0.4377)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_plne_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.1 Treatment emergent adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5297 (0.4242 to 0.6245)	0.4392 (0.3380 to 0.5358)	0.5733 (0.4179 to 0.7013)	0.2904 (0.1572 to 0.4377)	
Number of patients at risk[b]					
2 Months	65	53	33	24	
4 Months	54	44	30	20	
6 Months	47	37	25	15	
8 Months	43	36	21	13	
10 Months	43	32	18	13	
12 Months	36	30	17	10	
14 Months	21	21	12	6	
16 Months	12	9	7	0	
Cardiac disorders (days)					
Number (%) of events	5 (5.0)	14 (13.9)	1 (2.0)	8 (15.7)	0.4051
Number (%) of patients censored	95 (95.0)	87 (86.1)	48 (98.0)	43 (84.3)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.10 Treatment emergent severe adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	42 (42.0)	54 (53.5)	18 (36.7)	33 (64.7)	0.2513
Number (%) of patients censored	58 (58.0)	47 (46.5)	31 (63.3)	18 (35.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.9199 (0.7228 to 2.8255)	0.7228 (0.5585 to 0.8214)	1.4456 (0.5914 to 4.3039)	0.5914 (0.5257 to 0.7885)	
Median (95% CI)	NC (4.6653 to NC)	2.7926 (0.9199 to NC)	NC (2.8255 to NC)	1.9384 (0.7885 to 10.4476)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.4476 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0886		0.0078	
Hazard ratio (95% CI) vs Pd	-	1.42 (0.95 to 2.12)		2.15 (1.21 to 3.82)	
P-value	-	0.0902		0.0094	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.10 Treatment emergent severe adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.47 (0.26 to 0.83)		
Events probability (95% CI)[b]					
2 Months	0.6839 (0.5818 to 0.7660)	0.5403 (0.4379 to 0.6319)	0.6881 (0.5369 to 0.7988)	0.4894 (0.3470 to 0.6173)	
4 Months	0.6088 (0.5041 to 0.6980)	0.4897 (0.3886 to 0.5831)	0.6457 (0.4933 to 0.7628)	0.4078 (0.2725 to 0.5386)	
6 Months	0.5744 (0.4688 to 0.6664)	0.4897 (0.3886 to 0.5831)	0.6242 (0.4716 to 0.7442)	0.3875 (0.2545 to 0.5184)	
8 Months	0.5624 (0.4566 to 0.6554)	0.4768 (0.3755 to 0.5712)	0.6242 (0.4716 to 0.7442)	0.3875 (0.2545 to 0.5184)	
10 Months	0.5624 (0.4566 to 0.6554)	0.4495 (0.3478 to 0.5459)	0.6242 (0.4716 to 0.7442)	0.3875 (0.2545 to 0.5184)	
12 Months	0.5624 (0.4566 to 0.6554)	0.4495 (0.3478 to 0.5459)	0.6242 (0.4716 to 0.7442)	0.3576 (0.2253 to 0.4919)	
14 Months	0.5624 (0.4566 to 0.6554)	0.4495 (0.3478 to 0.5459)	0.6242 (0.4716 to 0.7442)	0.3066 (0.1678 to 0.4569)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_plne_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.10 Treatment emergent severe adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5624 (0.4566 to 0.6554)	0.4495 (0.3478 to 0.5459)	0.6242 (0.4716 to 0.7442)	0.3066 (0.1678 to 0.4569)	
Number of patients at risk[b]					
2 Months	66	54	33	24	
4 Months	56	45	30	20	
6 Months	50	38	26	16	
8 Months	45	37	22	14	
10 Months	45	33	20	13	
12 Months	37	31	19	10	
14 Months	22	21	13	6	
16 Months	13	9	8	0	
Gastrointestinal disorders (days)					
Number (%) of events	1 (1.0)	5 (5.0)	2 (4.1)	4 (7.8)	0.4927
Number (%) of patients censored	99 (99.0)	96 (95.0)	47 (95.9)	47 (92.2)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.1 Treatment emergent adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	25 (36.8)	46 (52.3)	40 (49.4)	43 (67.2)	0.7244
Number (%) of patients censored	43 (63.2)	42 (47.7)	41 (50.6)	21 (32.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.9384 (0.8871 to 5.0267)	0.6899 (0.5585 to 0.8542)	0.7556 (0.5257 to 1.1499)	0.6407 (0.5257 to 0.7885)	
Median (95% CI)	NC (8.6078 to NC)	4.2053 (1.0185 to NC)	4.9938 (2.0370 to NC)	0.9363 (0.7885 to 3.3183)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.4908 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0253		0.0548	
Hazard ratio (95% CI) vs Pd	-	1.73 (1.06 to 2.82)		1.52 (0.99 to 2.34)	
P-value	-	0.0271		0.0565	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.1 Treatment emergent adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.58 (0.35 to 0.94)				
Events probability (95% CI)[b]					
2 Months	0.7464 (0.6242 to 0.8340)	0.5747 (0.4641 to 0.6706)	0.6205 (0.5040 to 0.7173)	0.4375 (0.3145 to 0.5539)	
4 Months	0.6690 (0.5419 to 0.7682)	0.5153 (0.4055 to 0.6145)	0.5548 (0.4380 to 0.6567)	0.3743 (0.2575 to 0.4909)	
6 Months	0.6355 (0.5067 to 0.7392)	0.4914 (0.3822 to 0.5915)	0.4986 (0.3824 to 0.6041)	0.3743 (0.2575 to 0.4909)	
8 Months	0.6355 (0.5067 to 0.7392)	0.4914 (0.3822 to 0.5915)	0.4819 (0.3656 to 0.5889)	0.3510 (0.2344 to 0.4697)	
10 Months	0.6179 (0.4881 to 0.7238)	0.4607 (0.3511 to 0.5633)	0.4819 (0.3656 to 0.5889)	0.3510 (0.2344 to 0.4697)	
12 Months	0.6179 (0.4881 to 0.7238)	0.4607 (0.3511 to 0.5633)	0.4819 (0.3656 to 0.5889)	0.3276 (0.2120 to 0.4479)	
14 Months	0.6179 (0.4881 to 0.7238)	0.4607 (0.3511 to 0.5633)	0.4819 (0.3656 to 0.5889)	0.2866 (0.1665 to 0.4185)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.1 Treatment emergent adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.6179 (0.4881 to 0.7238)	0.4607 (0.3511 to 0.5633)	0.4819 (0.3656 to 0.5889)	0.2866 (0.1665 to 0.4185)	
Number of patients at risk[b]					
2 Months	50	49	48	28	
4 Months	43	43	41	21	
6 Months	38	35	34	17	
8 Months	36	34	28	15	
10 Months	33	30	28	15	
12 Months	27	27	26	13	
14 Months	18	20	15	7	
16 Months	12	7	7	2	
Cardiac disorders (days)					
Number (%) of events	3 (4.4)	13 (14.8)	3 (3.7)	9 (14.1)	0.9471
Number (%) of patients censored	65 (95.6)	75 (85.2)	78 (96.3)	55 (85.9)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.13 Treatment emergent severe adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	23 (33.8)	45 (51.1)	37 (45.7)	42 (65.6)	0.6952
Number (%) of patients censored	45 (66.2)	43 (48.9)	44 (54.3)	22 (34.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.9384 (0.8871 to NC)	0.6899 (0.5585 to 0.8542)	0.7556 (0.5257 to 1.4456)	0.6407 (0.5257 to 0.7885)	
Median (95% CI)	NC (NC to NC)	9.1663 (1.0185 to NC)	NC (2.8255 to NC)	0.9692 (0.8214 to 7.4908)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.4908 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0164		0.0394	
Hazard ratio (95% CI) vs Pd	-	1.83 (1.11 to 3.03)		1.59 (1.02 to 2.47)	
P-value	-	0.0181		0.0412	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.13 Treatment emergent severe adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.55 (0.33 to 0.90)		0.63 (0.40 to 0.98)		
Events probability (95% CI)[b]					
2 Months	0.7464 (0.6242 to 0.8340)	0.5747 (0.4641 to 0.6706)	0.6335 (0.5171 to 0.7290)	0.4531 (0.3289 to 0.5693)	
4 Months	0.6690 (0.5419 to 0.7682)	0.5153 (0.4055 to 0.6145)	0.5809 (0.4640 to 0.6811)	0.3900 (0.2714 to 0.5067)	
6 Months	0.6522 (0.5242 to 0.7537)	0.5033 (0.3938 to 0.6031)	0.5387 (0.4216 to 0.6422)	0.3900 (0.2714 to 0.5067)	
8 Months	0.6522 (0.5242 to 0.7537)	0.5033 (0.3938 to 0.6031)	0.5224 (0.4048 to 0.6274)	0.3671 (0.2487 to 0.4859)	
10 Months	0.6522 (0.5242 to 0.7537)	0.4728 (0.3627 to 0.5751)	0.5224 (0.4048 to 0.6274)	0.3671 (0.2487 to 0.4859)	
12 Months	0.6522 (0.5242 to 0.7537)	0.4728 (0.3627 to 0.5751)	0.5224 (0.4048 to 0.6274)	0.3441 (0.2266 to 0.4646)	
14 Months	0.6522 (0.5242 to 0.7537)	0.4728 (0.3627 to 0.5751)	0.5224 (0.4048 to 0.6274)	0.3011 (0.1772 to 0.4350)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.13 Treatment emergent severe adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.6522 (0.5242 to 0.7537)	0.4728 (0.3627 to 0.5751)	0.5224 (0.4048 to 0.6274)	0.3011 (0.1772 to 0.4350)	
Number of patients at risk[b]					
2 Months	50	49	49	29	
4 Months	43	43	43	22	
6 Months	39	36	37	18	
8 Months	37	35	30	16	
10 Months	35	30	30	16	
12 Months	28	27	28	14	
14 Months	19	20	16	7	
16 Months	13	7	8	2	
Gastrointestinal disorders (days)					
Number (%) of events	2 (2.9)	5 (5.7)	1 (1.2)	4 (6.3)	0.5095
Number (%) of patients censored	66 (97.1)	83 (94.3)	80 (98.8)	60 (93.8)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_sex_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.1 Treatment emergent adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	55 (45.1)	66 (56.9)	7 (36.8)	18 (75.0)	0.1253
Number (%) of patients censored	67 (54.9)	50 (43.1)	12 (63.2)	6 (25.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.8214 (0.7228 to 1.5770)	0.6242 (0.5257 to 0.7885)	1.9384 (0.5257 to NC)	0.6571 (0.2300 to 0.8542)	
Median (95% CI)	NC (3.3840 to NC)	2.6283 (0.8542 to NC)	NC (1.9384 to NC)	1.4456 (0.7228 to 9.3306)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	10.4476 (2.7926 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0594		0.0060	
Hazard ratio (95% CI) vs Pd	-	1.41 (0.98 to 2.02)		3.22 (1.33 to 7.75)	
P-value	-	0.0606		0.0093	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_race_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.1 Treatment emergent adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.31 (0.13 to 0.75)		
Events probability (95% CI)[b]					
2 Months	0.6667 (0.5746 to 0.7432)	0.5172 (0.4229 to 0.6035)	0.7368 (0.4789 to 0.8810)	0.4545 (0.2515 to 0.6374)	
4 Months	0.5798 (0.4856 to 0.6627)	0.4734 (0.3802 to 0.5608)	0.7368 (0.4789 to 0.8810)	0.3182 (0.1447 to 0.5075)	
6 Months	0.5423 (0.4477 to 0.6276)	0.4552 (0.3626 to 0.5430)	0.6842 (0.4279 to 0.8439)	0.3182 (0.1447 to 0.5075)	
8 Months	0.5423 (0.4477 to 0.6276)	0.4443 (0.3518 to 0.5327)	0.6272 (0.3725 to 0.8022)	0.3182 (0.1447 to 0.5075)	
10 Months	0.5315 (0.4365 to 0.6176)	0.4326 (0.3400 to 0.5217)	0.6272 (0.3725 to 0.8022)	0.2727 (0.1132 to 0.4608)	
12 Months	0.5315 (0.4365 to 0.6176)	0.4326 (0.3400 to 0.5217)	0.6272 (0.3725 to 0.8022)	0.2273 (0.0841 to 0.4121)	
14 Months	0.5315 (0.4365 to 0.6176)	0.4166 (0.3226 to 0.5078)	0.6272 (0.3725 to 0.8022)	0.2273 (0.0841 to 0.4121)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.1 Treatment emergent adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5315 (0.4365 to 0.6176)	0.4166 (0.3226 to 0.5078)	0.6272 (0.3725 to 0.8022)	0.2273 (0.0841 to 0.4121)	
Number of patients at risk[b]					
2 Months	79	60	14	10	
4 Months	66	52	14	7	
6 Months	56	43	13	7	
8 Months	50	40	11	7	
10 Months	47	37	11	6	
12 Months	43	35	8	3	
14 Months	28	23	3	2	
16 Months	16	9	1	0	
Cardiac disorders (days)					
Number (%) of events	6 (4.9)	18 (15.5)	0 (0.0)	4 (16.7)	0.9914
Number (%) of patients censored	116 (95.1)	98 (84.5)	19 (100.0)	20 (83.3)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.11 Treatment emergent severe adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	51 (41.8)	64 (55.2)	7 (36.8)	18 (75.0)	0.1570
Number (%) of patients censored	71 (58.2)	52 (44.8)	12 (63.2)	6 (25.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.8214 (0.7228 to 2.0370)	0.6242 (0.5257 to 0.7885)	1.9384 (0.5257 to NC)	0.6571 (0.2300 to 0.8542)	
Median (95% CI)	NC (4.3039 to NC)	2.8912 (0.8542 to NC)	NC (1.9384 to NC)	1.4456 (0.7228 to 9.3306)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	10.4476 (2.7926 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0412		0.0060	
Hazard ratio (95% CI) vs Pd	-	1.46 (1.01 to 2.12)		3.22 (1.33 to 7.75)	
P-value	-	0.0425		0.0093	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_race_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.11 Treatment emergent severe adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.68 (0.47 to 0.99)		0.31 (0.13 to 0.75)		
Events probability (95% CI)[b]					
2 Months	0.6751 (0.5834 to 0.7509)	0.5259 (0.4313 to 0.6119)	0.7368 (0.4789 to 0.8810)	0.4545 (0.2515 to 0.6374)	
4 Months	0.5969 (0.5029 to 0.6789)	0.4820 (0.3885 to 0.5693)	0.7368 (0.4789 to 0.8810)	0.3182 (0.1447 to 0.5075)	
6 Months	0.5689 (0.4743 to 0.6528)	0.4729 (0.3797 to 0.5604)	0.6842 (0.4279 to 0.8439)	0.3182 (0.1447 to 0.5075)	
8 Months	0.5689 (0.4743 to 0.6528)	0.4622 (0.3689 to 0.5503)	0.6272 (0.3725 to 0.8022)	0.3182 (0.1447 to 0.5075)	
10 Months	0.5689 (0.4743 to 0.6528)	0.4506 (0.3572 to 0.5394)	0.6272 (0.3725 to 0.8022)	0.2727 (0.1132 to 0.4608)	
12 Months	0.5689 (0.4743 to 0.6528)	0.4506 (0.3572 to 0.5394)	0.6272 (0.3725 to 0.8022)	0.2273 (0.0841 to 0.4121)	
14 Months	0.5689 (0.4743 to 0.6528)	0.4339 (0.3387 to 0.5253)	0.6272 (0.3725 to 0.8022)	0.2273 (0.0841 to 0.4121)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.11 Treatment emergent severe adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5689 (0.4743 to 0.6528)	0.4339 (0.3387 to 0.5253)	0.6272 (0.3725 to 0.8022)	0.2273 (0.0841 to 0.4121)	
Number of patients at risk[b]					
2 Months	80	61	14	10	
4 Months	68	53	14	7	
6 Months	59	45	13	7	
8 Months	52	42	11	7	
10 Months	50	38	11	6	
12 Months	46	36	8	3	
14 Months	30	23	3	2	
16 Months	18	9	1	0	
Gastrointestinal disorders (days)					
Number (%) of events	2 (1.6)	8 (6.9)	1 (5.3)	0 (0.0)	0.9935
Number (%) of patients censored	120 (98.4)	108 (93.1)	18 (94.7)	24 (100.0)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_race_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.1 Treatment emergent adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	1 (33.3)	2 (50.0)	58 (44.6)	76 (59.4)	0.9491
Number (%) of patients censored	2 (66.7)	2 (50.0)	72 (55.4)	52 (40.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	5.0267 (NC to NC)	0.6078 (0.4271 to NC)	0.9199 (0.7556 to 1.9384)	0.6242 (0.5585 to 0.7556)	
Median (95% CI)	5.0267 (NC to NC)	NC (0.4271 to NC)	NC (4.3039 to NC)	2.3655 (0.8542 to 9.3306)	
75% quantile (95% CI)	5.0267 (NC to NC)	NC (0.4271 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9358		0.0114	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.10 to 12.24)		1.55 (1.10 to 2.18)	
P-value	-	0.9358		0.0121	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.1 Treatment emergent adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.65 (0.46 to 0.91)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.6739 (0.5855 to 0.7474)	0.5154 (0.4257 to 0.5979)	
4 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.5934 (0.5028 to 0.6729)	0.4590 (0.3707 to 0.5427)	
6 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.5596 (0.4686 to 0.6411)	0.4423 (0.3546 to 0.5263)	
8 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.5499 (0.4586 to 0.6321)	0.4325 (0.3448 to 0.5169)	
10 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.5401 (0.4485 to 0.6230)	0.4114 (0.3237 to 0.4968)	
12 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.5401 (0.4485 to 0.6230)	0.4008 (0.3133 to 0.4867)	
14 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.5401 (0.4485 to 0.6230)	0.3848 (0.2958 to 0.4729)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.1 Treatment emergent adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.5401 (0.4485 to 0.6230)	0.3848 (0.2958 to 0.4729)	
Number of patients at risk[b]					
2 Months	2	2	86	65	
4 Months	2	2	73	55	
6 Months	0	2	64	46	
8 Months	0	2	56	43	
10 Months	0	2	53	39	
12 Months	0	2	46	34	
14 Months	0	2	28	21	
16 Months	0	0	16	8	
Cardiac disorders (days)					
Number (%) of events	0 (0.0)	0 (0.0)	5 (3.8)	20 (15.6)	0.9995
Number (%) of patients censored	3 (100.0)	4 (100.0)	125 (96.2)	108 (84.4)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.4 Treatment emergent serious adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	0 (0.0)	1 (25.0)	9 (6.9)	14 (10.9)	0.9892
Number (%) of patients censored	3 (100.0)	3 (75.0)	121 (93.1)	114 (89.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.4271 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (0.4271 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.4271 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.2666	
Hazard ratio (95% CI) vs Pd	-	NC		1.60 (0.69 to 3.70)	
P-value	-	0.9985		0.2710	
Events probability (95% CI)[b]					

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.4 Treatment emergent serious adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9455 (0.8891 to 0.9737)	0.9063 (0.8408 to 0.9456)	
4 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9375 (0.8788 to 0.9682)	0.8901 (0.8215 to 0.9334)	
6 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9375 (0.8788 to 0.9682)	0.8901 (0.8215 to 0.9334)	
8 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9375 (0.8788 to 0.9682)	0.8901 (0.8215 to 0.9334)	
10 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9268 (0.8634 to 0.9614)	0.8901 (0.8215 to 0.9334)	
12 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9268 (0.8634 to 0.9614)	0.8901 (0.8215 to 0.9334)	
14 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9268 (0.8634 to 0.9614)	0.8901 (0.8215 to 0.9334)	
16 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9268 (0.8634 to 0.9614)	0.8901 (0.8215 to 0.9334)	

Number of patients at risk[b]

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_ethn_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.4 Treatment emergent serious adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	2	3	119	115	
4 Months	2	3	113	108	
6 Months	1	3	102	100	
8 Months	1	3	92	96	
10 Months	1	3	87	92	
12 Months	0	3	75	80	
14 Months	0	3	47	53	
16 Months	0	1	22	23	
General disorders and administration site conditions (days)					
Number (%) of events	1 (33.3)	1 (25.0)	10 (7.7)	13 (10.2)	0.3919
Number (%) of patients censored	2 (66.7)	3 (75.0)	120 (92.3)	115 (89.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.3614 (0.3614 to NC)	NC (9.7248 to NC)	NC (NC to NC)	NC (15.9671 to NC)	
Median (95% CI)	NC (0.3614 to NC)	NC (9.7248 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (0.3614 to NC)	NC (9.7248 to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_ethn_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.10 Treatment emergent severe adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	0 (0.0)	2 (50.0)	54 (41.5)	74 (57.8)	0.9825
Number (%) of patients censored	3 (100.0)	2 (50.0)	76 (58.5)	54 (42.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.6078 (0.4271 to NC)	0.9199 (0.7556 to 2.0370)	0.6242 (0.5585 to 0.7556)	
Median (95% CI)	NC (NC to NC)	NC (0.4271 to NC)	NC (4.9938 to NC)	2.7926 (0.8542 to 13.8645)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.4271 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2807		0.0073	
Hazard ratio (95% CI) vs Pd	-	NC		1.61 (1.13 to 2.29)	
P-value	-	0.9979		0.0078	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.10 Treatment emergent severe adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.62 (0.44 to 0.88)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.6817 (0.5937 to 0.7546)	0.5232 (0.4333 to 0.6055)	
4 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.6093 (0.5189 to 0.6878)	0.4668 (0.3782 to 0.5505)	
6 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.5840 (0.4931 to 0.6642)	0.4585 (0.3701 to 0.5423)	
8 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.5744 (0.4831 to 0.6554)	0.4487 (0.3604 to 0.5330)	
10 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.5744 (0.4831 to 0.6554)	0.4279 (0.3394 to 0.5132)	
12 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.5744 (0.4831 to 0.6554)	0.4172 (0.3287 to 0.5030)	
14 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.5744 (0.4831 to 0.6554)	0.4005 (0.3102 to 0.4890)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.10 Treatment emergent severe adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.5744 (0.4831 to 0.6554)	0.4005 (0.3102 to 0.4890)	
Number of patients at risk[b]					
2 Months	2	2	87	66	
4 Months	2	2	75	56	
6 Months	1	2	67	48	
8 Months	1	2	58	45	
10 Months	1	2	56	40	
12 Months	0	2	49	35	
14 Months	0	2	30	21	
16 Months	0	0	18	8	
Gastrointestinal disorders (days)					
Number (%) of events	0 (0.0)	0 (0.0)	3 (2.3)	6 (4.7)	0.9998
Number (%) of patients censored	3 (100.0)	4 (100.0)	127 (97.7)	122 (95.3)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Blood and lymphatic system disorders (days)											
Number (%) of events	26 (35.1)	28 (50.9)	11 (55.0)	17 (60.7)	3 (60.0)	5 (71.4)	7 (46.7)	15 (71.4)	18 (51.4)	24 (58.5)	0.8421
Number (%) of patients censored	48 (64.9)	27 (49.1)	9 (45.0)	11 (39.3)	2 (40.0)	2 (28.6)	8 (53.3)	6 (28.6)	17 (48.6)	17 (41.5)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	0.9528 (0.6242 to 4.9938)	0.6899 (0.5257 to 0.8214)	0.7556 (0.2628 to 2.8255)	0.7556 (0.2957 to 0.8542)	2.8255 (0.2957 to NC)	0.5585 (0.4271 to 0.8542)	1.8398 (0.5257 to 7.6222)	0.7228 (0.2300 to 0.8542)	0.7885 (0.5257 to 2.8255)	0.6242 (0.4928 to 0.8542)	
Median (95% CI)	NC (NC to NC)	9.1663 (0.8214 to NC)	3.0883 (0.7556 to NC)	1.6920 (0.7885 to NC)	5.0267 (0.2957 to NC)	0.8542 (0.4271 to NC)	NC (1.5441 to NC)	1.9055 (0.7228 to 10.4476)	8.6078 (1.5770 to NC)	3.3183 (0.7885 to NC)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.0883 to NC)	NC (3.2854 to NC)	NC (0.2957 to NC)	NC (0.6571 to NC)	NC (NC to NC)	NC (2.7926 to NC)	NC (NC to NC)	NC (13.8645 to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.0817		0.7183		0.5682		0.0772		0.4768	
Hazard ratio (95% CI) vs Pd	-	1.60 (0.94 to 2.73)		1.15 (0.54 to 2.46)		1.52 (0.36 to 6.47)		2.21 (0.90 to 5.44)		1.25 (0.68 to 2.30)	
P-value	-	0.0846		0.7186		0.5708		0.0850		0.4777	
Events probability (95% CI)[b]											

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
2 Months	0.7100 (0.5906 to 0.8004)	0.5189 (0.3789 to 0.6417)	0.5789 (0.3321 to 0.7626)	0.5000 (0.3064 to 0.6662)	0.8000 (0.2038 to 0.9692)	0.4286 (0.0978 to 0.7344)	0.6667 (0.3753 to 0.8456)	0.4714 (0.2513 to 0.6640)	0.6571 (0.4760 to 0.7886)	0.5610 (0.3971 to 0.6964)	
4 Months	0.6662 (0.5442 to 0.7625)	0.5003 (0.3615 to 0.6242)	0.4737 (0.2444 to 0.6728)	0.4256 (0.2422 to 0.5977)	0.6000 (0.1257 to 0.8818)	0.2857 (0.0411 to 0.6115)	0.6667 (0.3753 to 0.8456)	0.3667 (0.1686 to 0.5681)	0.5377 (0.3597 to 0.6862)	0.4878 (0.3292 to 0.6289)	
6 Months	0.6345 (0.5106 to 0.7349)	0.5003 (0.3615 to 0.6242)	0.4211 (0.2037 to 0.6249)	0.4256 (0.2422 to 0.5977)	0.4000 (0.0520 to 0.7528)	0.2857 (0.0411 to 0.6115)	0.6000 (0.3176 to 0.7965)	0.3667 (0.1686 to 0.5681)	0.5041 (0.3273 to 0.6569)	0.4390 (0.2856 to 0.5823)	
8 Months	0.6345 (0.5106 to 0.7349)	0.5003 (0.3615 to 0.6242)	0.4211 (0.2037 to 0.6249)	0.3783 (0.1998 to 0.5561)	0.4000 (0.0520 to 0.7528)	0.2857 (0.0411 to 0.6115)	0.5333 (0.2632 to 0.7438)	0.3667 (0.1686 to 0.5681)	0.5041 (0.3273 to 0.6569)	0.4390 (0.2856 to 0.5823)	
10 Months	0.6345 (0.5106 to 0.7349)	0.4740 (0.3341 to 0.6015)	0.4211 (0.2037 to 0.6249)	0.3783 (0.1998 to 0.5561)	0.4000 (0.0520 to 0.7528)	0.2857 (0.0411 to 0.6115)	0.5333 (0.2632 to 0.7438)	0.3143 (0.1314 to 0.5168)	0.4621 (0.2848 to 0.6221)	0.4390 (0.2856 to 0.5823)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
12 Months	0.6345 (0.5106 to 0.7349)	0.4740 (0.3341 to 0.6015)	0.4211 (0.2037 to 0.6249)	0.3783 (0.1998 to 0.5561)	0.4000 (0.0520 to 0.7528)	0.2857 (0.0411 to 0.6115)	0.5333 (0.2632 to 0.7438)	0.2619 (0.0972 to 0.4630)	0.4621 (0.2848 to 0.6221)	0.4390 (0.2856 to 0.5823)	
14 Months	0.6345 (0.5106 to 0.7349)	0.4740 (0.3341 to 0.6015)	0.4211 (0.2037 to 0.6249)	0.3783 (0.1998 to 0.5561)	0.4000 (0.0520 to 0.7528)	0.2857 (0.0411 to 0.6115)	0.5333 (0.2632 to 0.7438)	0.2619 (0.0972 to 0.4630)	0.4621 (0.2848 to 0.6221)	0.4024 (0.2489 to 0.5511)	
16 Months	0.6345 (0.5106 to 0.7349)	0.4740 (0.3341 to 0.6015)	0.4211 (0.2037 to 0.6249)	0.3783 (0.1998 to 0.5561)	0.4000 (0.0520 to 0.7528)	0.2857 (0.0411 to 0.6115)	0.5333 (0.2632 to 0.7438)	0.2619 (0.0972 to 0.4630)	0.4621 (0.2848 to 0.6221)	0.4024 (0.2489 to 0.5511)	
Number of patients at risk[b]											
2 Months	50	28	11	14	4	3	10	9	23	23	
4 Months	44	24	9	11	3	2	10	7	18	20	
6 Months	40	19	7	9	2	1	9	7	14	16	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
8 Months	35	19	7	7	2	1	8	7	12	15	
10 Months	35	18	7	6	2	1	8	6	9	14	
12 Months	31	16	7	6	1	1	6	3	8	14	
14 Months	22	11	4	4	0	0	2	2	5	10	
16 Months	12	3	2	1	0	0	1	0	4	5	
Cardiac disorders (days)											
Number (%) of events	3 (4.1)	5 (9.1)	2 (10.0)	3 (10.7)	1 (20.0)	2 (28.6)	0 (0.0)	3 (14.3)	0 (0.0)	9 (22.0)	0.9737
Number (%) of patients censored	71 (95.9)	50 (90.9)	18 (90.0)	25 (89.3)	4 (80.0)	5 (71.4)	15 (100.0)	18 (85.7)	35 (100.0)	32 (78.0)	
Kaplan-Meier estimates of event in months											

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.9 Treatment emergent severe adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Blood and lymphatic system disorders (days)											
Number (%) of events	25 (33.8)	28 (50.9)	11 (55.0)	17 (60.7)	2 (40.0)	4 (57.1)	7 (46.7)	15 (71.4)	15 (42.9)	23 (56.1)	0.8903
Number (%) of patients censored	49 (66.2)	27 (49.1)	9 (45.0)	11 (39.3)	3 (60.0)	3 (42.9)	8 (53.3)	6 (28.6)	20 (57.1)	18 (43.9)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	0.9528 (0.6242 to 4.9938)	0.6899 (0.5257 to 0.8214)	0.7556 (0.2628 to 2.8255)	0.7556 (0.2957 to 0.8542)	2.8255 (0.2957 to NC)	0.5585 (0.4271 to 2.9569)	1.8398 (0.5257 to 7.6222)	0.7228 (0.2300 to 0.8542)	0.7885 (0.5257 to 2.9569)	0.6242 (0.4928 to 0.8542)	
Median (95% CI)	NC (NC to NC)	9.1663 (0.8214 to NC)	3.0883 (0.7556 to NC)	1.6920 (0.7885 to NC)	NC (0.2957 to NC)	2.9569 (0.4271 to NC)	NC (1.5441 to NC)	1.9055 (0.7228 to 10.4476)	NC (2.8255 to NC)	3.3183 (0.7885 to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.9 Treatment emergent severe adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=35)**	**IPd (N=41)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.0883 to NC)	NC (3.2854 to NC)	NC (0.2957 to NC)	NC (0.8542 to NC)	NC (NC to NC)	NC (2.7926 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.0626		0.7183		0.6466		0.0772		0.2510	
Hazard ratio (95% CI) vs Pd	-	1.66 (0.97 to 2.85)		1.15 (0.54 to 2.46)		1.49 (0.27 to 8.16)		2.21 (0.90 to 5.44)		1.46 (0.76 to 2.80)	
P-value	-	0.0654		0.7186		0.6487		0.0850		0.2538	
Events probability (95% CI)[b]											

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.9 Treatment emergent severe adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
2 Months	0.7100 (0.5906 to 0.8004)	0.5189 (0.3789 to 0.6417)	0.5789 (0.3321 to 0.7626)	0.5000 (0.3064 to 0.6662)	0.8000 (0.2038 to 0.9692)	0.5714 (0.1719 to 0.8371)	0.6667 (0.3753 to 0.8456)	0.4714 (0.2513 to 0.6640)	0.6857 (0.5048 to 0.8120)	0.5610 (0.3971 to 0.6964)	
4 Months	0.6807 (0.5594 to 0.7752)	0.5003 (0.3615 to 0.6242)	0.4737 (0.2444 to 0.6728)	0.4256 (0.2422 to 0.5977)	0.6000 (0.1257 to 0.8818)	0.4286 (0.0978 to 0.7344)	0.6667 (0.3753 to 0.8456)	0.3667 (0.1686 to 0.5681)	0.5665 (0.3865 to 0.7119)	0.4878 (0.3292 to 0.6289)	
6 Months	0.6490 (0.5256 to 0.7479)	0.5003 (0.3615 to 0.6242)	0.4211 (0.2037 to 0.6249)	0.4256 (0.2422 to 0.5977)	0.6000 (0.1257 to 0.8818)	0.4286 (0.0978 to 0.7344)	0.6000 (0.3176 to 0.7965)	0.3667 (0.1686 to 0.5681)	0.5665 (0.3865 to 0.7119)	0.4634 (0.3072 to 0.6058)	
8 Months	0.6490 (0.5256 to 0.7479)	0.5003 (0.3615 to 0.6242)	0.4211 (0.2037 to 0.6249)	0.3783 (0.1998 to 0.5561)	0.6000 (0.1257 to 0.8818)	0.4286 (0.0978 to 0.7344)	0.5333 (0.2632 to 0.7438)	0.3667 (0.1686 to 0.5681)	0.5665 (0.3865 to 0.7119)	0.4634 (0.3072 to 0.6058)	
10 Months	0.6490 (0.5256 to 0.7479)	0.4740 (0.3341 to 0.6015)	0.4211 (0.2037 to 0.6249)	0.3783 (0.1998 to 0.5561)	0.6000 (0.1257 to 0.8818)	0.4286 (0.0978 to 0.7344)	0.5333 (0.2632 to 0.7438)	0.3143 (0.1314 to 0.5168)	0.5665 (0.3865 to 0.7119)	0.4634 (0.3072 to 0.6058)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.9 Treatment emergent severe adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
12 Months	0.6490 (0.5256 to 0.7479)	0.4740 (0.3341 to 0.6015)	0.4211 (0.2037 to 0.6249)	0.3783 (0.1998 to 0.5561)	0.6000 (0.1257 to 0.8818)	0.4286 (0.0978 to 0.7344)	0.5333 (0.2632 to 0.7438)	0.2619 (0.0972 to 0.4630)	0.5665 (0.3865 to 0.7119)	0.4634 (0.3072 to 0.6058)	
14 Months	0.6490 (0.5256 to 0.7479)	0.4740 (0.3341 to 0.6015)	0.4211 (0.2037 to 0.6249)	0.3783 (0.1998 to 0.5561)	0.6000 (0.1257 to 0.8818)	0.4286 (0.0978 to 0.7344)	0.5333 (0.2632 to 0.7438)	0.2619 (0.0972 to 0.4630)	0.5665 (0.3865 to 0.7119)	0.4248 (0.2670 to 0.5740)	
16 Months	0.6490 (0.5256 to 0.7479)	0.4740 (0.3341 to 0.6015)	0.4211 (0.2037 to 0.6249)	0.3783 (0.1998 to 0.5561)	0.6000 (0.1257 to 0.8818)	0.4286 (0.0978 to 0.7344)	0.5333 (0.2632 to 0.7438)	0.2619 (0.0972 to 0.4630)	0.5665 (0.3865 to 0.7119)	0.4248 (0.2670 to 0.5740)	
Number of patients at risk[b]											
2 Months	50	28	11	14	4	4	10	9	24	23	
4 Months	45	24	9	11	3	3	10	7	19	20	
6 Months	41	19	7	9	3	2	9	7	16	17	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.9 Treatment emergent severe adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
8 Months	35	19	7	7	3	2	8	7	14	16	
10 Months	35	18	7	6	3	2	8	6	12	14	
12 Months	31	16	7	6	1	2	6	3	11	14	
14 Months	22	11	4	4	0	0	2	2	7	10	
16 Months	12	3	2	1	0	0	1	0	6	5	
Gastrointestinal disorders (days)											
Number (%) of events	0 (0.0)	5 (9.1)	1 (5.0)	0 (0.0)	0 (0.0)	1 (14.3)	1 (6.7)	0 (0.0)	1 (2.9)	3 (7.3)	1.0000
Number (%) of patients censored	74 (100.0)	50 (90.9)	19 (95.0)	28 (100.0)	5 (100.0)	6 (85.7)	14 (93.3)	21 (100.0)	34 (97.1)	38 (92.7)	
Kaplan-Meier estimates of event in months											

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.1 Treatment emergent adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	33 (35.1)	42 (54.5)	32 (58.2)	47 (62.7)	0.1988
Number (%) of patients censored	61 (64.9)	35 (45.5)	23 (41.8)	28 (37.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.1170 (0.7228 to 4.9938)	0.6899 (0.5257 to 0.8214)	0.7885 (0.5585 to 1.5441)	0.6242 (0.5257 to 0.7885)	
Median (95% CI)	NC (NC to NC)	2.8912 (0.8542 to NC)	2.9569 (1.5441 to NC)	2.3655 (0.8542 to 9.3306)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.4476 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0118		0.4002	
Hazard ratio (95% CI) vs Pd	-	1.78 (1.13 to 2.82)		1.21 (0.77 to 1.90)	
P-value	-	0.0130		0.4009	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.1 Treatment emergent adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.56 (0.35 to 0.89)				
Events probability (95% CI)[b]					
2 Months	0.7404 (0.6381 to 0.8179)	0.5267 (0.4090 to 0.6314)	0.5743 (0.4321 to 0.6931)	0.5063 (0.3885 to 0.6126)	
4 Months	0.6837 (0.5777 to 0.7685)	0.4740 (0.3587 to 0.5807)	0.4786 (0.3405 to 0.6041)	0.4363 (0.3220 to 0.5450)	
6 Months	0.6349 (0.5261 to 0.7252)	0.4740 (0.3587 to 0.5807)	0.4394 (0.3043 to 0.5665)	0.4082 (0.2959 to 0.5172)	
8 Months	0.6349 (0.5261 to 0.7252)	0.4740 (0.3587 to 0.5807)	0.4185 (0.2849 to 0.5465)	0.3925 (0.2811 to 0.5020)	
10 Months	0.6349 (0.5261 to 0.7252)	0.4551 (0.3391 to 0.5638)	0.3976 (0.2658 to 0.5262)	0.3746 (0.2639 to 0.4851)	
12 Months	0.6349 (0.5261 to 0.7252)	0.4551 (0.3391 to 0.5638)	0.3976 (0.2658 to 0.5262)	0.3568 (0.2470 to 0.4679)	
14 Months	0.6349 (0.5261 to 0.7252)	0.4298 (0.3110 to 0.5431)	0.3976 (0.2658 to 0.5262)	0.3568 (0.2470 to 0.4679)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.1 Treatment emergent adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.6349 (0.5261 to 0.7252)	0.4298 (0.3110 to 0.5431)	0.3976 (0.2658 to 0.5262)	0.3568 (0.2470 to 0.4679)	
Number of patients at risk[b]					
2 Months	67	40	31	37	
4 Months	59	33	25	31	
6 Months	51	26	21	26	
8 Months	44	25	20	24	
10 Months	42	24	19	21	
12 Months	37	22	16	18	
14 Months	25	15	8	12	
16 Months	14	4	5	5	
Cardiac disorders (days)					
Number (%) of events	4 (4.3)	10 (13.0)	2 (3.6)	12 (16.0)	0.7206
Number (%) of patients censored	90 (95.7)	67 (87.0)	53 (96.4)	63 (84.0)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.10 Treatment emergent severe adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	30 (31.9)	41 (53.2)	30 (54.5)	46 (61.3)	0.2083
Number (%) of patients censored	64 (68.1)	36 (46.8)	25 (45.5)	29 (38.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.1170 (0.7228 to NC)	0.6899 (0.5257 to 0.8214)	0.7885 (0.5585 to 1.5770)	0.6242 (0.5257 to 0.7885)	
Median (95% CI)	NC (NC to NC)	2.9569 (0.9199 to NC)	3.0883 (1.5770 to NC)	2.3655 (0.8542 to 9.3306)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0076		0.2981	
Hazard ratio (95% CI) vs Pd	-	1.88 (1.17 to 3.02)		1.28 (0.81 to 2.02)	
P-value	-	0.0086		0.2993	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.10 Treatment emergent severe adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.53 (0.33 to 0.85)				
Events probability (95% CI)[b]					
2 Months	0.7404 (0.6381 to 0.8179)	0.5399 (0.4218 to 0.6439)	0.5928 (0.4502 to 0.7099)	0.5063 (0.3885 to 0.6126)	
4 Months	0.6950 (0.5895 to 0.7784)	0.4872 (0.3712 to 0.5935)	0.4972 (0.3578 to 0.6218)	0.4363 (0.3220 to 0.5450)	
6 Months	0.6706 (0.5634 to 0.7571)	0.4872 (0.3712 to 0.5935)	0.4581 (0.3213 to 0.5847)	0.4223 (0.3089 to 0.5312)	
8 Months	0.6706 (0.5634 to 0.7571)	0.4872 (0.3712 to 0.5935)	0.4373 (0.3018 to 0.5649)	0.4066 (0.2940 to 0.5161)	
10 Months	0.6706 (0.5634 to 0.7571)	0.4685 (0.3517 to 0.5768)	0.4373 (0.3018 to 0.5649)	0.3889 (0.2769 to 0.4994)	
12 Months	0.6706 (0.5634 to 0.7571)	0.4685 (0.3517 to 0.5768)	0.4373 (0.3018 to 0.5649)	0.3704 (0.2590 to 0.4819)	
14 Months	0.6706 (0.5634 to 0.7571)	0.4424 (0.3223 to 0.5558)	0.4373 (0.3018 to 0.5649)	0.3704 (0.2590 to 0.4819)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_rreg_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.10 Treatment emergent severe adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.6706 (0.5634 to 0.7571)	0.4424 (0.3223 to 0.5558)	0.4373 (0.3018 to 0.5649)	0.3704 (0.2590 to 0.4819)	
Number of patients at risk[b]					
2 Months	67	41	32	37	
4 Months	60	34	26	31	
6 Months	54	27	22	27	
8 Months	46	26	21	25	
10 Months	44	25	21	21	
12 Months	38	23	18	18	
14 Months	25	15	10	12	
16 Months	14	4	7	5	
Gastrointestinal disorders (days)					
Number (%) of events	0 (0.0)	9 (11.7)	3 (5.5)	0 (0.0)	0.9926
Number (%) of patients censored	94 (100.0)	68 (88.3)	52 (94.5)	75 (100.0)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_rreg_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.1 Treatment emergent adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	58 (43.0)	80 (58.8)	7 (50.0)	9 (56.3)	0.6563
Number (%) of patients censored	77 (57.0)	56 (41.2)	7 (50.0)	7 (43.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.9856 (0.7885 to 2.8255)	0.6735 (0.5585 to 0.7885)	0.5257 (0.1643 to 1.8398)	0.5257 (0.0986 to 0.7885)	
Median (95% CI)	NC (4.9938 to NC)	2.3655 (0.9528 to 10.4476)	NC (0.4928 to NC)	0.8214 (0.5257 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.8398 to NC)	NC (0.8214 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0064		0.7098	
Hazard ratio (95% CI) vs Pd	-	1.59 (1.14 to 2.24)		1.21 (0.45 to 3.25)	
P-value	-	0.0069		0.7102	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_ecog_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.1 Treatment emergent adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.63 (0.45 to 0.88)				
Events probability (95% CI)[b]					
2 Months	0.6972 (0.6109 to 0.7679)	0.5218 (0.4346 to 0.6017)	0.5000 (0.2286 to 0.7221)	0.4688 (0.2137 to 0.6893)	
4 Months	0.6182 (0.5290 to 0.6954)	0.4537 (0.3683 to 0.5352)	0.5000 (0.2286 to 0.7221)	0.4688 (0.2137 to 0.6893)	
6 Months	0.5679 (0.4776 to 0.6485)	0.4381 (0.3532 to 0.5197)	0.5000 (0.2286 to 0.7221)	0.4688 (0.2137 to 0.6893)	
8 Months	0.5585 (0.4678 to 0.6397)	0.4288 (0.3439 to 0.5108)	0.5000 (0.2286 to 0.7221)	0.4688 (0.2137 to 0.6893)	
10 Months	0.5488 (0.4579 to 0.6308)	0.4188 (0.3339 to 0.5013)	0.5000 (0.2286 to 0.7221)	0.3516 (0.1100 to 0.6095)	
12 Months	0.5488 (0.4579 to 0.6308)	0.4088 (0.3240 to 0.4917)	0.5000 (0.2286 to 0.7221)	0.3516 (0.1100 to 0.6095)	
14 Months	0.5488 (0.4579 to 0.6308)	0.3952 (0.3094 to 0.4797)	0.5000 (0.2286 to 0.7221)	0.3516 (0.1100 to 0.6095)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.1 Treatment emergent adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5488 (0.4579 to 0.6308)	0.3952 (0.3094 to 0.4797)	0.5000 (0.2286 to 0.7221)	0.3516 (0.1100 to 0.6095)	
Number of patients at risk[b]					
2 Months	91	70	7	7	
4 Months	77	58	7	6	
6 Months	66	48	6	4	
8 Months	58	45	6	4	
10 Months	55	42	6	3	
12 Months	49	37	4	3	
14 Months	30	26	3	1	
16 Months	16	9	3	0	
Cardiac disorders (days)					
Number (%) of events	6 (4.4)	20 (14.7)	0 (0.0)	2 (12.5)	0.9898
Number (%) of patients censored	129 (95.6)	116 (85.3)	14 (100.0)	14 (87.5)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.10 Treatment emergent severe adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	53 (39.3)	78 (57.4)	7 (50.0)	9 (56.3)	0.5715
Number (%) of patients censored	82 (60.7)	58 (42.6)	7 (50.0)	7 (43.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.1170 (0.7885 to 2.8255)	0.6899 (0.5585 to 0.7885)	0.5257 (0.1643 to 1.8398)	0.5257 (0.0986 to 0.7885)	
Median (95% CI)	NC (NC to NC)	2.7926 (0.9856 to 13.8645)	NC (0.4928 to NC)	0.8214 (0.5257 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.8398 to NC)	NC (0.8214 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0029		0.7098	
Hazard ratio (95% CI) vs Pd	-	1.69 (1.19 to 2.40)		1.21 (0.45 to 3.25)	
P-value	-	0.0033		0.7102	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.10 Treatment emergent severe adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.59 (0.42 to 0.84)				
Events probability (95% CI)[b]					
2 Months	0.7048 (0.6190 to 0.7748)	0.5291 (0.4419 to 0.6089)	0.5000 (0.2286 to 0.7221)	0.4688 (0.2137 to 0.6893)	
4 Months	0.6337 (0.5449 to 0.7099)	0.4611 (0.3754 to 0.5425)	0.5000 (0.2286 to 0.7221)	0.4688 (0.2137 to 0.6893)	
6 Months	0.6004 (0.5104 to 0.6790)	0.4533 (0.3678 to 0.5348)	0.5000 (0.2286 to 0.7221)	0.4688 (0.2137 to 0.6893)	
8 Months	0.5910 (0.5006 to 0.6704)	0.4441 (0.3586 to 0.5259)	0.5000 (0.2286 to 0.7221)	0.4688 (0.2137 to 0.6893)	
10 Months	0.5910 (0.5006 to 0.6704)	0.4342 (0.3486 to 0.5166)	0.5000 (0.2286 to 0.7221)	0.3516 (0.1100 to 0.6095)	
12 Months	0.5910 (0.5006 to 0.6704)	0.4241 (0.3385 to 0.5070)	0.5000 (0.2286 to 0.7221)	0.3516 (0.1100 to 0.6095)	
14 Months	0.5910 (0.5006 to 0.6704)	0.4100 (0.3231 to 0.4947)	0.5000 (0.2286 to 0.7221)	0.3516 (0.1100 to 0.6095)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.10 Treatment emergent severe adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5910 (0.5006 to 0.6704)	0.4100 (0.3231 to 0.4947)	0.5000 (0.2286 to 0.7221)	0.3516 (0.1100 to 0.6095)	
Number of patients at risk[b]					
2 Months	92	71	7	7	
4 Months	79	59	7	6	
6 Months	70	50	6	4	
8 Months	61	47	6	4	
10 Months	59	43	6	3	
12 Months	52	38	4	3	
14 Months	32	26	3	1	
16 Months	18	9	3	0	
Gastrointestinal disorders (days)					
Number (%) of events	2 (1.5)	9 (6.6)	1 (7.1)	0 (0.0)	0.9920
Number (%) of patients censored	133 (98.5)	127 (93.4)	13 (92.9)	16 (100.0)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.1 Treatment emergent adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)							
Number (%) of events	22 (43.1)	37 (58.7)	21 (38.2)	29 (54.7)	21 (52.5)	23 (69.7)	0.9542
Number (%) of patients censored	29 (56.9)	26 (41.3)	34 (61.8)	24 (45.3)	19 (47.5)	10 (30.3)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	0.8214 (0.7228 to 4.9938)	0.7228 (0.5257 to 0.8542)	1.9384 (0.5914 to 4.5010)	0.6571 (0.5257 to 0.8542)	0.7556 (0.3285 to 1.1170)	0.5585 (0.4271 to 0.7556)	
Median (95% CI)	NC (3.0883 to NC)	2.1027 (0.8542 to NC)	NC (4.5010 to NC)	2.9569 (0.8542 to NC)	3.3840 (0.9856 to NC)	0.8214 (0.5585 to 4.0411)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.3655 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0652		0.0555		0.2075	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.1 Treatment emergent adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	1.64 (0.96 to 2.78)		1.72 (0.98 to 3.02)		1.46 (0.81 to 2.64)	
P-value	-	0.0679		0.0585		0.2102	
Events probability (95% CI)[b]							
2 Months	0.6863 (0.5399 to 0.7946)	0.5079 (0.3792 to 0.6230)	0.7401 (0.6007 to 0.8371)	0.5472 (0.4045 to 0.6692)	0.5829 (0.4116 to 0.7202)	0.4384 (0.2653 to 0.5990)	
4 Months	0.6471 (0.4998 to 0.7609)	0.4603 (0.3345 to 0.5771)	0.6642 (0.5209 to 0.7736)	0.4870 (0.3468 to 0.6134)	0.4560 (0.2882 to 0.6092)	0.3392 (0.1828 to 0.5027)	
6 Months	0.6078 (0.4606 to 0.7263)	0.4603 (0.3345 to 0.5771)	0.6037 (0.4587 to 0.7212)	0.4649 (0.3255 to 0.5930)	0.4180 (0.2518 to 0.5760)	0.3053 (0.1563 to 0.4683)	
8 Months	0.5876 (0.4405 to 0.7083)	0.4403 (0.3148 to 0.5587)	0.6037 (0.4587 to 0.7212)	0.4649 (0.3255 to 0.5930)	0.4180 (0.2518 to 0.5760)	0.3053 (0.1563 to 0.4683)	
10 Months	0.5666 (0.4197 to 0.6896)	0.4183 (0.2929 to 0.5386)	0.6037 (0.4587 to 0.7212)	0.4376 (0.2978 to 0.5689)	0.4180 (0.2518 to 0.5760)	0.3053 (0.1563 to 0.4683)	
12 Months	0.5666 (0.4197 to 0.6896)	0.4183 (0.2929 to 0.5386)	0.6037 (0.4587 to 0.7212)	0.4376 (0.2978 to 0.5689)	0.4180 (0.2518 to 0.5760)	0.2617 (0.1207 to 0.4274)	
14 Months	0.5666 (0.4197 to 0.6896)	0.3834 (0.2535 to 0.5119)	0.6037 (0.4587 to 0.7212)	0.4376 (0.2978 to 0.5689)	0.4180 (0.2518 to 0.5760)	0.2617 (0.1207 to 0.4274)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.1 Treatment emergent adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5666 (0.4197 to 0.6896)	0.3834 (0.2535 to 0.5119)	0.6037 (0.4587 to 0.7212)	0.4376 (0.2978 to 0.5689)	0.4180 (0.2518 to 0.5760)	0.2617 (0.1207 to 0.4274)	
Number of patients at risk[b]							
2 Months	35	32	39	28	22	14	
4 Months	33	29	35	22	14	10	
6 Months	31	23	29	18	10	8	
8 Months	28	22	25	17	9	7	
10 Months	27	19	23	16	9	7	
12 Months	25	15	18	16	8	6	
14 Months	15	10	12	11	6	3	
16 Months	11	4	5	5	3	0	
Cardiac disorders (days)							
Number (%) of events	2 (3.9)	6 (9.5)	4 (7.3)	11 (20.8)	0 (0.0)	5 (15.2)	0.9828
Number (%) of patients censored	49 (96.1)	57 (90.5)	51 (92.7)	42 (79.2)	40 (100.0)	28 (84.8)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.9 Treatment emergent severe adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)							
Number (%) of events	20 (39.2)	37 (58.7)	18 (32.7)	28 (52.8)	21 (52.5)	22 (66.7)	0.7875
Number (%) of patients censored	31 (60.8)	26 (41.3)	37 (67.3)	25 (47.2)	19 (47.5)	11 (33.3)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	0.8214 (0.7228 to 4.9938)	0.7228 (0.5257 to 0.8542)	1.9384 (0.5914 to NC)	0.6899 (0.5257 to 0.9199)	0.7556 (0.3285 to 1.1170)	0.5585 (0.4271 to 0.7556)	
Median (95% CI)	NC (4.9938 to NC)	2.1027 (0.8542 to NC)	NC (NC to NC)	4.2053 (0.8542 to NC)	3.3840 (0.9856 to NC)	0.8214 (0.5585 to 10.4476)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.3655 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0303		0.0319		0.2772	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_seiss_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.9 Treatment emergent severe adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	1.81 (1.05 to 3.13)		1.89 (1.05 to 3.43)		1.39 (0.76 to 2.54)	
P-value	-	0.0328		0.0349		0.2794	
Hazard ratio inverted (95% CI) vs IPd	0.55 (0.32 to 0.95)		0.53 (0.29 to 0.96)				
Events probability (95% CI)[b]							
2 Months	0.7059 (0.5603 to 0.8110)	0.5079 (0.3792 to 0.6230)	0.7401 (0.6007 to 0.8371)	0.5660 (0.4227 to 0.6865)	0.5829 (0.4116 to 0.7202)	0.4384 (0.2653 to 0.5990)	
4 Months	0.6667 (0.5198 to 0.7778)	0.4603 (0.3345 to 0.5771)	0.6832 (0.5405 to 0.7898)	0.5060 (0.3645 to 0.6314)	0.4560 (0.2882 to 0.6092)	0.3392 (0.1828 to 0.5027)	
6 Months	0.6275 (0.4801 to 0.7437)	0.4603 (0.3345 to 0.5771)	0.6636 (0.5202 to 0.7732)	0.4840 (0.3432 to 0.6113)	0.4180 (0.2518 to 0.5760)	0.3392 (0.1828 to 0.5027)	
8 Months	0.6072 (0.4598 to 0.7259)	0.4403 (0.3148 to 0.5587)	0.6636 (0.5202 to 0.7732)	0.4840 (0.3432 to 0.6113)	0.4180 (0.2518 to 0.5760)	0.3392 (0.1828 to 0.5027)	
10 Months	0.6072 (0.4598 to 0.7259)	0.4183 (0.2929 to 0.5386)	0.6636 (0.5202 to 0.7732)	0.4571 (0.3157 to 0.5877)	0.4180 (0.2518 to 0.5760)	0.3392 (0.1828 to 0.5027)	
12 Months	0.6072 (0.4598 to 0.7259)	0.4183 (0.2929 to 0.5386)	0.6636 (0.5202 to 0.7732)	0.4571 (0.3157 to 0.5877)	0.4180 (0.2518 to 0.5760)	0.2908 (0.1398 to 0.4604)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_seiss_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.9 Treatment emergent severe adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0.6072 (0.4598 to 0.7259)	0.3834 (0.2535 to 0.5119)	0.6636 (0.5202 to 0.7732)	0.4571 (0.3157 to 0.5877)	0.4180 (0.2518 to 0.5760)	0.2908 (0.1398 to 0.4604)	
16 Months	0.6072 (0.4598 to 0.7259)	0.3834 (0.2535 to 0.5119)	0.6636 (0.5202 to 0.7732)	0.4571 (0.3157 to 0.5877)	0.4180 (0.2518 to 0.5760)	0.2908 (0.1398 to 0.4604)	
Number of patients at risk[b]							
2 Months	36	32	39	29	22	14	
4 Months	34	29	36	23	14	10	
6 Months	32	23	32	19	10	9	
8 Months	29	22	27	18	9	8	
10 Months	29	19	25	17	9	7	
12 Months	27	15	19	17	8	6	
14 Months	17	10	12	11	6	3	
16 Months	13	4	5	5	3	0	
Gastrointestinal disorders (days)							
Number (%) of events	1 (2.0)	3 (4.8)	1 (1.8)	4 (7.5)	1 (2.5)	2 (6.1)	0.9049

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_seiss_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.1 Treatment emergent adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)							
Number (%) of events	13 (41.9)	23 (59.0)	39 (40.2)	57 (58.2)	13 (61.9)	9 (60.0)	0.4282
Number (%) of patients censored	18 (58.1)	16 (41.0)	58 (59.8)	41 (41.8)	8 (38.1)	6 (40.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	0.7885 (0.5257 to 8.6078)	0.6242 (0.3614 to 0.8542)	1.5441 (0.7556 to 2.8255)	0.6571 (0.5585 to 0.7885)	0.6242 (0.0657 to 1.1170)	0.5257 (0.4928 to 1.2485)	
Median (95% CI)	NC (0.9856 to NC)	2.7926 (0.7556 to NC)	NC (4.9938 to NC)	2.0370 (0.8542 to NC)	2.8255 (0.6242 to NC)	2.2834 (0.5257 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.8645 to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.8255 to NC)	NC (1.2485 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1514		0.0071		0.7583	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_seriss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.1 Treatment emergent adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	1.64 (0.83 to 3.24)		1.74 (1.16 to 2.62)		0.87 (0.37 to 2.05)	
P-value	-	0.1555		0.0079		0.7585	
Hazard ratio inverted (95% CI) vs IPd			0.57 (0.38 to 0.86)				
Events probability (95% CI)[b]							
2 Months	0.6774 (0.4835 to 0.8116)	0.5385 (0.3716 to 0.6790)	0.7159 (0.6136 to 0.7956)	0.5100 (0.4072 to 0.6037)	0.5042 (0.2749 to 0.6955)	0.5000 (0.2286 to 0.7221)	
4 Months	0.6452 (0.4515 to 0.7854)	0.4872 (0.3246 to 0.6316)	0.6510 (0.5456 to 0.7377)	0.4466 (0.3462 to 0.5420)	0.2988 (0.1057 to 0.5223)	0.4167 (0.1642 to 0.6543)	
6 Months	0.6452 (0.4515 to 0.7854)	0.4872 (0.3246 to 0.6316)	0.5822 (0.4749 to 0.6750)	0.4355 (0.3355 to 0.5311)	0.2988 (0.1057 to 0.5223)	0.3333 (0.1090 to 0.5801)	
8 Months	0.6129 (0.4202 to 0.7585)	0.4585 (0.2979 to 0.6053)	0.5822 (0.4749 to 0.6750)	0.4355 (0.3355 to 0.5311)	0.2988 (0.1057 to 0.5223)	0.3333 (0.1090 to 0.5801)	
10 Months	0.5789 (0.3872 to 0.7298)	0.4299 (0.2720 to 0.5784)	0.5822 (0.4749 to 0.6750)	0.4205 (0.3201 to 0.5173)	0.2988 (0.1057 to 0.5223)	0.3333 (0.1090 to 0.5801)	
12 Months	0.5789 (0.3872 to 0.7298)	0.4299 (0.2720 to 0.5784)	0.5822 (0.4749 to 0.6750)	0.4054 (0.3050 to 0.5034)	0.2988 (0.1057 to 0.5223)	0.3333 (0.1090 to 0.5801)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_seriss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.1 Treatment emergent adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0.5789 (0.3872 to 0.7298)	0.3869 (0.2281 to 0.5433)	0.5822 (0.4749 to 0.6750)	0.4054 (0.3050 to 0.5034)	0.2988 (0.1057 to 0.5223)	0.3333 (0.1090 to 0.5801)	
16 Months	0.5789 (0.3872 to 0.7298)	0.3869 (0.2281 to 0.5433)	0.5822 (0.4749 to 0.6750)	0.4054 (0.3050 to 0.5034)	0.2988 (0.1057 to 0.5223)	0.3333 (0.1090 to 0.5801)	
Number of patients at risk[b]							
2 Months	21	21	67	49	10	7	
4 Months	20	19	60	40	4	5	
6 Months	20	17	49	32	3	3	
8 Months	18	16	43	31	3	2	
10 Months	17	15	41	28	3	2	
12 Months	16	13	34	25	3	2	
14 Months	8	8	22	17	3	2	
16 Months	6	4	12	5	1	0	
Cardiac disorders (days)							
Number (%) of events	2 (6.5)	6 (15.4)	4 (4.1)	15 (15.3)	0 (0.0)	1 (6.7)	0.9225

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_seriss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.8 Treatment emergent severe adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)							
Number (%) of events	11 (35.5)	23 (59.0)	36 (37.1)	56 (57.1)	13 (61.9)	8 (53.3)	0.2411
Number (%) of patients censored	20 (64.5)	16 (41.0)	61 (62.9)	42 (42.9)	8 (38.1)	7 (46.7)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	0.7885 (0.5257 to NC)	0.6242 (0.3614 to 0.8542)	1.5441 (0.7556 to 2.9569)	0.6899 (0.5585 to 0.8214)	0.6242 (0.0657 to 1.1170)	0.5257 (0.4928 to 1.2485)	
Median (95% CI)	NC (3.0883 to NC)	2.7926 (0.7556 to NC)	NC (NC to NC)	2.3655 (0.8542 to NC)	2.8255 (0.6242 to NC)	2.2834 (0.5257 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.8645 to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.8255 to NC)	NC (1.2485 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0603		0.0042		0.6092	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_seriss_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.8 Treatment emergent severe adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	1.97 (0.96 to 4.04)		1.83 (1.20 to 2.78)		0.79 (0.33 to 1.92)	
P-value	-	0.0653		0.0048		0.6100	
Hazard ratio inverted (95% CI) vs IPd			0.55 (0.36 to 0.83)				
Events probability (95% CI)[b]							
2 Months	0.7097 (0.5162 to 0.8371)	0.5385 (0.3716 to 0.6790)	0.7159 (0.6136 to 0.7956)	0.5202 (0.4171 to 0.6136)	0.5042 (0.2749 to 0.6955)	0.5000 (0.2286 to 0.7221)	
4 Months	0.6774 (0.4835 to 0.8116)	0.4872 (0.3246 to 0.6316)	0.6618 (0.5569 to 0.7475)	0.4569 (0.3559 to 0.5521)	0.2988 (0.1057 to 0.5223)	0.4167 (0.1642 to 0.6543)	
6 Months	0.6774 (0.4835 to 0.8116)	0.4872 (0.3246 to 0.6316)	0.6161 (0.5094 to 0.7063)	0.4458 (0.3452 to 0.5413)	0.2988 (0.1057 to 0.5223)	0.4167 (0.1642 to 0.6543)	
8 Months	0.6452 (0.4515 to 0.7854)	0.4585 (0.2979 to 0.6053)	0.6161 (0.5094 to 0.7063)	0.4458 (0.3452 to 0.5413)	0.2988 (0.1057 to 0.5223)	0.4167 (0.1642 to 0.6543)	
10 Months	0.6452 (0.4515 to 0.7854)	0.4299 (0.2720 to 0.5784)	0.6161 (0.5094 to 0.7063)	0.4309 (0.3300 to 0.5277)	0.2988 (0.1057 to 0.5223)	0.4167 (0.1642 to 0.6543)	
12 Months	0.6452 (0.4515 to 0.7854)	0.4299 (0.2720 to 0.5784)	0.6161 (0.5094 to 0.7063)	0.4160 (0.3149 to 0.5139)	0.2988 (0.1057 to 0.5223)	0.4167 (0.1642 to 0.6543)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_seriss_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.8 Treatment emergent severe adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0.6452 (0.4515 to 0.7854)	0.3869 (0.2281 to 0.5433)	0.6161 (0.5094 to 0.7063)	0.4160 (0.3149 to 0.5139)	0.2988 (0.1057 to 0.5223)	0.4167 (0.1642 to 0.6543)	
16 Months	0.6452 (0.4515 to 0.7854)	0.3869 (0.2281 to 0.5433)	0.6161 (0.5094 to 0.7063)	0.4160 (0.3149 to 0.5139)	0.2988 (0.1057 to 0.5223)	0.4167 (0.1642 to 0.6543)	
Number of patients at risk[b]							
2 Months	22	21	67	50	10	7	
4 Months	21	19	61	41	4	5	
6 Months	21	17	52	33	3	4	
8 Months	19	16	45	32	3	3	
10 Months	19	15	43	29	3	2	
12 Months	18	13	35	26	3	2	
14 Months	10	8	22	17	3	2	
16 Months	8	4	12	5	1	0	
Gastrointestinal disorders (days)							
Number (%) of events	0 (0.0)	0 (0.0)	3 (3.1)	8 (8.2)	0 (0.0)	1 (6.7)	1.0000

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_seriss_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p)- Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	11 (52.4)	7 (50.0)	37 (39.8)	71 (61.2)	0.3216
Number (%) of patients censored	10 (47.6)	7 (50.0)	56 (60.2)	45 (38.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.7885 (0.0657 to 4.5010)	0.7556 (0.0986 to 1.2485)	1.4456 (0.7556 to 2.9569)	0.6899 (0.5257 to 0.7885)	
Median (95% CI)	4.9938 (0.7885 to NC)	1.2485 (0.5585 to NC)	NC (5.0267 to NC)	2.2012 (0.8542 to 7.4908)	
75% quantile (95% CI)	NC (4.9938 to NC)	NC (1.2485 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8309		0.0021	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.43 to 2.87)		1.85 (1.24 to 2.75)	
P-value	-	0.8310		0.0025	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.54 (0.36 to 0.81)		
Events probability (95% CI)[b]					
2 Months	0.6516 (0.4048 to 0.8164)	0.4643 (0.1934 to 0.6988)	0.7169 (0.6128 to 0.7976)	0.5086 (0.4144 to 0.5952)	
4 Months	0.6015 (0.3588 to 0.7772)	0.4643 (0.1934 to 0.6988)	0.6267 (0.5186 to 0.7171)	0.4384 (0.3467 to 0.5262)	
6 Months	0.4010 (0.1772 to 0.6172)	0.4643 (0.1934 to 0.6988)	0.6033 (0.4946 to 0.6957)	0.4201 (0.3293 to 0.5081)	
8 Months	0.4010 (0.1772 to 0.6172)	0.4643 (0.1934 to 0.6988)	0.5899 (0.4806 to 0.6837)	0.4093 (0.3187 to 0.4978)	
10 Months	0.4010 (0.1772 to 0.6172)	0.4643 (0.1934 to 0.6988)	0.5899 (0.4806 to 0.6837)	0.3866 (0.2963 to 0.4759)	
12 Months	0.4010 (0.1772 to 0.6172)	0.4643 (0.1934 to 0.6988)	0.5899 (0.4806 to 0.6837)	0.3752 (0.2853 to 0.4649)	
14 Months	0.4010 (0.1772 to 0.6172)	0.4643 (0.1934 to 0.6988)	0.5899 (0.4806 to 0.6837)	0.3752 (0.2853 to 0.4649)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.4010 (0.1772 to 0.6172)	0.4643 (0.1934 to 0.6988)	0.5899 (0.4806 to 0.6837)	0.3752 (0.2853 to 0.4649)	
Number of patients at risk[b]					
2 Months	13	6	65	59	
4 Months	11	5	55	48	
6 Months	6	3	50	40	
8 Months	6	3	43	37	
10 Months	6	2	41	34	
12 Months	6	2	37	29	
14 Months	6	2	25	20	
16 Months	4	0	13	7	
Cardiac disorders (days)					
Number (%) of events	0 (0.0)	3 (21.4)	4 (4.3)	15 (12.9)	0.9888
Number (%) of patients censored	21 (100.0)	11 (78.6)	89 (95.7)	101 (87.1)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.9 Treatment emergent severe adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	10 (47.6)	7 (50.0)	35 (37.6)	70 (60.3)	0.3891
Number (%) of patients censored	11 (52.4)	7 (50.0)	58 (62.4)	46 (39.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.7885 (0.0657 to 4.9938)	0.7556 (0.0986 to 1.2485)	1.4456 (0.7556 to 3.0883)	0.6899 (0.5257 to 0.7885)	
Median (95% CI)	4.9938 (0.7885 to NC)	1.2485 (0.5585 to NC)	NC (NC to NC)	2.2012 (0.8542 to 9.1663)	
75% quantile (95% CI)	NC (4.9938 to NC)	NC (1.2485 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6901		0.0013	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.46 to 3.22)		1.92 (1.28 to 2.89)	
P-value	-	0.6906		0.0016	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.9 Treatment emergent severe adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.52 (0.35 to 0.78)		
Events probability (95% CI)[b]					
2 Months	0.6516 (0.4048 to 0.8164)	0.4643 (0.1934 to 0.6988)	0.7169 (0.6128 to 0.7976)	0.5086 (0.4144 to 0.5952)	
4 Months	0.6015 (0.3588 to 0.7772)	0.4643 (0.1934 to 0.6988)	0.6379 (0.5301 to 0.7273)	0.4384 (0.3467 to 0.5262)	
6 Months	0.4678 (0.2310 to 0.6745)	0.4643 (0.1934 to 0.6988)	0.6263 (0.5182 to 0.7168)	0.4293 (0.3380 to 0.5172)	
8 Months	0.4678 (0.2310 to 0.6745)	0.4643 (0.1934 to 0.6988)	0.6130 (0.5040 to 0.7050)	0.4185 (0.3274 to 0.5069)	
10 Months	0.4678 (0.2310 to 0.6745)	0.4643 (0.1934 to 0.6988)	0.6130 (0.5040 to 0.7050)	0.3959 (0.3051 to 0.4852)	
12 Months	0.4678 (0.2310 to 0.6745)	0.4643 (0.1934 to 0.6988)	0.6130 (0.5040 to 0.7050)	0.3843 (0.2937 to 0.4740)	
14 Months	0.4678 (0.2310 to 0.6745)	0.4643 (0.1934 to 0.6988)	0.6130 (0.5040 to 0.7050)	0.3843 (0.2937 to 0.4740)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.9 Treatment emergent severe adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.4678 (0.2310 to 0.6745)	0.4643 (0.1934 to 0.6988)	0.6130 (0.5040 to 0.7050)	0.3843 (0.2937 to 0.4740)	
Number of patients at risk[b]					
2 Months	13	6	65	59	
4 Months	11	5	56	48	
6 Months	7	3	52	41	
8 Months	7	3	44	38	
10 Months	7	2	42	34	
12 Months	7	2	37	29	
14 Months	6	2	25	20	
16 Months	4	0	13	7	
Gastrointestinal disorders (days)					
Number (%) of events	0 (0.0)	1 (7.1)	1 (1.1)	7 (6.0)	0.9931
Number (%) of patients censored	21 (100.0)	13 (92.9)	92 (98.9)	109 (94.0)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	18 (52.9)	15 (65.2)	29 (38.2)	62 (60.2)	0.7335
Number (%) of patients censored	16 (47.1)	8 (34.8)	47 (61.8)	41 (39.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.7556 (0.2628 to 2.8255)	0.5585 (0.0986 to 0.7885)	1.5441 (0.7885 to 3.3840)	0.6899 (0.5257 to 0.8214)	
Median (95% CI)	4.9938 (1.1170 to NC)	0.8214 (0.5585 to NC)	NC (7.6222 to NC)	2.7926 (0.9528 to 9.3306)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.8214 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1868		0.0034	
Hazard ratio (95% CI) vs Pd	-	1.59 (0.79 to 3.18)		1.91 (1.23 to 2.97)	
P-value	-	0.1904		0.0040	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.52 (0.34 to 0.81)		
Events probability (95% CI)[b]					
2 Months	0.6382 (0.4516 to 0.7760)	0.3188 (0.1421 to 0.5119)	0.7325 (0.6166 to 0.8184)	0.5340 (0.4333 to 0.6246)	
4 Months	0.5775 (0.3930 to 0.7241)	0.3188 (0.1421 to 0.5119)	0.6357 (0.5152 to 0.7339)	0.4548 (0.3565 to 0.5477)	
6 Months	0.4331 (0.2567 to 0.5975)	0.3188 (0.1421 to 0.5119)	0.6216 (0.5007 to 0.7212)	0.4341 (0.3368 to 0.5274)	
8 Months	0.4331 (0.2567 to 0.5975)	0.3188 (0.1421 to 0.5119)	0.6048 (0.4828 to 0.7066)	0.4220 (0.3249 to 0.5158)	
10 Months	0.4331 (0.2567 to 0.5975)	0.3188 (0.1421 to 0.5119)	0.6048 (0.4828 to 0.7066)	0.3965 (0.2998 to 0.4914)	
12 Months	0.4331 (0.2567 to 0.5975)	0.3188 (0.1421 to 0.5119)	0.6048 (0.4828 to 0.7066)	0.3837 (0.2874 to 0.4791)	
14 Months	0.4331 (0.2567 to 0.5975)	0.3188 (0.1421 to 0.5119)	0.6048 (0.4828 to 0.7066)	0.3837 (0.2874 to 0.4791)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.4331 (0.2567 to 0.5975)	0.3188 (0.1421 to 0.5119)	0.6048 (0.4828 to 0.7066)	0.3837 (0.2874 to 0.4791)	
Number of patients at risk[b]					
2 Months	21	7	54	55	
4 Months	18	6	46	44	
6 Months	12	4	42	36	
8 Months	12	3	35	34	
10 Months	12	2	33	31	
12 Months	11	2	30	26	
14 Months	9	2	21	18	
16 Months	6	0	11	6	
Cardiac disorders (days)					
Number (%) of events	0 (0.0)	3 (13.0)	4 (5.3)	15 (14.6)	0.9899
Number (%) of patients censored	34 (100.0)	20 (87.0)	72 (94.7)	88 (85.4)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.13 Treatment emergent severe adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	16 (47.1)	15 (65.2)	28 (36.8)	61 (59.2)	0.9191
Number (%) of patients censored	18 (52.9)	8 (34.8)	48 (63.2)	42 (40.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.7556 (0.2628 to 2.8255)	0.5585 (0.0986 to 0.7885)	1.5441 (0.7885 to 3.7454)	0.6899 (0.5257 to 0.8214)	
Median (95% CI)	NC (1.1170 to NC)	0.8214 (0.5585 to NC)	NC (7.6222 to NC)	2.7926 (0.9528 to 10.4476)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.8214 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1228		0.0030	
Hazard ratio (95% CI) vs Pd	-	1.74 (0.85 to 3.56)		1.95 (1.24 to 3.05)	
P-value	-	0.1273		0.0036	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.13 Treatment emergent severe adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.51 (0.33 to 0.80)		
Events probability (95% CI)[b]					
2 Months	0.6382 (0.4516 to 0.7760)	0.3188 (0.1421 to 0.5119)	0.7325 (0.6166 to 0.8184)	0.5340 (0.4333 to 0.6246)	
4 Months	0.5775 (0.3930 to 0.7241)	0.3188 (0.1421 to 0.5119)	0.6495 (0.5293 to 0.7463)	0.4548 (0.3565 to 0.5477)	
6 Months	0.5053 (0.3223 to 0.6626)	0.3188 (0.1421 to 0.5119)	0.6354 (0.5148 to 0.7337)	0.4444 (0.3466 to 0.5376)	
8 Months	0.5053 (0.3223 to 0.6626)	0.3188 (0.1421 to 0.5119)	0.6187 (0.4968 to 0.7192)	0.4324 (0.3348 to 0.5261)	
10 Months	0.5053 (0.3223 to 0.6626)	0.3188 (0.1421 to 0.5119)	0.6187 (0.4968 to 0.7192)	0.4070 (0.3097 to 0.5019)	
12 Months	0.5053 (0.3223 to 0.6626)	0.3188 (0.1421 to 0.5119)	0.6187 (0.4968 to 0.7192)	0.3939 (0.2968 to 0.4893)	
14 Months	0.5053 (0.3223 to 0.6626)	0.3188 (0.1421 to 0.5119)	0.6187 (0.4968 to 0.7192)	0.3939 (0.2968 to 0.4893)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.13 Treatment emergent severe adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5053 (0.3223 to 0.6626)	0.3188 (0.1421 to 0.5119)	0.6187 (0.4968 to 0.7192)	0.3939 (0.2968 to 0.4893)	
Number of patients at risk[b]					
2 Months	21	7	54	55	
4 Months	18	6	47	44	
6 Months	14	4	43	37	
8 Months	14	3	35	35	
10 Months	14	2	33	31	
12 Months	12	2	30	26	
14 Months	9	2	21	18	
16 Months	6	0	11	6	
Gastrointestinal disorders (days)					
Number (%) of events	0 (0.0)	4 (17.4)	1 (1.3)	4 (3.9)	0.9921
Number (%) of patients censored	34 (100.0)	19 (82.6)	75 (98.7)	99 (96.1)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.1 Treatment emergent adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	38 (43.2)	42 (51.9)	27 (44.3)	47 (66.2)	0.6319
Number (%) of patients censored	50 (56.8)	39 (48.1)	34 (55.7)	24 (33.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.9856 (0.7556 to 2.8255)	0.6571 (0.5585 to 0.7885)	0.7885 (0.5257 to 1.9384)	0.6571 (0.5257 to 0.8214)	
Median (95% CI)	NC (4.3039 to NC)	3.3183 (0.8542 to NC)	NC (2.5626 to NC)	1.8398 (0.8542 to 4.2053)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.3306 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1180		0.0329	
Hazard ratio (95% CI) vs Pd	-	1.42 (0.91 to 2.20)		1.67 (1.04 to 2.68)	
P-value	-	0.1199		0.0348	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.1 Treatment emergent adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.60 (0.37 to 0.96)		
Events probability (95% CI)[b]					
2 Months	0.7037 (0.5962 to 0.7876)	0.5502 (0.4349 to 0.6513)	0.6405 (0.5034 to 0.7488)	0.4789 (0.3593 to 0.5888)	
4 Months	0.6209 (0.5101 to 0.7136)	0.4980 (0.3840 to 0.6019)	0.5871 (0.4497 to 0.7013)	0.4085 (0.2940 to 0.5194)	
6 Months	0.5696 (0.4576 to 0.6669)	0.4980 (0.3840 to 0.6019)	0.5498 (0.4125 to 0.6676)	0.3793 (0.2675 to 0.4903)	
8 Months	0.5554 (0.4429 to 0.6540)	0.4814 (0.3670 to 0.5868)	0.5498 (0.4125 to 0.6676)	0.3793 (0.2675 to 0.4903)	
10 Months	0.5554 (0.4429 to 0.6540)	0.4814 (0.3670 to 0.5868)	0.5278 (0.3899 to 0.6482)	0.3432 (0.2335 to 0.4555)	
12 Months	0.5554 (0.4429 to 0.6540)	0.4814 (0.3670 to 0.5868)	0.5278 (0.3899 to 0.6482)	0.3251 (0.2169 to 0.4377)	
14 Months	0.5554 (0.4429 to 0.6540)	0.4531 (0.3332 to 0.5653)	0.5278 (0.3899 to 0.6482)	0.3251 (0.2169 to 0.4377)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.1 Treatment emergent adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5554 (0.4429 to 0.6540)	0.4531 (0.3332 to 0.5653)	0.5278 (0.3899 to 0.6482)	0.3251 (0.2169 to 0.4377)	
Number of patients at risk[b]					
2 Months	61	43	37	34	
4 Months	51	36	33	28	
6 Months	43	31	29	21	
8 Months	39	28	25	21	
10 Months	37	26	24	19	
12 Months	34	23	19	17	
14 Months	22	16	11	11	
16 Months	13	4	6	5	
Cardiac disorders (days)					
Number (%) of events	6 (6.8)	7 (8.6)	0 (0.0)	15 (21.1)	0.9866
Number (%) of patients censored	82 (93.2)	74 (91.4)	61 (100.0)	56 (78.9)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.11 Treatment emergent severe adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	36 (40.9)	42 (51.9)	24 (39.3)	45 (63.4)	0.6410
Number (%) of patients censored	52 (59.1)	39 (48.1)	37 (60.7)	26 (36.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.9856 (0.7556 to 2.8255)	0.6571 (0.5585 to 0.7885)	0.7885 (0.5257 to 1.9384)	0.6899 (0.5257 to 0.8214)	
Median (95% CI)	NC (4.6653 to NC)	3.3183 (0.8542 to NC)	NC (2.9569 to NC)	1.9055 (0.8542 to 9.3306)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.4476 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0716		0.0240	
Hazard ratio (95% CI) vs Pd	-	1.50 (0.96 to 2.35)		1.76 (1.07 to 2.89)	
P-value	-	0.0735		0.0259	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.11 Treatment emergent severe adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.57 (0.35 to 0.93)		
Events probability (95% CI)[b]					
2 Months	0.7152 (0.6083 to 0.7977)	0.5502 (0.4349 to 0.6513)	0.6405 (0.5034 to 0.7488)	0.4930 (0.3726 to 0.6025)	
4 Months	0.6324 (0.5219 to 0.7242)	0.4980 (0.3840 to 0.6019)	0.6049 (0.4674 to 0.7173)	0.4225 (0.3069 to 0.5335)	
6 Months	0.5942 (0.4824 to 0.6896)	0.4980 (0.3840 to 0.6019)	0.5860 (0.4482 to 0.7005)	0.4080 (0.2935 to 0.5191)	
8 Months	0.5801 (0.4676 to 0.6769)	0.4814 (0.3670 to 0.5868)	0.5860 (0.4482 to 0.7005)	0.4080 (0.2935 to 0.5191)	
10 Months	0.5801 (0.4676 to 0.6769)	0.4814 (0.3670 to 0.5868)	0.5860 (0.4482 to 0.7005)	0.3725 (0.2597 to 0.4852)	
12 Months	0.5801 (0.4676 to 0.6769)	0.4814 (0.3670 to 0.5868)	0.5860 (0.4482 to 0.7005)	0.3539 (0.2421 to 0.4673)	
14 Months	0.5801 (0.4676 to 0.6769)	0.4531 (0.3332 to 0.5653)	0.5860 (0.4482 to 0.7005)	0.3539 (0.2421 to 0.4673)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.11 Treatment emergent severe adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5801 (0.4676 to 0.6769)	0.4531 (0.3332 to 0.5653)	0.5860 (0.4482 to 0.7005)	0.3539 (0.2421 to 0.4673)	
Number of patients at risk[b]					
2 Months	62	43	37	35	
4 Months	52	36	34	29	
6 Months	45	31	31	23	
8 Months	41	28	26	23	
10 Months	39	26	26	20	
12 Months	35	23	21	18	
14 Months	23	16	12	11	
16 Months	14	4	7	5	
Gastrointestinal disorders (days)					
Number (%) of events	1 (1.1)	6 (7.4)	2 (3.3)	3 (4.2)	0.2267
Number (%) of patients censored	87 (98.9)	75 (92.6)	59 (96.7)	68 (95.8)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.1 Treatment emergent adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	0 (0.0)	1 (50.0)	65 (44.2)	88 (58.7)	0.9822
Number (%) of patients censored	2 (100.0)	1 (50.0)	82 (55.8)	62 (41.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	2.0370 (2.0370 to NC)	0.9528 (0.7556 to 1.9384)	0.6571 (0.5585 to 0.7556)	
Median (95% CI)	NC (NC to NC)	NC (2.0370 to NC)	NC (4.6653 to NC)	2.3655 (0.9199 to 9.3306)	
75% quantile (95% CI)	NC (NC to NC)	NC (2.0370 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.0090	
Hazard ratio (95% CI) vs Pd	-	NC		1.53 (1.11 to 2.11)	
P-value	-	0.9990		0.0095	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.1 Treatment emergent adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.65 (0.47 to 0.90)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.6739 (0.5907 to 0.7438)	0.5101 (0.4272 to 0.5869)	
4 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.6017 (0.5163 to 0.6767)	0.4549 (0.3733 to 0.5327)	
6 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.5552 (0.4690 to 0.6330)	0.4404 (0.3593 to 0.5185)	
8 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.5466 (0.4601 to 0.6249)	0.4316 (0.3504 to 0.5101)	
10 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.5378 (0.4510 to 0.6167)	0.4129 (0.3315 to 0.4923)	
12 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.5378 (0.4510 to 0.6167)	0.4035 (0.3221 to 0.4833)	
14 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.5378 (0.4510 to 0.6167)	0.3905 (0.3081 to 0.4718)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.1 Treatment emergent adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.5378 (0.4510 to 0.6167)	0.3905 (0.3081 to 0.4718)	
Number of patients at risk[b]					
2 Months	2	2	96	75	
4 Months	2	1	82	63	
6 Months	2	1	70	51	
8 Months	2	1	62	48	
10 Months	1	1	60	44	
12 Months	1	1	52	39	
14 Months	1	0	32	27	
16 Months	0	0	19	9	
Cardiac disorders (days)					
Number (%) of events	0 (0.0)	0 (0.0)	6 (4.1)	22 (14.7)	0.9995
Number (%) of patients censored	2 (100.0)	2 (100.0)	141 (95.9)	128 (85.3)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.11 Treatment emergent severe adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	0 (0.0)	1 (50.0)	60 (40.8)	86 (57.3)	0.9829
Number (%) of patients censored	2 (100.0)	1 (50.0)	87 (59.2)	64 (42.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	2.0370 (2.0370 to NC)	0.9528 (0.7556 to 2.0370)	0.6571 (0.5585 to 0.7885)	
Median (95% CI)	NC (NC to NC)	NC (2.0370 to NC)	NC (4.9938 to NC)	2.7926 (0.9199 to 10.4476)	
75% quantile (95% CI)	NC (NC to NC)	NC (2.0370 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.0044	
Hazard ratio (95% CI) vs Pd	-	NC		1.61 (1.16 to 2.24)	
P-value	-	0.9990		0.0048	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_allt_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.11 Treatment emergent severe adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.62 (0.45 to 0.87)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.6809 (0.5980 to 0.7503)	0.5168 (0.4337 to 0.5935)	
4 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.6159 (0.5308 to 0.6901)	0.4616 (0.3798 to 0.5394)	
6 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.5851 (0.4991 to 0.6613)	0.4544 (0.3728 to 0.5323)	
8 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.5765 (0.4902 to 0.6534)	0.4457 (0.3640 to 0.5240)	
10 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.5765 (0.4902 to 0.6534)	0.4271 (0.3452 to 0.5064)	
12 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.5765 (0.4902 to 0.6534)	0.4176 (0.3356 to 0.4974)	
14 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.5765 (0.4902 to 0.6534)	0.4041 (0.3209 to 0.4857)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.11 Treatment emergent severe adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.5765 (0.4902 to 0.6534)	0.4041 (0.3209 to 0.4857)	
Number of patients at risk[b]					
2 Months	2	2	97	76	
4 Months	2	1	84	64	
6 Months	2	1	74	53	
8 Months	2	1	65	50	
10 Months	1	1	64	45	
12 Months	1	1	55	40	
14 Months	1	0	34	27	
16 Months	0	0	21	9	
Gastrointestinal disorders (days)					
Number (%) of events	0 (0.0)	0 (0.0)	3 (2.0)	9 (6.0)	0.9998
Number (%) of patients censored	2 (100.0)	2 (100.0)	144 (98.0)	141 (94.0)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	41 (41.8)	58 (56.3)	18 (45.0)	24 (75.0)	0.2816
Number (%) of patients censored	57 (58.2)	45 (43.7)	22 (55.0)	8 (25.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.1499 (0.7556 to 2.8255)	0.7228 (0.5585 to 0.8214)	0.7885 (0.4928 to 1.8398)	0.5749 (0.4928 to 0.7556)	
Median (95% CI)	NC (4.6653 to NC)	3.3183 (0.9528 to NC)	NC (0.9528 to NC)	0.8542 (0.5914 to 1.9055)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	7.4908 (0.8542 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0349		0.0152	
Hazard ratio (95% CI) vs Pd	-	1.53 (1.03 to 2.29)		2.11 (1.14 to 3.90)	
P-value	-	0.0363		0.0175	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.65 (0.44 to 0.97)		0.47 (0.26 to 0.88)		
Events probability (95% CI)[b]					
2 Months	0.7191 (0.6176 to 0.7980)	0.5494 (0.4479 to 0.6397)	0.6162 (0.4460 to 0.7480)	0.3125 (0.1638 to 0.4734)	
4 Months	0.6341 (0.5291 to 0.7219)	0.4905 (0.3905 to 0.5830)	0.5882 (0.4179 to 0.7241)	0.2813 (0.1404 to 0.4406)	
6 Months	0.5890 (0.4828 to 0.6806)	0.4701 (0.3707 to 0.5631)	0.5294 (0.3599 to 0.6731)	0.2813 (0.1404 to 0.4406)	
8 Months	0.5767 (0.4701 to 0.6694)	0.4701 (0.3707 to 0.5631)	0.5294 (0.3599 to 0.6731)	0.2461 (0.1141 to 0.4043)	
10 Months	0.5642 (0.4572 to 0.6579)	0.4446 (0.3452 to 0.5393)	0.5294 (0.3599 to 0.6731)	0.2461 (0.1141 to 0.4043)	
12 Months	0.5642 (0.4572 to 0.6579)	0.4319 (0.3326 to 0.5272)	0.5294 (0.3599 to 0.6731)	0.2461 (0.1141 to 0.4043)	
14 Months	0.5642 (0.4572 to 0.6579)	0.4132 (0.3121 to 0.5112)	0.5294 (0.3599 to 0.6731)	0.2461 (0.1141 to 0.4043)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5642 (0.4572 to 0.6579)	0.4132 (0.3121 to 0.5112)	0.5294 (0.3599 to 0.6731)	0.2461 (0.1141 to 0.4043)	
Number of patients at risk[b]					
2 Months	68	56	24	10	
4 Months	59	48	21	9	
6 Months	50	41	18	8	
8 Months	46	39	14	7	
10 Months	43	35	14	7	
12 Months	37	30	13	7	
14 Months	24	21	6	4	
16 Months	13	7	4	1	
Cardiac disorders (days)					
Number (%) of events	5 (5.1)	14 (13.6)	1 (2.5)	8 (25.0)	0.5067
Number (%) of patients censored	93 (94.9)	89 (86.4)	39 (97.5)	24 (75.0)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.13 Treatment emergent severe adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	37 (37.8)	57 (55.3)	17 (42.5)	23 (71.9)	0.3246
Number (%) of patients censored	61 (62.2)	46 (44.7)	23 (57.5)	9 (28.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.4456 (0.7556 to 3.3840)	0.7228 (0.5585 to 0.8214)	0.7885 (0.4928 to 1.8398)	0.5749 (0.4928 to 0.7885)	
Median (95% CI)	NC (NC to NC)	3.3183 (0.9528 to NC)	NC (0.9528 to NC)	0.8542 (0.5914 to 2.8912)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.9856 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0138		0.0228	
Hazard ratio (95% CI) vs Pd	-	1.67 (1.11 to 2.53)		2.05 (1.09 to 3.84)	
P-value	-	0.0148		0.0258	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.13 Treatment emergent severe adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.60 (0.39 to 0.90)		0.49 (0.26 to 0.92)		
Events probability (95% CI)[b]					
2 Months	0.7296 (0.6288 to 0.8072)	0.5494 (0.4479 to 0.6397)	0.6162 (0.4460 to 0.7480)	0.3438 (0.1879 to 0.5056)	
4 Months	0.6553 (0.5508 to 0.7411)	0.4905 (0.3905 to 0.5830)	0.5882 (0.4179 to 0.7241)	0.3125 (0.1638 to 0.4734)	
6 Months	0.6215 (0.5158 to 0.7107)	0.4803 (0.3806 to 0.5730)	0.5588 (0.3885 to 0.6989)	0.3125 (0.1638 to 0.4734)	
8 Months	0.6094 (0.5030 to 0.6997)	0.4803 (0.3806 to 0.5730)	0.5588 (0.3885 to 0.6989)	0.2778 (0.1369 to 0.4382)	
10 Months	0.6094 (0.5030 to 0.6997)	0.4550 (0.3551 to 0.5494)	0.5588 (0.3885 to 0.6989)	0.2778 (0.1369 to 0.4382)	
12 Months	0.6094 (0.5030 to 0.6997)	0.4420 (0.3421 to 0.5372)	0.5588 (0.3885 to 0.6989)	0.2778 (0.1369 to 0.4382)	
14 Months	0.6094 (0.5030 to 0.6997)	0.4228 (0.3209 to 0.5210)	0.5588 (0.3885 to 0.6989)	0.2778 (0.1369 to 0.4382)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.13 Treatment emergent severe adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.6094 (0.5030 to 0.6997)	0.4228 (0.3209 to 0.5210)	0.5588 (0.3885 to 0.6989)	0.2778 (0.1369 to 0.4382)	
Number of patients at risk[b]					
2 Months	69	56	24	11	
4 Months	61	48	21	10	
6 Months	53	42	19	9	
8 Months	48	40	15	8	
10 Months	46	35	15	8	
12 Months	40	30	13	8	
14 Months	26	21	6	4	
16 Months	15	7	4	1	
Gastrointestinal disorders (days)					
Number (%) of events	1 (1.0)	4 (3.9)	2 (5.0)	3 (9.4)	0.8921
Number (%) of patients censored	97 (99.0)	99 (96.1)	38 (95.0)	29 (90.6)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	41 (42.3)	56 (55.4)	24 (47.1)	32 (64.0)	0.7782
Number (%) of patients censored	56 (57.7)	45 (44.6)	27 (52.9)	18 (36.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.1170 (0.7556 to 2.8255)	0.7228 (0.5585 to 0.8214)	0.7885 (0.5585 to 1.5770)	0.5914 (0.5257 to 0.7885)	
Median (95% CI)	NC (4.6653 to NC)	4.0411 (0.9199 to NC)	NC (1.5441 to NC)	1.0021 (0.7556 to 7.4908)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.2854 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0549		0.0737	
Hazard ratio (95% CI) vs Pd	-	1.48 (0.99 to 2.22)		1.62 (0.95 to 2.75)	
P-value	-	0.0564		0.0764	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.7161 (0.6138 to 0.7957)	0.5604 (0.4577 to 0.6510)	0.6005 (0.4518 to 0.7208)	0.4383 (0.2987 to 0.5694)	
4 Months	0.6302 (0.5245 to 0.7187)	0.5003 (0.3990 to 0.5934)	0.5560 (0.4072 to 0.6815)	0.3712 (0.2381 to 0.5044)	
6 Months	0.5846 (0.4777 to 0.6769)	0.4795 (0.3787 to 0.5732)	0.5097 (0.3615 to 0.6399)	0.3712 (0.2381 to 0.5044)	
8 Months	0.5721 (0.4649 to 0.6655)	0.4795 (0.3787 to 0.5732)	0.5097 (0.3615 to 0.6399)	0.3375 (0.2046 to 0.4754)	
10 Months	0.5594 (0.4519 to 0.6539)	0.4536 (0.3526 to 0.5490)	0.5097 (0.3615 to 0.6399)	0.3375 (0.2046 to 0.4754)	
12 Months	0.5594 (0.4519 to 0.6539)	0.4406 (0.3397 to 0.5367)	0.5097 (0.3615 to 0.6399)	0.3375 (0.2046 to 0.4754)	
14 Months	0.5594 (0.4519 to 0.6539)	0.4214 (0.3187 to 0.5205)	0.5097 (0.3615 to 0.6399)	0.3375 (0.2046 to 0.4754)	
16 Months	0.5594 (0.4519 to 0.6539)	0.4214 (0.3187 to 0.5205)	0.5097 (0.3615 to 0.6399)	0.3375 (0.2046 to 0.4754)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_dghc_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	67	56	30	21	
4 Months	58	48	25	16	
6 Months	49	41	22	11	
8 Months	45	39	18	10	
10 Months	42	35	18	10	
12 Months	36	30	16	10	
14 Months	23	21	9	6	
16 Months	12	7	6	2	
Cardiac disorders (days)					
Number (%) of events	5 (5.2)	14 (13.9)	1 (2.0)	8 (16.0)	0.3320
Number (%) of patients censored	92 (94.8)	87 (86.1)	50 (98.0)	42 (84.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.6612 to NC)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.14 Treatment emergent severe adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	37 (38.1)	55 (54.5)	23 (45.1)	31 (62.0)	0.9729
Number (%) of patients censored	60 (61.9)	46 (45.5)	28 (54.9)	19 (38.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.1499 (0.7556 to 3.0883)	0.7228 (0.5585 to 0.8214)	0.7885 (0.5585 to 1.5770)	0.5914 (0.5257 to 0.8214)	
Median (95% CI)	NC (7.6222 to NC)	4.2053 (0.9199 to NC)	NC (1.5441 to NC)	1.4292 (0.7885 to 7.4908)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.4908 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0228		0.0904	
Hazard ratio (95% CI) vs Pd	-	1.62 (1.06 to 2.45)		1.59 (0.93 to 2.73)	
P-value	-	0.0241		0.0933	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_dghc_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.14 Treatment emergent severe adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.62 (0.41 to 0.94)				
Events probability (95% CI)[b]					
2 Months	0.7268 (0.6252 to 0.8051)	0.5604 (0.4577 to 0.6510)	0.6005 (0.4518 to 0.7208)	0.4583 (0.3168 to 0.5889)	
4 Months	0.6516 (0.5464 to 0.7382)	0.5003 (0.3990 to 0.5934)	0.5560 (0.4072 to 0.6815)	0.3916 (0.2559 to 0.5249)	
6 Months	0.6175 (0.5111 to 0.7074)	0.4899 (0.3888 to 0.5833)	0.5328 (0.3841 to 0.6609)	0.3916 (0.2559 to 0.5249)	
8 Months	0.6051 (0.4982 to 0.6962)	0.4899 (0.3888 to 0.5833)	0.5328 (0.3841 to 0.6609)	0.3590 (0.2233 to 0.4966)	
10 Months	0.6051 (0.4982 to 0.6962)	0.4641 (0.3627 to 0.5593)	0.5328 (0.3841 to 0.6609)	0.3590 (0.2233 to 0.4966)	
12 Months	0.6051 (0.4982 to 0.6962)	0.4508 (0.3494 to 0.5469)	0.5328 (0.3841 to 0.6609)	0.3590 (0.2233 to 0.4966)	
14 Months	0.6051 (0.4982 to 0.6962)	0.4312 (0.3277 to 0.5305)	0.5328 (0.3841 to 0.6609)	0.3590 (0.2233 to 0.4966)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.14 Treatment emergent severe adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.6051 (0.4982 to 0.6962)	0.4312 (0.3277 to 0.5305)	0.5328 (0.3841 to 0.6609)	0.3590 (0.2233 to 0.4966)	
Number of patients at risk[b]					
2 Months	68	56	30	22	
4 Months	60	48	25	17	
6 Months	52	42	23	12	
8 Months	47	40	19	11	
10 Months	45	35	19	11	
12 Months	39	30	16	11	
14 Months	25	21	9	6	
16 Months	14	7	6	2	
Gastrointestinal disorders (days)					
Number (%) of events	1 (1.0)	3 (3.0)	2 (3.9)	5 (10.0)	0.9588
Number (%) of patients censored	96 (99.0)	98 (97.0)	49 (96.1)	45 (90.0)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.1 Treatment emergent adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	1 (10.0)	8 (57.1)	64 (46.0)	81 (58.7)	0.1776
Number (%) of patients censored	9 (90.0)	6 (42.9)	75 (54.0)	57 (41.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (0.7556 to NC)	0.7556 (0.5257 to 1.9055)	0.9199 (0.7556 to 1.8398)	0.6571 (0.5585 to 0.7885)	
Median (95% CI)	NC (0.7556 to NC)	1.9713 (0.6242 to NC)	NC (4.3039 to NC)	2.7926 (0.8542 to 9.3306)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.9055 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0387		0.0190	
Hazard ratio (95% CI) vs Pd	-	6.69 (0.83 to 53.67)		1.48 (1.06 to 2.05)	
P-value	-	0.0735		0.0198	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.1 Treatment emergent adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.68 (0.49 to 0.94)		
Events probability (95% CI)[b]					
2 Months	0.8889 (0.4330 to 0.9836)	0.5000 (0.2286 to 0.7221)	0.6641 (0.5783 to 0.7365)	0.5183 (0.4316 to 0.5981)	
4 Months	0.8889 (0.4330 to 0.9836)	0.4286 (0.1773 to 0.6604)	0.5896 (0.5021 to 0.6669)	0.4582 (0.3729 to 0.5393)	
6 Months	0.8889 (0.4330 to 0.9836)	0.4286 (0.1773 to 0.6604)	0.5428 (0.4550 to 0.6225)	0.4424 (0.3576 to 0.5237)	
8 Months	0.8889 (0.4330 to 0.9836)	0.4286 (0.1773 to 0.6604)	0.5343 (0.4464 to 0.6145)	0.4328 (0.3479 to 0.5146)	
10 Months	0.8889 (0.4330 to 0.9836)	0.4286 (0.1773 to 0.6604)	0.5257 (0.4377 to 0.6063)	0.4122 (0.3271 to 0.4951)	
12 Months	0.8889 (0.4330 to 0.9836)	0.4286 (0.1773 to 0.6604)	0.5257 (0.4377 to 0.6063)	0.4019 (0.3168 to 0.4853)	
14 Months	0.8889 (0.4330 to 0.9836)	0.4286 (0.1773 to 0.6604)	0.5257 (0.4377 to 0.6063)	0.3875 (0.3014 to 0.4727)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.1 Treatment emergent adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.8889 (0.4330 to 0.9836)	0.4286 (0.1773 to 0.6604)	0.5257 (0.4377 to 0.6063)	0.3875 (0.3014 to 0.4727)	
Number of patients at risk[b]					
2 Months	8	7	90	70	
4 Months	6	6	78	58	
6 Months	4	5	68	47	
8 Months	2	5	62	44	
10 Months	2	5	59	40	
12 Months	2	4	51	36	
14 Months	2	3	31	24	
16 Months	0	2	19	7	
Cardiac disorders (days)					
Number (%) of events	0 (0.0)	2 (14.3)	6 (4.3)	20 (14.5)	0.9889
Number (%) of patients censored	10 (100.0)	12 (85.7)	133 (95.7)	118 (85.5)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.9 Treatment emergent severe adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	1 (10.0)	8 (57.1)	59 (42.4)	79 (57.2)	0.1927
Number (%) of patients censored	9 (90.0)	6 (42.9)	80 (57.6)	59 (42.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (0.7556 to NC)	0.7556 (0.5257 to 1.9055)	0.9199 (0.7556 to 1.9384)	0.6571 (0.5585 to 0.7885)	
Median (95% CI)	NC (0.7556 to NC)	1.9713 (0.6242 to NC)	NC (4.9938 to NC)	2.7926 (0.9199 to 13.8645)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.9055 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0387		0.0102	
Hazard ratio (95% CI) vs Pd	-	6.69 (0.83 to 53.67)		1.55 (1.11 to 2.17)	
P-value	-	0.0735		0.0109	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.9 Treatment emergent severe adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.64 (0.46 to 0.90)		
Events probability (95% CI)[b]					
2 Months	0.8889 (0.4330 to 0.9836)	0.5000 (0.2286 to 0.7221)	0.6715 (0.5859 to 0.7432)	0.5256 (0.4388 to 0.6052)	
4 Months	0.8889 (0.4330 to 0.9836)	0.4286 (0.1773 to 0.6604)	0.6044 (0.5170 to 0.6808)	0.4655 (0.3800 to 0.5465)	
6 Months	0.8889 (0.4330 to 0.9836)	0.4286 (0.1773 to 0.6604)	0.5733 (0.4854 to 0.6516)	0.4576 (0.3723 to 0.5388)	
8 Months	0.8889 (0.4330 to 0.9836)	0.4286 (0.1773 to 0.6604)	0.5648 (0.4768 to 0.6437)	0.4481 (0.3627 to 0.5298)	
10 Months	0.8889 (0.4330 to 0.9836)	0.4286 (0.1773 to 0.6604)	0.5648 (0.4768 to 0.6437)	0.4277 (0.3420 to 0.5106)	
12 Months	0.8889 (0.4330 to 0.9836)	0.4286 (0.1773 to 0.6604)	0.5648 (0.4768 to 0.6437)	0.4173 (0.3315 to 0.5007)	
14 Months	0.8889 (0.4330 to 0.9836)	0.4286 (0.1773 to 0.6604)	0.5648 (0.4768 to 0.6437)	0.4024 (0.3152 to 0.4879)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.9 Treatment emergent severe adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.8889 (0.4330 to 0.9836)	0.4286 (0.1773 to 0.6604)	0.5648 (0.4768 to 0.6437)	0.4024 (0.3152 to 0.4879)	
Number of patients at risk[b]					
2 Months	8	7	91	71	
4 Months	6	6	80	59	
6 Months	4	5	72	49	
8 Months	2	5	65	46	
10 Months	2	5	63	41	
12 Months	2	4	54	37	
14 Months	2	3	33	24	
16 Months	0	2	21	7	
Gastrointestinal disorders (days)					
Number (%) of events	0 (0.0)	0 (0.0)	3 (2.2)	9 (6.5)	0.9997
Number (%) of patients censored	10 (100.0)	14 (100.0)	136 (97.8)	129 (93.5)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.1 Treatment emergent adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	39 (41.5)	50 (58.1)	23 (48.9)	34 (63.0)	0.8430
Number (%) of patients censored	55 (58.5)	36 (41.9)	24 (51.1)	20 (37.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.9856 (0.7556 to 2.8255)	0.6899 (0.5585 to 0.8542)	0.7885 (0.4928 to 2.8255)	0.5585 (0.4271 to 0.7885)	
Median (95% CI)	NC (4.9938 to NC)	2.3655 (0.9528 to NC)	4.6653 (1.5770 to NC)	0.9692 (0.7885 to 10.4476)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.4476 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0208		0.1422	
Hazard ratio (95% CI) vs Pd	-	1.63 (1.07 to 2.48)		1.48 (0.87 to 2.52)	
P-value	-	0.0221		0.1448	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_crcl_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.1 Treatment emergent adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.61 (0.40 to 0.93)				
Events probability (95% CI)[b]					
2 Months	0.6877 (0.5826 to 0.7714)	0.5225 (0.4121 to 0.6217)	0.6531 (0.4975 to 0.7711)	0.4815 (0.3439 to 0.6062)	
4 Months	0.6316 (0.5244 to 0.7210)	0.4750 (0.3663 to 0.5759)	0.5419 (0.3878 to 0.6727)	0.4044 (0.2734 to 0.5316)	
6 Months	0.5951 (0.4866 to 0.6880)	0.4625 (0.3543 to 0.5638)	0.4967 (0.3453 to 0.6310)	0.3852 (0.2563 to 0.5124)	
8 Months	0.5819 (0.4728 to 0.6761)	0.4481 (0.3400 to 0.5502)	0.4967 (0.3453 to 0.6310)	0.3852 (0.2563 to 0.5124)	
10 Months	0.5684 (0.4588 to 0.6639)	0.4182 (0.3107 to 0.5220)	0.4967 (0.3453 to 0.6310)	0.3852 (0.2563 to 0.5124)	
12 Months	0.5684 (0.4588 to 0.6639)	0.4182 (0.3107 to 0.5220)	0.4967 (0.3453 to 0.6310)	0.3595 (0.2318 to 0.4887)	
14 Months	0.5684 (0.4588 to 0.6639)	0.3962 (0.2869 to 0.5033)	0.4967 (0.3453 to 0.6310)	0.3595 (0.2318 to 0.4887)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.1 Treatment emergent adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5684 (0.4588 to 0.6639)	0.3962 (0.2869 to 0.5033)	0.4967 (0.3453 to 0.6310)	0.3595 (0.2318 to 0.4887)	
Number of patients at risk[b]					
2 Months	63	44	30	26	
4 Months	56	38	24	21	
6 Months	47	32	22	18	
8 Months	43	31	18	16	
10 Months	40	28	18	15	
12 Months	35	24	16	14	
14 Months	19	16	12	9	
16 Months	11	7	6	2	
Cardiac disorders (days)					
Number (%) of events	5 (5.3)	10 (11.6)	1 (2.1)	12 (22.2)	0.1772
Number (%) of patients censored	89 (94.7)	76 (88.4)	46 (97.9)	42 (77.8)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.10 Treatment emergent severe adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	36 (38.3)	50 (58.1)	22 (46.8)	32 (59.3)	0.5808
Number (%) of patients censored	58 (61.7)	36 (41.9)	25 (53.2)	22 (40.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.1170 (0.7556 to 3.0883)	0.6899 (0.5585 to 0.8542)	0.7885 (0.4928 to 2.8255)	0.5585 (0.4271 to 0.7885)	
Median (95% CI)	NC (7.6222 to NC)	2.3655 (0.9528 to NC)	NC (1.5770 to NC)	1.9055 (0.7885 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0076		0.1964	
Hazard ratio (95% CI) vs Pd	-	1.78 (1.16 to 2.73)		1.43 (0.83 to 2.46)	
P-value	-	0.0085		0.1988	
Hazard ratio inverted (95% CI) vs IPd	0.56 (0.37 to 0.86)				

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.10 Treatment emergent severe adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.6986 (0.5941 to 0.7810)	0.5225 (0.4121 to 0.6217)	0.6531 (0.4975 to 0.7711)	0.5000 (0.3612 to 0.6239)	
4 Months	0.6538 (0.5473 to 0.7412)	0.4750 (0.3663 to 0.5759)	0.5419 (0.3878 to 0.6727)	0.4231 (0.2900 to 0.5500)	
6 Months	0.6175 (0.5092 to 0.7086)	0.4625 (0.3543 to 0.5638)	0.5193 (0.3664 to 0.6520)	0.4231 (0.2900 to 0.5500)	
8 Months	0.6043 (0.4954 to 0.6969)	0.4481 (0.3400 to 0.5502)	0.5193 (0.3664 to 0.6520)	0.4231 (0.2900 to 0.5500)	
10 Months	0.6043 (0.4954 to 0.6969)	0.4182 (0.3107 to 0.5220)	0.5193 (0.3664 to 0.6520)	0.4231 (0.2900 to 0.5500)	
12 Months	0.6043 (0.4954 to 0.6969)	0.4182 (0.3107 to 0.5220)	0.5193 (0.3664 to 0.6520)	0.3966 (0.2639 to 0.5263)	
14 Months	0.6043 (0.4954 to 0.6969)	0.3962 (0.2869 to 0.5033)	0.5193 (0.3664 to 0.6520)	0.3966 (0.2639 to 0.5263)	
16 Months	0.6043 (0.4954 to 0.6969)	0.3962 (0.2869 to 0.5033)	0.5193 (0.3664 to 0.6520)	0.3966 (0.2639 to 0.5263)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.10 Treatment emergent severe adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	64	44	30	27	
4 Months	58	38	24	22	
6 Months	49	32	23	20	
8 Months	44	31	19	18	
10 Months	42	28	19	16	
12 Months	37	24	17	15	
14 Months	21	16	12	9	
16 Months	13	7	6	2	
Gastrointestinal disorders (days)					
Number (%) of events	2 (2.1)	5 (5.8)	1 (2.1)	3 (5.6)	0.9456
Number (%) of patients censored	92 (97.9)	81 (94.2)	46 (97.9)	51 (94.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.1 Treatment emergent adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	1 (50.0)	0 (0.0)	64 (43.5)	89 (59.3)	0.9797
Number (%) of patients censored	1 (50.0)	2 (100.0)	83 (56.5)	61 (40.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.1643 (0.1643 to NC)	NC (NC to NC)	0.9856 (0.7556 to 2.0370)	0.6571 (0.5585 to 0.7556)	
Median (95% CI)	NC (0.1643 to NC)	NC (NC to NC)	NC (4.9938 to NC)	2.1027 (0.9199 to 9.1663)	
75% quantile (95% CI)	NC (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.0041	
Hazard ratio (95% CI) vs Pd	-	NC		1.60 (1.16 to 2.20)	
P-value	-	0.9990		0.0044	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.1 Treatment emergent adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.63 (0.45 to 0.86)		
Events probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.6807 (0.5978 to 0.7502)	0.5101 (0.4272 to 0.5869)	
4 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.6085 (0.5233 to 0.6832)	0.4481 (0.3667 to 0.5260)	
6 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.5628 (0.4767 to 0.6402)	0.4336 (0.3527 to 0.5117)	
8 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.5543 (0.4679 to 0.6322)	0.4248 (0.3439 to 0.5032)	
10 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.5456 (0.4590 to 0.6241)	0.4059 (0.3248 to 0.4853)	
12 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.5456 (0.4590 to 0.6241)	0.3964 (0.3154 to 0.4762)	
14 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.5456 (0.4590 to 0.6241)	0.3828 (0.3006 to 0.4643)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.1 Treatment emergent adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.5456 (0.4590 to 0.6241)	0.3828 (0.3006 to 0.4643)	
Number of patients at risk[b]					
2 Months	1	2	97	75	
4 Months	1	2	83	62	
6 Months	0	2	72	50	
8 Months	0	2	64	47	
10 Months	0	2	61	43	
12 Months	0	2	53	38	
14 Months	0	2	33	25	
16 Months	0	0	19	9	
Cardiac disorders (days)					
Number (%) of events	0 (0.0)	0 (0.0)	6 (4.1)	22 (14.7)	0.9996
Number (%) of patients censored	2 (100.0)	2 (100.0)	141 (95.9)	128 (85.3)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.9 Treatment emergent severe adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	1 (50.0)	0 (0.0)	59 (40.1)	87 (58.0)	0.9804
Number (%) of patients censored	1 (50.0)	2 (100.0)	88 (59.9)	63 (42.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.1643 (0.1643 to NC)	NC (NC to NC)	0.9856 (0.7556 to 2.8255)	0.6571 (0.5585 to 0.7885)	
Median (95% CI)	NC (0.1643 to NC)	NC (NC to NC)	NC (7.6222 to NC)	2.3655 (0.9199 to 9.3306)	
75% quantile (95% CI)	NC (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.0019	
Hazard ratio (95% CI) vs Pd	-	NC		1.68 (1.21 to 2.34)	
P-value	-	0.9990		0.0021	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.9 Treatment emergent severe adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.60 (0.43 to 0.83)		
Events probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.6877 (0.6051 to 0.7566)	0.5168 (0.4337 to 0.5935)	
4 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.6228 (0.5378 to 0.6966)	0.4548 (0.3732 to 0.5327)	
6 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.5924 (0.5066 to 0.6682)	0.4476 (0.3662 to 0.5256)	
8 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.5839 (0.4978 to 0.6604)	0.4388 (0.3574 to 0.5172)	
10 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.5839 (0.4978 to 0.6604)	0.4201 (0.3385 to 0.4995)	
12 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.5839 (0.4978 to 0.6604)	0.4106 (0.3289 to 0.4904)	
14 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.5839 (0.4978 to 0.6604)	0.3964 (0.3133 to 0.4783)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.9 Treatment emergent severe adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.5839 (0.4978 to 0.6604)	0.3964 (0.3133 to 0.4783)	
Number of patients at risk[b]					
2 Months	1	2	98	76	
4 Months	1	2	85	63	
6 Months	0	2	76	52	
8 Months	0	2	67	49	
10 Months	0	2	65	44	
12 Months	0	2	56	39	
14 Months	0	2	35	25	
16 Months	0	0	21	9	
Gastrointestinal disorders (days)					
Number (%) of events	0 (0.0)	0 (0.0)	3 (2.0)	9 (6.0)	0.9998
Number (%) of patients censored	2 (100.0)	2 (100.0)	144 (98.0)	141 (94.0)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	50 (45.0)	70 (59.8)	15 (39.5)	19 (54.3)	0.6293
Number (%) of patients censored	61 (55.0)	47 (40.2)	23 (60.5)	16 (45.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.8871 (0.7228 to 1.5770)	0.7556 (0.5585 to 0.8214)	1.9384 (0.4928 to 7.6222)	0.5585 (0.4271 to 0.7228)	
Median (95% CI)	NC (3.3840 to NC)	2.7926 (0.9528 to 9.3306)	NC (2.9569 to NC)	1.2485 (0.5914 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0305		0.1239	
Hazard ratio (95% CI) vs Pd	-	1.49 (1.04 to 2.14)		1.69 (0.86 to 3.34)	
P-value	-	0.0316		0.1281	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.67 (0.47 to 0.97)				
Events probability (95% CI)[b]					
2 Months	0.6605 (0.5633 to 0.7410)	0.5257 (0.4311 to 0.6118)	0.7308 (0.5574 to 0.8452)	0.4857 (0.3142 to 0.6374)	
4 Months	0.5837 (0.4847 to 0.6702)	0.4553 (0.3627 to 0.5431)	0.6756 (0.4998 to 0.8012)	0.4571 (0.2890 to 0.6105)	
6 Months	0.5427 (0.4432 to 0.6319)	0.4371 (0.3452 to 0.5252)	0.6169 (0.4396 to 0.7528)	0.4571 (0.2890 to 0.6105)	
8 Months	0.5427 (0.4432 to 0.6319)	0.4256 (0.3337 to 0.5143)	0.5844 (0.4062 to 0.7259)	0.4571 (0.2890 to 0.6105)	
10 Months	0.5311 (0.4313 to 0.6212)	0.4006 (0.3084 to 0.4909)	0.5844 (0.4062 to 0.7259)	0.4571 (0.2890 to 0.6105)	
12 Months	0.5311 (0.4313 to 0.6212)	0.3880 (0.2960 to 0.4790)	0.5844 (0.4062 to 0.7259)	0.4571 (0.2890 to 0.6105)	
14 Months	0.5311 (0.4313 to 0.6212)	0.3704 (0.2769 to 0.4638)	0.5844 (0.4062 to 0.7259)	0.4571 (0.2890 to 0.6105)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5311 (0.4313 to 0.6212)	0.3704 (0.2769 to 0.4638)	0.5844 (0.4062 to 0.7259)	0.4571 (0.2890 to 0.6105)	
Number of patients at risk[b]					
2 Months	71	60	27	17	
4 Months	60	50	24	14	
6 Months	51	39	21	13	
8 Months	47	36	17	13	
10 Months	44	32	17	13	
12 Months	39	28	14	12	
14 Months	24	19	9	8	
16 Months	13	8	6	1	
Cardiac disorders (days)					
Number (%) of events	3 (2.7)	19 (16.2)	3 (7.9)	3 (8.6)	0.0830
Number (%) of patients censored	108 (97.3)	98 (83.8)	35 (92.1)	32 (91.4)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.11 Treatment emergent severe adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	46 (41.4)	68 (58.1)	14 (36.8)	19 (54.3)	0.5773
Number (%) of patients censored	65 (58.6)	49 (41.9)	24 (63.2)	16 (45.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.8871 (0.7228 to 1.5770)	0.7556 (0.5585 to 0.8214)	2.8255 (0.4928 to 7.6222)	0.5585 (0.4271 to 0.7228)	
Median (95% CI)	NC (3.7454 to NC)	2.7926 (0.9856 to 10.4476)	NC (4.6653 to NC)	1.2485 (0.5914 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0200		0.0846	
Hazard ratio (95% CI) vs Pd	-	1.55 (1.07 to 2.26)		1.82 (0.91 to 3.65)	
P-value	-	0.0210		0.0892	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.11 Treatment emergent severe adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.64 (0.44 to 0.94)				
Events probability (95% CI)[b]					
2 Months	0.6605 (0.5633 to 0.7410)	0.5344 (0.4396 to 0.6202)	0.7579 (0.5862 to 0.8660)	0.4857 (0.3142 to 0.6374)	
4 Months	0.5933 (0.4943 to 0.6792)	0.4640 (0.3710 to 0.5517)	0.7027 (0.5275 to 0.8232)	0.4571 (0.2890 to 0.6105)	
6 Months	0.5730 (0.4736 to 0.6603)	0.4549 (0.3622 to 0.5428)	0.6442 (0.4665 to 0.7760)	0.4571 (0.2890 to 0.6105)	
8 Months	0.5730 (0.4736 to 0.6603)	0.4435 (0.3508 to 0.5320)	0.6120 (0.4328 to 0.7498)	0.4571 (0.2890 to 0.6105)	
10 Months	0.5730 (0.4736 to 0.6603)	0.4189 (0.3258 to 0.5090)	0.6120 (0.4328 to 0.7498)	0.4571 (0.2890 to 0.6105)	
12 Months	0.5730 (0.4736 to 0.6603)	0.4062 (0.3130 to 0.4971)	0.6120 (0.4328 to 0.7498)	0.4571 (0.2890 to 0.6105)	
14 Months	0.5730 (0.4736 to 0.6603)	0.3877 (0.2926 to 0.4816)	0.6120 (0.4328 to 0.7498)	0.4571 (0.2890 to 0.6105)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.11 Treatment emergent severe adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5730 (0.4736 to 0.6603)	0.3877 (0.2926 to 0.4816)	0.6120 (0.4328 to 0.7498)	0.4571 (0.2890 to 0.6105)	
Number of patients at risk[b]					
2 Months	71	61	28	17	
4 Months	61	51	25	14	
6 Months	54	41	22	13	
8 Months	49	38	18	13	
10 Months	47	33	18	13	
12 Months	41	29	15	12	
14 Months	25	19	10	8	
16 Months	14	8	7	1	
Gastrointestinal disorders (days)					
Number (%) of events	3 (2.7)	7 (6.0)	0 (0.0)	2 (5.7)	0.9925
Number (%) of patients censored	108 (97.3)	110 (94.0)	38 (100.0)	33 (94.3)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	58 (41.4)	85 (58.6)	7 (77.8)	4 (57.1)	0.1951
Number (%) of patients censored	82 (58.6)	60 (41.4)	2 (22.2)	3 (42.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.9528 (0.7556 to 2.5626)	0.6571 (0.5585 to 0.7885)	0.9856 (0.5914 to 2.8255)	0.7228 (0.5585 to 9.3306)	
Median (95% CI)	NC (4.9938 to NC)	2.1027 (0.8542 to 9.1663)	2.8255 (0.5914 to NC)	9.3306 (0.5585 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	8.6078 (0.9856 to NC)	NC (1.4456 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0035		0.5307	
Hazard ratio (95% CI) vs Pd	-	1.64 (1.17 to 2.29)		0.67 (0.20 to 2.33)	
P-value	-	0.0039		0.5332	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.61 (0.44 to 0.85)				
Events probability (95% CI)[b]					
2 Months	0.6866 (0.6017 to 0.7571)	0.5139 (0.4294 to 0.5919)	0.5556 (0.2042 to 0.8045)	0.5714 (0.1719 to 0.8371)	
4 Months	0.6181 (0.5307 to 0.6940)	0.4497 (0.3669 to 0.5289)	0.4444 (0.1359 to 0.7193)	0.5714 (0.1719 to 0.8371)	
6 Months	0.5773 (0.4888 to 0.6559)	0.4347 (0.3523 to 0.5141)	0.3333 (0.0783 to 0.6226)	0.5714 (0.1719 to 0.8371)	
8 Months	0.5682 (0.4793 to 0.6475)	0.4255 (0.3430 to 0.5053)	0.3333 (0.0783 to 0.6226)	0.5714 (0.1719 to 0.8371)	
10 Months	0.5682 (0.4793 to 0.6475)	0.4158 (0.3333 to 0.4961)	0.2222 (0.0337 to 0.5131)	0.3810 (0.0612 to 0.7164)	
12 Months	0.5682 (0.4793 to 0.6475)	0.4061 (0.3236 to 0.4869)	0.2222 (0.0337 to 0.5131)	0.3810 (0.0612 to 0.7164)	
14 Months	0.5682 (0.4793 to 0.6475)	0.3921 (0.3083 to 0.4747)	0.2222 (0.0337 to 0.5131)	0.3810 (0.0612 to 0.7164)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5682 (0.4793 to 0.6475)	0.3921 (0.3083 to 0.4747)	0.2222 (0.0337 to 0.5131)	0.3810 (0.0612 to 0.7164)	
Number of patients at risk[b]					
2 Months	93	73	5	4	
4 Months	80	60	4	4	
6 Months	69	48	3	4	
8 Months	61	46	3	3	
10 Months	59	43	2	2	
12 Months	51	38	2	2	
14 Months	32	25	1	2	
16 Months	19	9	0	0	
Cardiac disorders (days)					
Number (%) of events	5 (3.6)	20 (13.8)	1 (11.1)	2 (28.6)	0.8534
Number (%) of patients censored	135 (96.4)	125 (86.2)	8 (88.9)	5 (71.4)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.9 Treatment emergent severe adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	55 (39.3)	83 (57.2)	5 (55.6)	4 (57.1)	0.5213
Number (%) of patients censored	85 (60.7)	62 (42.8)	4 (44.4)	3 (42.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.9528 (0.7556 to 2.8255)	0.6571 (0.5585 to 0.7885)	0.9856 (0.5914 to 4.6653)	0.7228 (0.5585 to 9.3306)	
Median (95% CI)	NC (NC to NC)	2.3655 (0.9199 to 13.8645)	4.6653 (0.5914 to NC)	9.3306 (0.5585 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.8255 to NC)	NC (1.4456 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0030		0.8898	
Hazard ratio (95% CI) vs Pd	-	1.67 (1.19 to 2.35)		1.10 (0.29 to 4.09)	
P-value	-	0.0033		0.8898	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.9 Treatment emergent severe adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.60 (0.43 to 0.84)				
Events probability (95% CI)[b]					
2 Months	0.6866 (0.6017 to 0.7571)	0.5208 (0.4363 to 0.5987)	0.6667 (0.2817 to 0.8783)	0.5714 (0.1719 to 0.8371)	
4 Months	0.6257 (0.5385 to 0.7010)	0.4567 (0.3736 to 0.5358)	0.5556 (0.2042 to 0.8045)	0.5714 (0.1719 to 0.8371)	
6 Months	0.6013 (0.5133 to 0.6784)	0.4492 (0.3663 to 0.5285)	0.4444 (0.1359 to 0.7193)	0.5714 (0.1719 to 0.8371)	
8 Months	0.5922 (0.5037 to 0.6701)	0.4400 (0.3571 to 0.5197)	0.4444 (0.1359 to 0.7193)	0.5714 (0.1719 to 0.8371)	
10 Months	0.5922 (0.5037 to 0.6701)	0.4304 (0.3474 to 0.5107)	0.4444 (0.1359 to 0.7193)	0.3810 (0.0612 to 0.7164)	
12 Months	0.5922 (0.5037 to 0.6701)	0.4207 (0.3375 to 0.5014)	0.4444 (0.1359 to 0.7193)	0.3810 (0.0612 to 0.7164)	
14 Months	0.5922 (0.5037 to 0.6701)	0.4062 (0.3214 to 0.4891)	0.4444 (0.1359 to 0.7193)	0.3810 (0.0612 to 0.7164)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.9 Treatment emergent severe adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5922 (0.5037 to 0.6701)	0.4062 (0.3214 to 0.4891)	0.4444 (0.1359 to 0.7193)	0.3810 (0.0612 to 0.7164)	
Number of patients at risk[b]					
2 Months	93	74	6	4	
4 Months	81	61	5	4	
6 Months	72	50	4	4	
8 Months	63	48	4	3	
10 Months	61	44	4	2	
12 Months	52	39	4	2	
14 Months	32	25	3	2	
16 Months	19	9	2	0	
Gastrointestinal disorders (days)					
Number (%) of events	3 (2.1)	9 (6.2)	0 (0.0)	0 (0.0)	0.9997
Number (%) of patients censored	137 (97.9)	136 (93.8)	9 (100.0)	7 (100.0)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	36 (41.4)	51 (56.0)	29 (46.8)	38 (62.3)	0.6945
Number (%) of patients censored	51 (58.6)	40 (44.0)	33 (53.2)	23 (37.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.7885 (0.6242 to 2.8255)	0.5585 (0.4928 to 0.7556)	1.4456 (0.7556 to 2.8255)	0.7885 (0.5914 to 0.8542)	
Median (95% CI)	NC (4.9938 to NC)	2.1027 (0.8214 to NC)	8.6078 (2.8255 to NC)	2.9569 (0.9199 to 10.4476)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.4476 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0307		0.1096	
Hazard ratio (95% CI) vs Pd	-	1.60 (1.04 to 2.45)		1.48 (0.91 to 2.40)	
P-value	-	0.0322		0.1122	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.63 (0.41 to 0.96)				
Events probability (95% CI)[b]					
2 Months	0.6750 (0.5651 to 0.7628)	0.5005 (0.3936 to 0.5983)	0.6822 (0.5479 to 0.7843)	0.5405 (0.4080 to 0.6556)	
4 Months	0.6266 (0.5150 to 0.7194)	0.4439 (0.3395 to 0.5430)	0.5785 (0.4426 to 0.6924)	0.4723 (0.3429 to 0.5912)	
6 Months	0.5882 (0.4756 to 0.6846)	0.4439 (0.3395 to 0.5430)	0.5224 (0.3869 to 0.6414)	0.4373 (0.3102 to 0.5575)	
8 Months	0.5745 (0.4615 to 0.6722)	0.4291 (0.3247 to 0.5292)	0.5224 (0.3869 to 0.6414)	0.4373 (0.3102 to 0.5575)	
10 Months	0.5745 (0.4615 to 0.6722)	0.4291 (0.3247 to 0.5292)	0.4997 (0.3636 to 0.6214)	0.3913 (0.2650 to 0.5154)	
12 Months	0.5745 (0.4615 to 0.6722)	0.4291 (0.3247 to 0.5292)	0.4997 (0.3636 to 0.6214)	0.3683 (0.2432 to 0.4937)	
14 Months	0.5745 (0.4615 to 0.6722)	0.4291 (0.3247 to 0.5292)	0.4997 (0.3636 to 0.6214)	0.3400 (0.2153 to 0.4686)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5745 (0.4615 to 0.6722)	0.4291 (0.3247 to 0.5292)	0.4997 (0.3636 to 0.6214)	0.3400 (0.2153 to 0.4686)	
Number of patients at risk[b]					
2 Months	58	45	40	32	
4 Months	51	37	33	27	
6 Months	46	30	26	22	
8 Months	41	29	23	20	
10 Months	41	28	20	17	
12 Months	35	26	18	14	
14 Months	22	16	11	11	
16 Months	12	5	7	4	
Cardiac disorders (days)					
Number (%) of events	2 (2.3)	10 (11.0)	4 (6.5)	12 (19.7)	0.6183
Number (%) of patients censored	85 (97.7)	81 (89.0)	58 (93.5)	49 (80.3)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.14 Treatment emergent severe adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Blood and lymphatic system disorders (days)					
Number (%) of events	34 (39.1)	51 (56.0)	26 (41.9)	36 (59.0)	0.6807
Number (%) of patients censored	53 (60.9)	40 (44.0)	36 (58.1)	25 (41.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.7885 (0.6242 to 2.8255)	0.5585 (0.4928 to 0.7556)	1.5441 (0.7556 to 3.0883)	0.7885 (0.5914 to 0.9199)	
Median (95% CI)	NC (7.6222 to NC)	2.1027 (0.8214 to NC)	NC (3.0883 to NC)	3.2854 (0.9528 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.8645 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0167		0.0861	
Hazard ratio (95% CI) vs Pd	-	1.69 (1.09 to 2.61)		1.55 (0.94 to 2.57)	
P-value	-	0.0180		0.0886	
Hazard ratio inverted (95% CI) vs IPd	0.59 (0.38 to 0.91)				

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.14 Treatment emergent severe adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.6750 (0.5651 to 0.7628)	0.5005 (0.3936 to 0.5983)	0.6993 (0.5657 to 0.7988)	0.5569 (0.4239 to 0.6708)	
4 Months	0.6386 (0.5273 to 0.7303)	0.4439 (0.3395 to 0.5430)	0.5956 (0.4595 to 0.7080)	0.4888 (0.3583 to 0.6071)	
6 Months	0.6131 (0.5009 to 0.7073)	0.4439 (0.3395 to 0.5430)	0.5589 (0.4227 to 0.6750)	0.4714 (0.3418 to 0.5904)	
8 Months	0.5994 (0.4867 to 0.6951)	0.4291 (0.3247 to 0.5292)	0.5589 (0.4227 to 0.6750)	0.4714 (0.3418 to 0.5904)	
10 Months	0.5994 (0.4867 to 0.6951)	0.4291 (0.3247 to 0.5292)	0.5589 (0.4227 to 0.6750)	0.4265 (0.2970 to 0.5498)	
12 Months	0.5994 (0.4867 to 0.6951)	0.4291 (0.3247 to 0.5292)	0.5589 (0.4227 to 0.6750)	0.4028 (0.2738 to 0.5281)	
14 Months	0.5994 (0.4867 to 0.6951)	0.4291 (0.3247 to 0.5292)	0.5589 (0.4227 to 0.6750)	0.3718 (0.2416 to 0.5020)	
16 Months	0.5994 (0.4867 to 0.6951)	0.4291 (0.3247 to 0.5292)	0.5589 (0.4227 to 0.6750)	0.3718 (0.2416 to 0.5020)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.14 Treatment emergent severe adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	58	45	41	33	
4 Months	52	37	34	28	
6 Months	48	30	28	24	
8 Months	42	29	25	22	
10 Months	42	28	23	18	
12 Months	36	26	20	15	
14 Months	22	16	13	11	
16 Months	12	5	9	4	
Gastrointestinal disorders (days)					
Number (%) of events	1 (1.1)	3 (3.3)	2 (3.2)	6 (9.8)	0.9851
Number (%) of patients censored	86 (98.9)	88 (96.7)	60 (96.8)	55 (90.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.1 Treatment emergent adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0.6164 (0.4860 to 0.7228)	0.4582 (0.3213 to 0.5848)	0.4963 (0.3499 to 0.6266)	0.3927 (0.2675 to 0.5156)	0.4560 (0.2656 to 0.6280)	0.3008 (0.1508 to 0.4664)	
16 Months	0.6164 (0.4860 to 0.7228)	0.4582 (0.3213 to 0.5848)	0.4963 (0.3499 to 0.6266)	0.3927 (0.2675 to 0.5156)	0.4560 (0.2656 to 0.6280)	0.3008 (0.1508 to 0.4664)	
Number of patients at risk[b]							
2 Months	50	28	32	35	16	14	
4 Months	44	21	25	33	15	10	
6 Months	37	18	24	26	11	8	
8 Months	33	16	22	25	9	8	
10 Months	31	15	21	22	9	8	
12 Months	29	13	18	20	6	7	
14 Months	19	10	11	12	3	5	
16 Months	13	2	4	6	2	1	
Cardiac disorders (days)							
Number (%) of events	1 (1.5)	6 (11.1)	4 (7.5)	10 (15.2)	1 (3.6)	6 (18.8)	0.5034

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.1 Treatment emergent adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of patients censored	67 (98.5)	48 (88.9)	49 (92.5)	56 (84.8)	27 (96.4)	26 (81.3)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (9.8234 to NC)	NC (NC to NC)	NC (6.9651 to NC)	NC (9.7248 to NC)	NC (2.6612 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0247		0.2134		0.1096	
Hazard ratio (95% CI) vs Pd	-	7.76 (0.93 to 64.42)		2.06 (0.64 to 6.55)		4.78 (0.58 to 39.74)	
P-value	-	0.0578		0.2233		0.1476	
Events probability (95% CI)[b]							
2 Months	1.0000 (1.0000 to 1.0000)	0.9256 (0.8137 to 0.9714)	0.9804 (0.8689 to 0.9972)	0.9233 (0.8255 to 0.9673)	1.0000 (1.0000 to 1.0000)	0.9375 (0.7725 to 0.9840)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.1 Treatment emergent adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	1.0000 (1.0000 to 1.0000)	0.9256 (0.8137 to 0.9714)	0.9804 (0.8689 to 0.9972)	0.8920 (0.7867 to 0.9470)	1.0000 (1.0000 to 1.0000)	0.9052 (0.7340 to 0.9684)	
6 Months	0.9831 (0.8857 to 0.9976)	0.9256 (0.8137 to 0.9714)	0.9600 (0.8492 to 0.9898)	0.8761 (0.7673 to 0.9360)	1.0000 (1.0000 to 1.0000)	0.8704 (0.6899 to 0.9494)	
8 Months	0.9831 (0.8857 to 0.9976)	0.9256 (0.8137 to 0.9714)	0.9366 (0.8152 to 0.9792)	0.8582 (0.7448 to 0.9237)	1.0000 (1.0000 to 1.0000)	0.8341 (0.6452 to 0.9277)	
10 Months	0.9831 (0.8857 to 0.9976)	0.8741 (0.7379 to 0.9422)	0.9366 (0.8152 to 0.9792)	0.8391 (0.7207 to 0.9104)	0.9333 (0.6126 to 0.9903)	0.7978 (0.6029 to 0.9041)	
12 Months	0.9831 (0.8857 to 0.9976)	0.8741 (0.7379 to 0.9422)	0.9366 (0.8152 to 0.9792)	0.8391 (0.7207 to 0.9104)	0.9333 (0.6126 to 0.9903)	0.7978 (0.6029 to 0.9041)	
14 Months	0.9831 (0.8857 to 0.9976)	0.8741 (0.7379 to 0.9422)	0.9082 (0.7706 to 0.9650)	0.8391 (0.7207 to 0.9104)	0.9333 (0.6126 to 0.9903)	0.7978 (0.6029 to 0.9041)	
16 Months	0.9831 (0.8857 to 0.9976)	0.8741 (0.7379 to 0.9422)	0.9082 (0.7706 to 0.9650)	0.8391 (0.7207 to 0.9104)	0.9333 (0.6126 to 0.9903)	0.7978 (0.6029 to 0.9041)	
Number of patients at risk[b]							
2 Months	66	49	50	59	26	30	
4 Months	62	46	48	57	24	26	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_age_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.1 Treatment emergent adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	53	42	44	50	18	24	
8 Months	48	38	39	48	16	23	
10 Months	46	34	38	43	14	21	
12 Months	40	30	33	39	10	18	
14 Months	25	19	18	28	8	13	
16 Months	14	10	7	9	4	3	
Eye disorders (days)							
Number (%) of events	7 (10.3)	4 (7.4)	6 (11.3)	7 (10.6)	2 (7.1)	2 (6.3)	0.9539
Number (%) of patients censored	61 (89.7)	50 (92.6)	47 (88.7)	59 (89.4)	26 (92.9)	30 (93.8)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.4312 to NC)	NC (9.1663 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.1 Treatment emergent adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5297 (0.4242 to 0.6245)	0.4392 (0.3380 to 0.5358)	0.5733 (0.4179 to 0.7013)	0.2904 (0.1572 to 0.4377)	
Number of patients at risk[b]					
2 Months	65	53	33	24	
4 Months	54	44	30	20	
6 Months	47	37	25	15	
8 Months	43	36	21	13	
10 Months	43	32	18	13	
12 Months	36	30	17	10	
14 Months	21	21	12	6	
16 Months	12	9	7	0	
Cardiac disorders (days)					
Number (%) of events	5 (5.0)	14 (13.9)	1 (2.0)	8 (15.7)	0.4051
Number (%) of patients censored	95 (95.0)	87 (86.1)	48 (98.0)	43 (84.3)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.1 Treatment emergent adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.3450 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0365		0.0259	
Hazard ratio (95% CI) vs Pd	-	2.83 (1.02 to 7.87)		7.46 (0.93 to 59.68)	
P-value	-	0.0456		0.0582	
Hazard ratio inverted (95% CI) vs IPd	0.35 (0.13 to 0.98)				
Events probability (95% CI)[b]					
2 Months	0.9897 (0.9291 to 0.9985)	0.9299 (0.8586 to 0.9659)	1.0000 (1.0000 to 1.0000)	0.9216 (0.8044 to 0.9698)	
4 Months	0.9897 (0.9291 to 0.9985)	0.8992 (0.8208 to 0.9445)	1.0000 (1.0000 to 1.0000)	0.9216 (0.8044 to 0.9698)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.1 Treatment emergent adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9780 (0.9148 to 0.9945)	0.8883 (0.8072 to 0.9365)	0.9778 (0.8525 to 0.9968)	0.9011 (0.7785 to 0.9576)	
8 Months	0.9650 (0.8948 to 0.9886)	0.8759 (0.7915 to 0.9277)	0.9778 (0.8525 to 0.9968)	0.8791 (0.7501 to 0.9439)	
10 Months	0.9512 (0.8744 to 0.9815)	0.8496 (0.7581 to 0.9085)	0.9778 (0.8525 to 0.9968)	0.8315 (0.6898 to 0.9124)	
12 Months	0.9512 (0.8744 to 0.9815)	0.8496 (0.7581 to 0.9085)	0.9778 (0.8525 to 0.9968)	0.8315 (0.6898 to 0.9124)	
14 Months	0.9345 (0.8478 to 0.9726)	0.8496 (0.7581 to 0.9085)	0.9778 (0.8525 to 0.9968)	0.8315 (0.6898 to 0.9124)	
16 Months	0.9345 (0.8478 to 0.9726)	0.8496 (0.7581 to 0.9085)	0.9778 (0.8525 to 0.9968)	0.8315 (0.6898 to 0.9124)	
Number of patients at risk[b]					
2 Months	94	92	48	46	
4 Months	89	83	45	46	
6 Months	78	74	37	42	
8 Months	71	71	32	38	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.1 Treatment emergent adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	69	64	29	34	
12 Months	57	59	26	28	
14 Months	34	40	17	20	
16 Months	15	15	10	7	
Eye disorders (days)					
Number (%) of events	9 (9.0)	8 (7.9)	6 (12.2)	5 (9.8)	0.8493
Number (%) of patients censored	91 (91.0)	93 (92.1)	43 (87.8)	46 (90.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.9795 to NC)	NC (10.6119 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6641		0.5370	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.1 Treatment emergent adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.6179 (0.4881 to 0.7238)	0.4607 (0.3511 to 0.5633)	0.4819 (0.3656 to 0.5889)	0.2866 (0.1665 to 0.4185)	
Number of patients at risk[b]					
2 Months	50	49	48	28	
4 Months	43	43	41	21	
6 Months	38	35	34	17	
8 Months	36	34	28	15	
10 Months	33	30	28	15	
12 Months	27	27	26	13	
14 Months	18	20	15	7	
16 Months	12	7	7	2	
Cardiac disorders (days)					
Number (%) of events	3 (4.4)	13 (14.8)	3 (3.7)	9 (14.1)	0.9471
Number (%) of patients censored	65 (95.6)	75 (85.2)	78 (96.3)	55 (85.9)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.1 Treatment emergent adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (9.8234 to NC)	NC (NC to NC)	NC (8.3450 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0386		0.0355	
Hazard ratio (95% CI) vs Pd	-	3.47 (0.99 to 12.17)		3.70 (1.00 to 13.65)	
P-value	-	0.0523		0.0499	
Hazard ratio inverted (95% CI) vs IPd			0.27 (0.07 to 1.00)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9079 (0.8242 to 0.9528)	0.9873 (0.9135 to 0.9982)	0.9529 (0.8609 to 0.9846)	
4 Months	1.0000 (1.0000 to 1.0000)	0.8961 (0.8098 to 0.9445)	0.9873 (0.9135 to 0.9982)	0.9211 (0.8208 to 0.9664)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.1 Treatment emergent adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9836 (0.8893 to 0.9977)	0.8717 (0.7802 to 0.9269)	0.9730 (0.8961 to 0.9932)	0.9211 (0.8208 to 0.9664)	
8 Months	0.9647 (0.8656 to 0.9911)	0.8717 (0.7802 to 0.9269)	0.9730 (0.8961 to 0.9932)	0.8831 (0.7694 to 0.9428)	
10 Months	0.9647 (0.8656 to 0.9911)	0.8424 (0.7431 to 0.9057)	0.9540 (0.8614 to 0.9852)	0.8434 (0.7191 to 0.9158)	
12 Months	0.9647 (0.8656 to 0.9911)	0.8424 (0.7431 to 0.9057)	0.9540 (0.8614 to 0.9852)	0.8434 (0.7191 to 0.9158)	
14 Months	0.9400 (0.8220 to 0.9806)	0.8424 (0.7431 to 0.9057)	0.9540 (0.8614 to 0.9852)	0.8434 (0.7191 to 0.9158)	
16 Months	0.9400 (0.8220 to 0.9806)	0.8424 (0.7431 to 0.9057)	0.9540 (0.8614 to 0.9852)	0.8434 (0.7191 to 0.9158)	
Number of patients at risk[b]					
2 Months	65	78	77	60	
4 Months	62	74	72	55	
6 Months	54	66	61	50	
8 Months	51	63	52	46	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.1 Treatment emergent adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	48	56	50	42	
12 Months	39	49	44	38	
14 Months	24	33	27	27	
16 Months	14	13	11	9	
Eye disorders (days)					
Number (%) of events	6 (8.8)	6 (6.8)	9 (11.1)	7 (10.9)	0.8410
Number (%) of patients censored	62 (91.2)	82 (93.2)	72 (88.9)	57 (89.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.3634 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5846		0.7505	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.1 Treatment emergent adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5315 (0.4365 to 0.6176)	0.4166 (0.3226 to 0.5078)	0.6272 (0.3725 to 0.8022)	0.2273 (0.0841 to 0.4121)	
Number of patients at risk[b]					
2 Months	79	60	14	10	
4 Months	66	52	14	7	
6 Months	56	43	13	7	
8 Months	50	40	11	7	
10 Months	47	37	11	6	
12 Months	43	35	8	3	
14 Months	28	23	3	2	
16 Months	16	9	1	0	
Cardiac disorders (days)					
Number (%) of events	6 (4.9)	18 (15.5)	0 (0.0)	4 (16.7)	0.9914
Number (%) of patients censored	116 (95.1)	98 (84.5)	19 (100.0)	20 (83.3)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_race_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.1 Treatment emergent adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.0842 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0112		0.0579	
Hazard ratio (95% CI) vs Pd	-	3.11 (1.23 to 7.83)		NC	
P-value	-	0.0162		0.9968	
Hazard ratio inverted (95% CI) vs IPd	0.32 (0.13 to 0.81)				
Events probability (95% CI)[b]					
2 Months	0.9916 (0.9419 to 0.9988)	0.9138 (0.8457 to 0.9527)	1.0000 (1.0000 to 1.0000)	0.9583 (0.7392 to 0.9940)	
4 Months	0.9916 (0.9419 to 0.9988)	0.8965 (0.8249 to 0.9398)	1.0000 (1.0000 to 1.0000)	0.9148 (0.7000 to 0.9780)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.1 Treatment emergent adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9727 (0.9176 to 0.9911)	0.8782 (0.8029 to 0.9260)	1.0000 (1.0000 to 1.0000)	0.9148 (0.7000 to 0.9780)	
8 Months	0.9615 (0.9001 to 0.9855)	0.8683 (0.7909 to 0.9185)	1.0000 (1.0000 to 1.0000)	0.8666 (0.6399 to 0.9551)	
10 Months	0.9492 (0.8811 to 0.9787)	0.8363 (0.7520 to 0.8939)	1.0000 (1.0000 to 1.0000)	0.8185 (0.5843 to 0.9280)	
12 Months	0.9492 (0.8811 to 0.9787)	0.8363 (0.7520 to 0.8939)	1.0000 (1.0000 to 1.0000)	0.8185 (0.5843 to 0.9280)	
14 Months	0.9352 (0.8596 to 0.9708)	0.8363 (0.7520 to 0.8939)	1.0000 (1.0000 to 1.0000)	0.8185 (0.5843 to 0.9280)	
16 Months	0.9352 (0.8596 to 0.9708)	0.8363 (0.7520 to 0.8939)	1.0000 (1.0000 to 1.0000)	0.8185 (0.5843 to 0.9280)	
Number of patients at risk[b]					
2 Months	116	106	19	22	
4 Months	109	100	19	21	
6 Months	92	90	19	21	
8 Months	81	86	18	18	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.1 Treatment emergent adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	77	77	17	16	
12 Months	68	68	13	14	
14 Months	46	45	3	11	
16 Months	22	17	1	4	
Eye disorders (days)					
Number (%) of events	11 (9.0)	10 (8.6)	4 (21.1)	3 (12.5)	0.6847
Number (%) of patients censored	111 (91.0)	106 (91.4)	15 (78.9)	21 (87.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.9856 to NC)	NC (2.4969 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6954		0.4717	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.1 Treatment emergent adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.5401 (0.4485 to 0.6230)	0.3848 (0.2958 to 0.4729)	
Number of patients at risk[b]					
2 Months	2	2	86	65	
4 Months	2	2	73	55	
6 Months	0	2	64	46	
8 Months	0	2	56	43	
10 Months	0	2	53	39	
12 Months	0	2	46	34	
14 Months	0	2	28	21	
16 Months	0	0	16	8	
Cardiac disorders (days)					
Number (%) of events	0 (0.0)	0 (0.0)	5 (3.8)	20 (15.6)	0.9995
Number (%) of patients censored	3 (100.0)	4 (100.0)	125 (96.2)	108 (84.4)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.1 Treatment emergent adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0022	
Hazard ratio (95% CI) vs Pd	-	NC		4.09 (1.54 to 10.90)	
P-value	-			0.0048	
Hazard ratio inverted (95% CI) vs IPd			0.24 (0.09 to 0.65)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9922 (0.9458 to 0.9989)	0.9296 (0.8690 to 0.9627)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9922 (0.9458 to 0.9989)	0.9059 (0.8402 to 0.9454)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.1 Treatment emergent adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9751 (0.9246 to 0.9919)	0.8892 (0.8201 to 0.9329)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9650 (0.9091 to 0.9868)	0.8710 (0.7978 to 0.9190)	
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9539 (0.8920 to 0.9807)	0.8319 (0.7508 to 0.8885)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9539 (0.8920 to 0.9807)	0.8319 (0.7508 to 0.8885)	
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9539 (0.8920 to 0.9807)	0.8319 (0.7508 to 0.8885)	
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9539 (0.8920 to 0.9807)	0.8319 (0.7508 to 0.8885)	
Number of patients at risk[b]					
2 Months	2	4	125	118	
4 Months	2	4	119	111	
6 Months	1	4	103	101	
8 Months	1	4	91	94	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.1 Treatment emergent adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	1	4	86	83	
12 Months	0	4	73	72	
14 Months	0	4	46	49	
16 Months	0	1	22	18	
Eye disorders (days)					
Number (%) of events	1 (33.3)	1 (25.0)	14 (10.8)	11 (8.6)	0.6612
Number (%) of patients censored	2 (66.7)	3 (75.0)	116 (89.2)	117 (91.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.1314 (0.1314 to NC)	NC (11.3018 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (0.1314 to NC)	NC (11.3018 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (0.1314 to NC)	NC (11.3018 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2482		0.4106	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
8 Months	35	19	7	7	2	1	8	7	12	15	
10 Months	35	18	7	6	2	1	8	6	9	14	
12 Months	31	16	7	6	1	1	6	3	8	14	
14 Months	22	11	4	4	0	0	2	2	5	10	
16 Months	12	3	2	1	0	0	1	0	4	5	
Cardiac disorders (days)											
Number (%) of events	3 (4.1)	5 (9.1)	2 (10.0)	3 (10.7)	1 (20.0)	2 (28.6)	0 (0.0)	3 (14.3)	0 (0.0)	9 (22.0)	0.9737
Number (%) of patients censored	71 (95.9)	50 (90.9)	18 (90.0)	25 (89.3)	4 (80.0)	5 (71.4)	15 (100.0)	18 (85.7)	35 (100.0)	32 (78.0)	
Kaplan-Meier estimates of event in months											

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.3368 to NC)	NC (1.0185 to NC)	NC (6.7351 to NC)	1.0842 (0.4600 to NC)	NC (NC to NC)	NC (1.0842 to NC)	NC (NC to NC)	NC (2.7926 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.7351 to NC)	NC (0.4600 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.7351 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.2486		0.9775		0.6193		0.1227		0.0077	
Hazard ratio (95% CI) vs Pd	-	2.27 (0.54 to 9.50)		1.03 (0.17 to 6.14)		1.83 (0.16 to 20.47)		NC		NC	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
P-value	-	0.2618		0.9776		0.6244		0.9973		0.9926	
Events probability (95% CI)[b]											
2 Months	0.9859 (0.9042 to 0.9980)	0.9626 (0.8586 to 0.9905)	1.0000 (1.0000 to 1.0000)	0.9286 (0.7435 to 0.9816)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.9524 (0.7072 to 0.9932)	1.0000 (1.0000 to 1.0000)	0.9024 (0.7606 to 0.9622)	
4 Months	0.9859 (0.9042 to 0.9980)	0.9437 (0.8356 to 0.9815)	1.0000 (1.0000 to 1.0000)	0.9286 (0.7435 to 0.9816)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.9023 (0.6623 to 0.9747)	1.0000 (1.0000 to 1.0000)	0.8780 (0.7315 to 0.9473)	
6 Months	0.9859 (0.9042 to 0.9980)	0.9223 (0.8055 to 0.9702)	0.8889 (0.6242 to 0.9710)	0.8914 (0.6999 to 0.9637)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.9023 (0.6623 to 0.9747)	1.0000 (1.0000 to 1.0000)	0.8780 (0.7315 to 0.9473)	
8 Months	0.9859 (0.9042 to 0.9980)	0.9223 (0.8055 to 0.9702)	0.8889 (0.6242 to 0.9710)	0.8914 (0.6999 to 0.9637)	0.8000 (0.2038 to 0.9692)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.9023 (0.6623 to 0.9747)	1.0000 (1.0000 to 1.0000)	0.8240 (0.6652 to 0.9121)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
10 Months	0.9662 (0.8690 to 0.9916)	0.8959 (0.7653 to 0.9559)	0.8889 (0.6242 to 0.9710)	0.8914 (0.6999 to 0.9637)	0.8000 (0.2038 to 0.9692)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.8492 (0.6010 to 0.9489)	1.0000 (1.0000 to 1.0000)	0.7661 (0.5970 to 0.8714)	
12 Months	0.9662 (0.8690 to 0.9916)	0.8959 (0.7653 to 0.9559)	0.8889 (0.6242 to 0.9710)	0.8914 (0.6999 to 0.9637)	0.8000 (0.2038 to 0.9692)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.8492 (0.6010 to 0.9489)	1.0000 (1.0000 to 1.0000)	0.7661 (0.5970 to 0.8714)	
14 Months	0.9437 (0.8322 to 0.9819)	0.8959 (0.7653 to 0.9559)	0.8889 (0.6242 to 0.9710)	0.8914 (0.6999 to 0.9637)	0.8000 (0.2038 to 0.9692)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.8492 (0.6010 to 0.9489)	1.0000 (1.0000 to 1.0000)	0.7661 (0.5970 to 0.8714)	
16 Months	0.9437 (0.8322 to 0.9819)	0.8959 (0.7653 to 0.9559)	0.8889 (0.6242 to 0.9710)	0.8914 (0.6999 to 0.9637)	0.8000 (0.2038 to 0.9692)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.8492 (0.6010 to 0.9489)	1.0000 (1.0000 to 1.0000)	0.7661 (0.5970 to 0.8714)	
Number of patients at risk[b]											
2 Months	69	51	19	26	5	5	15	19	34	37	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.1 Treatment emergent adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.6349 (0.5261 to 0.7252)	0.4298 (0.3110 to 0.5431)	0.3976 (0.2658 to 0.5262)	0.3568 (0.2470 to 0.4679)	
Number of patients at risk[b]					
2 Months	67	40	31	37	
4 Months	59	33	25	31	
6 Months	51	26	21	26	
8 Months	44	25	20	24	
10 Months	42	24	19	21	
12 Months	37	22	16	18	
14 Months	25	15	8	12	
16 Months	14	4	5	5	
Cardiac disorders (days)					
Number (%) of events	4 (4.3)	10 (13.0)	2 (3.6)	12 (16.0)	0.7206
Number (%) of patients censored	90 (95.7)	67 (87.0)	53 (96.4)	63 (84.0)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.1 Treatment emergent adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (9.8234 to NC)	NC (NC to NC)	NC (9.0678 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0424		0.0323	
Hazard ratio (95% CI) vs Pd	-	3.12 (0.98 to 9.95)		4.45 (1.00 to 19.87)	
P-value	-	0.0544		0.0507	
Events probability (95% CI)[b]					
2 Months	0.9890 (0.9246 to 0.9984)	0.9342 (0.8491 to 0.9721)	1.0000 (1.0000 to 1.0000)	0.9198 (0.8302 to 0.9632)	
4 Months	0.9890 (0.9246 to 0.9984)	0.9208 (0.8322 to 0.9636)	1.0000 (1.0000 to 1.0000)	0.8925 (0.7966 to 0.9448)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.1 Treatment emergent adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9890 (0.9246 to 0.9984)	0.9062 (0.8131 to 0.9542)	0.9600 (0.8494 to 0.9898)	0.8788 (0.7800 to 0.9350)	
8 Months	0.9747 (0.9013 to 0.9937)	0.8723 (0.7677 to 0.9319)	0.9600 (0.8494 to 0.9898)	0.8788 (0.7800 to 0.9350)	
10 Months	0.9587 (0.8757 to 0.9867)	0.8542 (0.7440 to 0.9194)	0.9600 (0.8494 to 0.9898)	0.8322 (0.7228 to 0.9013)	
12 Months	0.9587 (0.8757 to 0.9867)	0.8542 (0.7440 to 0.9194)	0.9600 (0.8494 to 0.9898)	0.8322 (0.7228 to 0.9013)	
14 Months	0.9403 (0.8460 to 0.9776)	0.8542 (0.7440 to 0.9194)	0.9600 (0.8494 to 0.9898)	0.8322 (0.7228 to 0.9013)	
16 Months	0.9403 (0.8460 to 0.9776)	0.8542 (0.7440 to 0.9194)	0.9600 (0.8494 to 0.9898)	0.8322 (0.7228 to 0.9013)	
Number of patients at risk[b]					
2 Months	89	70	53	68	
4 Months	82	64	52	65	
6 Months	75	55	40	61	
8 Months	63	51	40	58	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.1 Treatment emergent adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	60	47	38	51	
12 Months	52	41	31	46	
14 Months	34	26	17	34	
16 Months	16	9	9	13	
Eye disorders (days)					
Number (%) of events	9 (9.6)	6 (7.8)	6 (10.9)	7 (9.3)	0.9350
Number (%) of patients censored	85 (90.4)	71 (92.2)	49 (89.1)	68 (90.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.9795 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5666		0.6248	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.1 Treatment emergent adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5488 (0.4579 to 0.6308)	0.3952 (0.3094 to 0.4797)	0.5000 (0.2286 to 0.7221)	0.3516 (0.1100 to 0.6095)	
Number of patients at risk[b]					
2 Months	91	70	7	7	
4 Months	77	58	7	6	
6 Months	66	48	6	4	
8 Months	58	45	6	4	
10 Months	55	42	6	3	
12 Months	49	37	4	3	
14 Months	30	26	3	1	
16 Months	16	9	3	0	
Cardiac disorders (days)					
Number (%) of events	6 (4.4)	20 (14.7)	0 (0.0)	2 (12.5)	0.9898
Number (%) of patients censored	129 (95.6)	116 (85.3)	14 (100.0)	14 (87.5)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.1 Treatment emergent adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.6612 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.5996 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0068		0.1474	
Hazard ratio (95% CI) vs Pd	-	3.28 (1.32 to 8.17)		NC	
P-value	-	0.0107		0.9977	
Hazard ratio inverted (95% CI) vs IPd	0.30 (0.12 to 0.76)				
Events probability (95% CI)[b]					
2 Months	0.9924 (0.9471 to 0.9989)	0.9189 (0.8584 to 0.9543)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9924 (0.9471 to 0.9989)	0.9041 (0.8405 to 0.9431)	1.0000 (1.0000 to 1.0000)	0.9231 (0.5664 to 0.9888)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.1 Treatment emergent adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9755 (0.9260 to 0.9921)	0.8964 (0.8313 to 0.9373)	1.0000 (1.0000 to 1.0000)	0.8308 (0.4717 to 0.9553)	
8 Months	0.9658 (0.9110 to 0.9871)	0.8794 (0.8105 to 0.9244)	1.0000 (1.0000 to 1.0000)	0.8308 (0.4717 to 0.9553)	
10 Months	0.9552 (0.8949 to 0.9812)	0.8432 (0.7669 to 0.8962)	1.0000 (1.0000 to 1.0000)	0.8308 (0.4717 to 0.9553)	
12 Months	0.9552 (0.8949 to 0.9812)	0.8432 (0.7669 to 0.8962)	1.0000 (1.0000 to 1.0000)	0.8308 (0.4717 to 0.9553)	
14 Months	0.9428 (0.8755 to 0.9742)	0.8432 (0.7669 to 0.8962)	1.0000 (1.0000 to 1.0000)	0.8308 (0.4717 to 0.9553)	
16 Months	0.9428 (0.8755 to 0.9742)	0.8432 (0.7669 to 0.8962)	1.0000 (1.0000 to 1.0000)	0.8308 (0.4717 to 0.9553)	
Number of patients at risk[b]					
2 Months	128	124	14	14	
4 Months	121	118	13	11	
6 Months	105	109	10	7	
8 Months	94	102	9	7	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.1 Treatment emergent adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	90	91	8	7	
12 Months	77	80	6	7	
14 Months	47	56	4	4	
16 Months	22	20	3	2	
Eye disorders (days)					
Number (%) of events	13 (9.6)	10 (7.4)	2 (14.3)	3 (18.8)	0.4630
Number (%) of patients censored	122 (90.4)	126 (92.6)	12 (85.7)	13 (81.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.7084 to NC)	8.8871 (6.1437 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.1437 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.3018 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3641		0.6972	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.1 Treatment emergent adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5666 (0.4197 to 0.6896)	0.3834 (0.2535 to 0.5119)	0.6037 (0.4587 to 0.7212)	0.4376 (0.2978 to 0.5689)	0.4180 (0.2518 to 0.5760)	0.2617 (0.1207 to 0.4274)	
Number of patients at risk[b]							
2 Months	35	32	39	28	22	14	
4 Months	33	29	35	22	14	10	
6 Months	31	23	29	18	10	8	
8 Months	28	22	25	17	9	7	
10 Months	27	19	23	16	9	7	
12 Months	25	15	18	16	8	6	
14 Months	15	10	12	11	6	3	
16 Months	11	4	5	5	3	0	
Cardiac disorders (days)							
Number (%) of events	2 (3.9)	6 (9.5)	4 (7.3)	11 (20.8)	0 (0.0)	5 (15.2)	0.9828
Number (%) of patients censored	49 (96.1)	57 (90.5)	51 (92.7)	42 (79.2)	40 (100.0)	28 (84.8)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.1 Treatment emergent adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.3326 to NC)	NC (NC to NC)	NC (2.6612 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2268		0.0425		0.0234	
Hazard ratio (95% CI) vs Pd	-	2.59 (0.52 to 12.83)		3.08 (0.98 to 9.68)		NC	
P-value	-	0.2443		0.0541		0.9964	
Events probability (95% CI)[b]							
2 Months	1.0000 (1.0000 to 1.0000)	0.9524 (0.8596 to 0.9844)	0.9815 (0.8757 to 0.9974)	0.8856 (0.7628 to 0.9469)	1.0000 (1.0000 to 1.0000)	0.9384 (0.7754 to 0.9842)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9365 (0.8396 to 0.9757)	0.9815 (0.8757 to 0.9974)	0.8659 (0.7390 to 0.9337)	1.0000 (1.0000 to 1.0000)	0.9061 (0.7361 to 0.9687)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_seiss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.1 Treatment emergent adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9800 (0.8664 to 0.9972)	0.9365 (0.8396 to 0.9757)	0.9622 (0.8573 to 0.9904)	0.8237 (0.6880 to 0.9043)	1.0000 (1.0000 to 1.0000)	0.9061 (0.7361 to 0.9687)	
8 Months	0.9800 (0.8664 to 0.9972)	0.9185 (0.8149 to 0.9653)	0.9393 (0.8225 to 0.9802)	0.8014 (0.6614 to 0.8882)	1.0000 (1.0000 to 1.0000)	0.9061 (0.7361 to 0.9687)	
10 Months	0.9582 (0.8428 to 0.9894)	0.8998 (0.7897 to 0.9538)	0.9393 (0.8225 to 0.9802)	0.7764 (0.6308 to 0.8702)	1.0000 (1.0000 to 1.0000)	0.8155 (0.6049 to 0.9205)	
12 Months	0.9582 (0.8428 to 0.9894)	0.8998 (0.7897 to 0.9538)	0.9393 (0.8225 to 0.9802)	0.7764 (0.6308 to 0.8702)	1.0000 (1.0000 to 1.0000)	0.8155 (0.6049 to 0.9205)	
14 Months	0.9582 (0.8428 to 0.9894)	0.8998 (0.7897 to 0.9538)	0.9045 (0.7563 to 0.9646)	0.7764 (0.6308 to 0.8702)	1.0000 (1.0000 to 1.0000)	0.8155 (0.6049 to 0.9205)	
16 Months	0.9582 (0.8428 to 0.9894)	0.8998 (0.7897 to 0.9538)	0.9045 (0.7563 to 0.9646)	0.7764 (0.6308 to 0.8702)	1.0000 (1.0000 to 1.0000)	0.8155 (0.6049 to 0.9205)	
Number of patients at risk[b]							
2 Months	51	60	53	45	35	30	
4 Months	50	59	53	41	29	26	
6 Months	49	53	44	37	20	23	
8 Months	46	51	38	35	17	20	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_seiss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.1 Treatment emergent adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	44	48	36	30	16	17	
12 Months	40	43	27	25	14	16	
14 Months	25	29	16	17	10	11	
16 Months	14	13	7	4	4	5	
Eye disorders (days)							
Number (%) of events	3 (5.9)	9 (14.3)	7 (12.7)	3 (5.7)	4 (10.0)	1 (3.0)	0.0661
Number (%) of patients censored	48 (94.1)	54 (85.7)	48 (87.3)	50 (94.3)	36 (90.0)	32 (97.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (10.6119 to NC)	NC (4.2053 to NC)	NC (NC to NC)	NC (5.9795 to NC)	NC (6.4723 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1337		0.1714		0.1624	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.1 Treatment emergent adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0.5789 (0.3872 to 0.7298)	0.3869 (0.2281 to 0.5433)	0.5822 (0.4749 to 0.6750)	0.4054 (0.3050 to 0.5034)	0.2988 (0.1057 to 0.5223)	0.3333 (0.1090 to 0.5801)	
16 Months	0.5789 (0.3872 to 0.7298)	0.3869 (0.2281 to 0.5433)	0.5822 (0.4749 to 0.6750)	0.4054 (0.3050 to 0.5034)	0.2988 (0.1057 to 0.5223)	0.3333 (0.1090 to 0.5801)	
Number of patients at risk[b]							
2 Months	21	21	67	49	10	7	
4 Months	20	19	60	40	4	5	
6 Months	20	17	49	32	3	3	
8 Months	18	16	43	31	3	2	
10 Months	17	15	41	28	3	2	
12 Months	16	13	34	25	3	2	
14 Months	8	8	22	17	3	2	
16 Months	6	4	12	5	1	0	
Cardiac disorders (days)							
Number (%) of events	2 (6.5)	6 (15.4)	4 (4.1)	15 (15.3)	0 (0.0)	1 (6.7)	0.9225

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.1 Treatment emergent adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of patients censored	29 (93.5)	33 (84.6)	93 (95.9)	83 (84.7)	21 (100.0)	14 (93.3)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (2.7926 to NC)	NC (NC to NC)	NC (9.4620 to NC)	NC (NC to NC)	NC (2.6612 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2283		0.0105		0.3006	
Hazard ratio (95% CI) vs Pd	-	2.58 (0.52 to 12.79)		3.81 (1.27 to 11.49)		NC	
P-value	-	0.2457		0.0174		0.9984	
Hazard ratio inverted (95% CI) vs IPd			0.26 (0.09 to 0.79)				
Events probability (95% CI)[b]							

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_seriss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.1 Treatment emergent adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	0.9231 (0.7802 to 0.9745)	0.9895 (0.9276 to 0.9985)	0.9180 (0.8428 to 0.9581)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
4 Months	1.0000 (1.0000 to 1.0000)	0.8974 (0.7494 to 0.9602)	0.9895 (0.9276 to 0.9985)	0.9076 (0.8299 to 0.9508)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	
6 Months	0.9677 (0.7923 to 0.9954)	0.8974 (0.7494 to 0.9602)	0.9784 (0.9162 to 0.9945)	0.8856 (0.8028 to 0.9350)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	
8 Months	0.9677 (0.7923 to 0.9954)	0.8702 (0.7157 to 0.9439)	0.9650 (0.8945 to 0.9886)	0.8733 (0.7873 to 0.9261)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	
10 Months	0.9344 (0.7621 to 0.9832)	0.8430 (0.6833 to 0.9263)	0.9650 (0.8945 to 0.9886)	0.8335 (0.7379 to 0.8967)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	
12 Months	0.9344 (0.7621 to 0.9832)	0.8430 (0.6833 to 0.9263)	0.9650 (0.8945 to 0.9886)	0.8335 (0.7379 to 0.8967)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	
14 Months	0.9344 (0.7621 to 0.9832)	0.8430 (0.6833 to 0.9263)	0.9464 (0.8595 to 0.9801)	0.8335 (0.7379 to 0.8967)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	
16 Months	0.9344 (0.7621 to 0.9832)	0.8430 (0.6833 to 0.9263)	0.9464 (0.8595 to 0.9801)	0.8335 (0.7379 to 0.8967)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	

Number of patients at risk[b]

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.1 Treatment emergent adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	31	36	94	88	17	14	
4 Months	31	35	91	83	12	11	
6 Months	30	33	78	74	7	9	
8 Months	29	32	68	70	6	7	
10 Months	28	31	64	61	6	6	
12 Months	26	28	52	53	5	6	
14 Months	15	17	32	37	4	6	
16 Months	9	8	15	12	1	2	
Eye disorders (days)							
Number (%) of events	3 (9.7)	4 (10.3)	10 (10.3)	9 (9.2)	2 (9.5)	0 (0.0)	0.9589
Number (%) of patients censored	28 (90.3)	35 (89.7)	87 (89.7)	89 (90.8)	19 (90.5)	15 (100.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (3.1211 to NC)	NC (11.3018 to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.1314 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.9795 to NC)	NC (NC to NC)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_seriss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.4010 (0.1772 to 0.6172)	0.4643 (0.1934 to 0.6988)	0.5899 (0.4806 to 0.6837)	0.3752 (0.2853 to 0.4649)	
Number of patients at risk[b]					
2 Months	13	6	65	59	
4 Months	11	5	55	48	
6 Months	6	3	50	40	
8 Months	6	3	43	37	
10 Months	6	2	41	34	
12 Months	6	2	37	29	
14 Months	6	2	25	20	
16 Months	4	0	13	7	
Cardiac disorders (days)					
Number (%) of events	0 (0.0)	3 (21.4)	4 (4.3)	15 (12.9)	0.9888
Number (%) of patients censored	21 (100.0)	11 (78.6)	89 (95.7)	101 (87.1)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	4.4353 (1.9384 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (2.6612 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0339		0.0384	
Hazard ratio (95% CI) vs Pd	-	NC		3.03 (1.00 to 9.13)	
P-value	-	0.9972		0.0490	
Hazard ratio inverted (95% CI) vs IPd			0.33 (0.11 to 1.00)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9167 (0.5390 to 0.9878)	0.9891 (0.9253 to 0.9985)	0.9224 (0.8562 to 0.9589)	
4 Months	1.0000 (1.0000 to 1.0000)	0.8333 (0.4817 to 0.9555)	0.9891 (0.9253 to 0.9985)	0.9050 (0.8350 to 0.9462)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	1.0000 (1.0000 to 1.0000)	0.7292 (0.3677 to 0.9051)	0.9778 (0.9140 to 0.9944)	0.8959 (0.8239 to 0.9395)	
8 Months	1.0000 (1.0000 to 1.0000)	0.7292 (0.3677 to 0.9051)	0.9640 (0.8918 to 0.9883)	0.8959 (0.8239 to 0.9395)	
10 Months	1.0000 (1.0000 to 1.0000)	0.7292 (0.3677 to 0.9051)	0.9640 (0.8918 to 0.9883)	0.8648 (0.7853 to 0.9164)	
12 Months	1.0000 (1.0000 to 1.0000)	0.7292 (0.3677 to 0.9051)	0.9640 (0.8918 to 0.9883)	0.8648 (0.7853 to 0.9164)	
14 Months	1.0000 (1.0000 to 1.0000)	0.7292 (0.3677 to 0.9051)	0.9458 (0.8587 to 0.9798)	0.8648 (0.7853 to 0.9164)	
16 Months	1.0000 (1.0000 to 1.0000)	0.7292 (0.3677 to 0.9051)	0.9458 (0.8587 to 0.9798)	0.8648 (0.7853 to 0.9164)	
Number of patients at risk[b]					
2 Months	18	11	91	107	
4 Months	15	8	87	101	
6 Months	10	6	75	93	
8 Months	10	5	67	91	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	10	4	64	82	
12 Months	10	4	53	72	
14 Months	9	3	34	52	
16 Months	4	1	17	19	
Eye disorders (days)					
Number (%) of events	0 (0.0)	1 (7.1)	11 (11.8)	9 (7.8)	0.9919
Number (%) of patients censored	21 (100.0)	13 (92.9)	82 (88.2)	107 (92.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (9.3634 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (9.3634 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (9.3634 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1573		0.2395	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.4331 (0.2567 to 0.5975)	0.3188 (0.1421 to 0.5119)	0.6048 (0.4828 to 0.7066)	0.3837 (0.2874 to 0.4791)	
Number of patients at risk[b]					
2 Months	21	7	54	55	
4 Months	18	6	46	44	
6 Months	12	4	42	36	
8 Months	12	3	35	34	
10 Months	12	2	33	31	
12 Months	11	2	30	26	
14 Months	9	2	21	18	
16 Months	6	0	11	6	
Cardiac disorders (days)					
Number (%) of events	0 (0.0)	3 (13.0)	4 (5.3)	15 (14.6)	0.9899
Number (%) of patients censored	34 (100.0)	20 (87.0)	72 (94.7)	88 (85.4)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (1.9384 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0365		0.0532	
Hazard ratio (95% CI) vs Pd	-	NC		2.83 (0.94 to 8.53)	
P-value	-	0.9972		0.0644	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9524 (0.7072 to 0.9932)	0.9867 (0.9091 to 0.9981)	0.9126 (0.8388 to 0.9535)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9048 (0.6700 to 0.9753)	0.9867 (0.9091 to 0.9981)	0.8930 (0.8151 to 0.9393)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	1.0000 (1.0000 to 1.0000)	0.8515 (0.6060 to 0.9497)	0.9732 (0.8969 to 0.9932)	0.8826 (0.8025 to 0.9316)	
8 Months	1.0000 (1.0000 to 1.0000)	0.8515 (0.6060 to 0.9497)	0.9567 (0.8708 to 0.9859)	0.8826 (0.8025 to 0.9316)	
10 Months	1.0000 (1.0000 to 1.0000)	0.8515 (0.6060 to 0.9497)	0.9567 (0.8708 to 0.9859)	0.8471 (0.7585 to 0.9052)	
12 Months	1.0000 (1.0000 to 1.0000)	0.8515 (0.6060 to 0.9497)	0.9567 (0.8708 to 0.9859)	0.8471 (0.7585 to 0.9052)	
14 Months	1.0000 (1.0000 to 1.0000)	0.8515 (0.6060 to 0.9497)	0.9349 (0.8320 to 0.9757)	0.8471 (0.7585 to 0.9052)	
16 Months	1.0000 (1.0000 to 1.0000)	0.8515 (0.6060 to 0.9497)	0.9349 (0.8320 to 0.9757)	0.8471 (0.7585 to 0.9052)	
Number of patients at risk[b]					
2 Months	31	20	74	94	
4 Months	27	17	73	88	
6 Months	20	15	63	80	
8 Months	20	13	55	79	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	20	12	52	70	
12 Months	17	10	44	62	
14 Months	13	7	29	45	
16 Months	7	2	14	17	
Eye disorders (days)					
Number (%) of events	0 (0.0)	2 (8.7)	11 (14.5)	7 (6.8)	0.9895
Number (%) of patients censored	34 (100.0)	21 (91.3)	65 (85.5)	96 (93.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (6.5051 to NC)	NC (5.9795 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0840		0.0726	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.1 Treatment emergent adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5554 (0.4429 to 0.6540)	0.4531 (0.3332 to 0.5653)	0.5278 (0.3899 to 0.6482)	0.3251 (0.2169 to 0.4377)	
Number of patients at risk[b]					
2 Months	61	43	37	34	
4 Months	51	36	33	28	
6 Months	43	31	29	21	
8 Months	39	28	25	21	
10 Months	37	26	24	19	
12 Months	34	23	19	17	
14 Months	22	16	11	11	
16 Months	13	4	6	5	
Cardiac disorders (days)					
Number (%) of events	6 (6.8)	7 (8.6)	0 (0.0)	15 (21.1)	0.9866
Number (%) of patients censored	82 (93.2)	74 (91.4)	61 (100.0)	56 (78.9)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.1 Treatment emergent adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.7926 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6774		0.0003	
Hazard ratio (95% CI) vs Pd	-	1.26 (0.42 to 3.75)		NC	
P-value	-	0.6781		0.9904	
Events probability (95% CI)[b]					
2 Months	0.9886 (0.9221 to 0.9984)	0.9625 (0.8882 to 0.9877)	1.0000 (1.0000 to 1.0000)	0.8873 (0.7873 to 0.9420)	
4 Months	0.9886 (0.9221 to 0.9984)	0.9625 (0.8882 to 0.9877)	1.0000 (1.0000 to 1.0000)	0.8439 (0.7358 to 0.9104)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.1 Treatment emergent adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9633 (0.8903 to 0.9880)	0.9491 (0.8700 to 0.9806)	1.0000 (1.0000 to 1.0000)	0.8286 (0.7177 to 0.8989)	
8 Months	0.9485 (0.8678 to 0.9805)	0.9341 (0.8483 to 0.9721)	1.0000 (1.0000 to 1.0000)	0.8120 (0.6979 to 0.8864)	
10 Months	0.9329 (0.8452 to 0.9717)	0.9007 (0.8014 to 0.9518)	1.0000 (1.0000 to 1.0000)	0.7785 (0.6588 to 0.8605)	
12 Months	0.9329 (0.8452 to 0.9717)	0.9007 (0.8014 to 0.9518)	1.0000 (1.0000 to 1.0000)	0.7785 (0.6588 to 0.8605)	
14 Months	0.9150 (0.8184 to 0.9614)	0.9007 (0.8014 to 0.9518)	1.0000 (1.0000 to 1.0000)	0.7785 (0.6588 to 0.8605)	
16 Months	0.9150 (0.8184 to 0.9614)	0.9007 (0.8014 to 0.9518)	1.0000 (1.0000 to 1.0000)	0.7785 (0.6588 to 0.8605)	
Number of patients at risk[b]					
2 Months	86	76	56	62	
4 Months	81	72	53	57	
6 Months	69	66	46	50	
8 Months	63	60	40	49	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.1 Treatment emergent adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	60	54	38	44	
12 Months	52	48	31	39	
14 Months	32	33	19	27	
16 Months	16	14	9	8	
Eye disorders (days)					
Number (%) of events	10 (11.4)	4 (4.9)	5 (8.2)	9 (12.7)	0.1256
Number (%) of patients censored	78 (88.6)	77 (95.1)	56 (91.8)	62 (87.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.3018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1048		0.5579	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.1 Treatment emergent adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.5378 (0.4510 to 0.6167)	0.3905 (0.3081 to 0.4718)	
Number of patients at risk[b]					
2 Months	2	2	96	75	
4 Months	2	1	82	63	
6 Months	2	1	70	51	
8 Months	2	1	62	48	
10 Months	1	1	60	44	
12 Months	1	1	52	39	
14 Months	1	0	32	27	
16 Months	0	0	19	9	
Cardiac disorders (days)					
Number (%) of events	0 (0.0)	0 (0.0)	6 (4.1)	22 (14.7)	0.9995
Number (%) of patients censored	2 (100.0)	2 (100.0)	141 (95.9)	128 (85.3)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.1 Treatment emergent adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0027	
Hazard ratio (95% CI) vs Pd	-	NC		3.63 (1.47 to 8.96)	
P-value	-			0.0051	
Hazard ratio inverted (95% CI) vs IPd			0.28 (0.11 to 0.68)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9930 (0.9514 to 0.9990)	0.9261 (0.8705 to 0.9584)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9930 (0.9514 to 0.9990)	0.9055 (0.8456 to 0.9429)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.1 Treatment emergent adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9775 (0.9317 to 0.9927)	0.8910 (0.8282 to 0.9318)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9684 (0.9175 to 0.9881)	0.8749 (0.8084 to 0.9194)	
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9585 (0.9024 to 0.9826)	0.8406 (0.7673 to 0.8925)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9585 (0.9024 to 0.9826)	0.8406 (0.7673 to 0.8925)	
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9468 (0.8838 to 0.9761)	0.8406 (0.7673 to 0.8925)	
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9468 (0.8838 to 0.9761)	0.8406 (0.7673 to 0.8925)	
Number of patients at risk[b]					
2 Months	2	2	140	136	
4 Months	2	2	132	127	
6 Months	2	2	113	114	
8 Months	2	2	101	107	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.1 Treatment emergent adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	1	2	97	96	
12 Months	1	1	82	86	
14 Months	1	0	50	60	
16 Months	0	0	25	22	
Eye disorders (days)					
Number (%) of events	1 (50.0)	0 (0.0)	14 (9.5)	13 (8.7)	0.9880
Number (%) of patients censored	1 (50.0)	2 (100.0)	133 (90.5)	137 (91.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.8255 (2.8255 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (2.8255 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (2.8255 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.6209	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5642 (0.4572 to 0.6579)	0.4132 (0.3121 to 0.5112)	0.5294 (0.3599 to 0.6731)	0.2461 (0.1141 to 0.4043)	
Number of patients at risk[b]					
2 Months	68	56	24	10	
4 Months	59	48	21	9	
6 Months	50	41	18	8	
8 Months	46	39	14	7	
10 Months	43	35	14	7	
12 Months	37	30	13	7	
14 Months	24	21	6	4	
16 Months	13	7	4	1	
Cardiac disorders (days)					
Number (%) of events	5 (5.1)	14 (13.6)	1 (2.5)	8 (25.0)	0.5067
Number (%) of patients censored	93 (94.9)	89 (86.4)	39 (97.5)	24 (75.0)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	9.4620 (1.0842 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0538		0.0054	
Hazard ratio (95% CI) vs Pd	-	2.63 (0.95 to 7.30)		10.64 (1.33 to 85.09)	
P-value	-	0.0636		0.0258	
Hazard ratio inverted (95% CI) vs IPd			0.09 (0.01 to 0.75)		
Events probability (95% CI)[b]					
2 Months	0.9896 (0.9284 to 0.9985)	0.9413 (0.8739 to 0.9732)	1.0000 (1.0000 to 1.0000)	0.8438 (0.6646 to 0.9318)	
4 Months	0.9896 (0.9284 to 0.9985)	0.9315 (0.8616 to 0.9667)	1.0000 (1.0000 to 1.0000)	0.7788 (0.5911 to 0.8880)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9783 (0.9161 to 0.9945)	0.9105 (0.8350 to 0.9524)	0.9697 (0.8037 to 0.9957)	0.7788 (0.5911 to 0.8880)	
8 Months	0.9646 (0.8932 to 0.9885)	0.8876 (0.8059 to 0.9363)	0.9697 (0.8037 to 0.9957)	0.7788 (0.5911 to 0.8880)	
10 Months	0.9497 (0.8701 to 0.9811)	0.8509 (0.7603 to 0.9093)	0.9697 (0.8037 to 0.9957)	0.7434 (0.5510 to 0.8629)	
12 Months	0.9497 (0.8701 to 0.9811)	0.8509 (0.7603 to 0.9093)	0.9697 (0.8037 to 0.9957)	0.7434 (0.5510 to 0.8629)	
14 Months	0.9321 (0.8419 to 0.9717)	0.8509 (0.7603 to 0.9093)	0.9697 (0.8037 to 0.9957)	0.7434 (0.5510 to 0.8629)	
16 Months	0.9321 (0.8419 to 0.9717)	0.8509 (0.7603 to 0.9093)	0.9697 (0.8037 to 0.9957)	0.7434 (0.5510 to 0.8629)	
Number of patients at risk[b]					
2 Months	94	96	38	26	
4 Months	91	91	34	24	
6 Months	75	83	32	23	
8 Months	67	76	28	23	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	64	67	27	21	
12 Months	54	58	23	20	
14 Months	33	40	12	13	
16 Months	17	13	6	4	
Eye disorders (days)					
Number (%) of events	9 (9.2)	8 (7.8)	5 (12.5)	4 (12.5)	0.9752
Number (%) of patients censored	89 (90.8)	95 (92.2)	35 (87.5)	28 (87.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.6283 to NC)	NC (6.5051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5510		0.8874	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	67	56	30	21	
4 Months	58	48	25	16	
6 Months	49	41	22	11	
8 Months	45	39	18	10	
10 Months	42	35	18	10	
12 Months	36	30	16	10	
14 Months	23	21	9	6	
16 Months	12	7	6	2	
Cardiac disorders (days)					
Number (%) of events	5 (5.2)	14 (13.9)	1 (2.0)	8 (16.0)	0.3320
Number (%) of patients censored	92 (94.8)	87 (86.1)	50 (98.0)	42 (84.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.6612 to NC)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0509		0.0161	
Hazard ratio (95% CI) vs Pd	-	2.66 (0.96 to 7.38)		8.40 (1.05 to 67.13)	
P-value	-	0.0606		0.0449	
Hazard ratio inverted (95% CI) vs IPd			0.12 (0.01 to 0.95)		
Events probability (95% CI)[b]					
2 Months	0.9895 (0.9276 to 0.9985)	0.9401 (0.8715 to 0.9726)	1.0000 (1.0000 to 1.0000)	0.8991 (0.7744 to 0.9567)	
4 Months	0.9895 (0.9276 to 0.9985)	0.9301 (0.8589 to 0.9660)	1.0000 (1.0000 to 1.0000)	0.8568 (0.7227 to 0.9291)	
6 Months	0.9781 (0.9152 to 0.9945)	0.9087 (0.8318 to 0.9515)	0.9762 (0.8428 to 0.9966)	0.8568 (0.7227 to 0.9291)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.9641 (0.8919 to 0.9884)	0.8853 (0.8020 to 0.9349)	0.9762 (0.8428 to 0.9966)	0.8568 (0.7227 to 0.9291)	
10 Months	0.9491 (0.8685 to 0.9808)	0.8476 (0.7553 to 0.9072)	0.9762 (0.8428 to 0.9966)	0.8308 (0.6886 to 0.9120)	
12 Months	0.9491 (0.8685 to 0.9808)	0.8476 (0.7553 to 0.9072)	0.9762 (0.8428 to 0.9966)	0.8308 (0.6886 to 0.9120)	
14 Months	0.9312 (0.8397 to 0.9713)	0.8476 (0.7553 to 0.9072)	0.9762 (0.8428 to 0.9966)	0.8308 (0.6886 to 0.9120)	
16 Months	0.9312 (0.8397 to 0.9713)	0.8476 (0.7553 to 0.9072)	0.9762 (0.8428 to 0.9966)	0.8308 (0.6886 to 0.9120)	
Number of patients at risk[b]					
2 Months	93	94	48	43	
4 Months	90	89	43	39	
6 Months	74	81	40	34	
8 Months	66	74	36	34	
10 Months	63	65	34	32	
12 Months	53	56	29	30	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	32	39	18	21	
16 Months	16	13	8	9	
Eye disorders (days)					
Number (%) of events	9 (9.3)	7 (6.9)	6 (11.8)	6 (12.0)	0.6270
Number (%) of patients censored	88 (90.7)	94 (93.1)	45 (88.2)	44 (88.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.0883 to NC)	NC (7.1294 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3894		0.9724	
Hazard ratio (95% CI) vs Pd	-	0.65 (0.24 to 1.75)		0.98 (0.32 to 3.04)	
P-value	-	0.3930		0.9724	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.1 Treatment emergent adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.8889 (0.4330 to 0.9836)	0.4286 (0.1773 to 0.6604)	0.5257 (0.4377 to 0.6063)	0.3875 (0.3014 to 0.4727)	
Number of patients at risk[b]					
2 Months	8	7	90	70	
4 Months	6	6	78	58	
6 Months	4	5	68	47	
8 Months	2	5	62	44	
10 Months	2	5	59	40	
12 Months	2	4	51	36	
14 Months	2	3	31	24	
16 Months	0	2	19	7	
Cardiac disorders (days)					
Number (%) of events	0 (0.0)	2 (14.3)	6 (4.3)	20 (14.5)	0.9889
Number (%) of patients censored	10 (100.0)	12 (85.7)	133 (95.7)	118 (85.5)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.1 Treatment emergent adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (2.6612 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (9.0678 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4054		0.0045	
Hazard ratio (95% CI) vs Pd	-	NC		3.46 (1.39 to 8.63)	
P-value	-	0.9972		0.0076	
Hazard ratio inverted (95% CI) vs IPd			0.29 (0.12 to 0.72)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9926 (0.9490 to 0.9990)	0.9196 (0.8595 to 0.9546)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9926 (0.9490 to 0.9990)	0.9046 (0.8414 to 0.9435)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.1 Treatment emergent adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9766 (0.9292 to 0.9924)	0.8888 (0.8223 to 0.9315)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9673 (0.9150 to 0.9877)	0.8715 (0.8011 to 0.9182)	
10 Months	1.0000 (1.0000 to 1.0000)	0.8357 (0.4804 to 0.9570)	0.9574 (0.9000 to 0.9821)	0.8436 (0.7674 to 0.8965)	
12 Months	1.0000 (1.0000 to 1.0000)	0.8357 (0.4804 to 0.9570)	0.9574 (0.9000 to 0.9821)	0.8436 (0.7674 to 0.8965)	
14 Months	1.0000 (1.0000 to 1.0000)	0.8357 (0.4804 to 0.9570)	0.9455 (0.8814 to 0.9755)	0.8436 (0.7674 to 0.8965)	
16 Months	1.0000 (1.0000 to 1.0000)	0.8357 (0.4804 to 0.9570)	0.9455 (0.8814 to 0.9755)	0.8436 (0.7674 to 0.8965)	
Number of patients at risk[b]					
2 Months	9	14	133	124	
4 Months	7	13	127	116	
6 Months	5	11	110	105	
8 Months	2	10	101	99	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.1 Treatment emergent adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	2	9	96	89	
12 Months	2	7	81	80	
14 Months	2	6	49	54	
16 Months	0	4	25	18	
Eye disorders (days)					
Number (%) of events	0 (0.0)	1 (7.1)	15 (10.8)	12 (8.7)	0.9876
Number (%) of patients censored	10 (100.0)	13 (92.9)	124 (89.2)	126 (91.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (9.3634 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (9.3634 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6547		0.4457	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.1 Treatment emergent adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5684 (0.4588 to 0.6639)	0.3962 (0.2869 to 0.5033)	0.4967 (0.3453 to 0.6310)	0.3595 (0.2318 to 0.4887)	
Number of patients at risk[b]					
2 Months	63	44	30	26	
4 Months	56	38	24	21	
6 Months	47	32	22	18	
8 Months	43	31	18	16	
10 Months	40	28	18	15	
12 Months	35	24	16	14	
14 Months	19	16	12	9	
16 Months	11	7	6	2	
Cardiac disorders (days)					
Number (%) of events	5 (5.3)	10 (11.6)	1 (2.1)	12 (22.2)	0.1772
Number (%) of patients censored	89 (94.7)	76 (88.4)	46 (97.9)	42 (77.8)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.1 Treatment emergent adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.6612 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1499		0.0055	
Hazard ratio (95% CI) vs Pd	-	2.16 (0.74 to 6.32)		10.25 (1.33 to 78.85)	
P-value	-	0.1601		0.0254	
Hazard ratio inverted (95% CI) vs IPd			0.10 (0.01 to 0.75)		
Events probability (95% CI)[b]					
2 Months	0.9892 (0.9261 to 0.9985)	0.9414 (0.8650 to 0.9752)	1.0000 (1.0000 to 1.0000)	0.8889 (0.7693 to 0.9485)	
4 Months	0.9892 (0.9261 to 0.9985)	0.9297 (0.8501 to 0.9678)	1.0000 (1.0000 to 1.0000)	0.8514 (0.7248 to 0.9228)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.1 Treatment emergent adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9654 (0.8964 to 0.9887)	0.9054 (0.8196 to 0.9515)	1.0000 (1.0000 to 1.0000)	0.8514 (0.7248 to 0.9228)	
8 Months	0.9654 (0.8964 to 0.9887)	0.8922 (0.8030 to 0.9425)	0.9677 (0.7923 to 0.9954)	0.8290 (0.6965 to 0.9074)	
10 Months	0.9512 (0.8745 to 0.9815)	0.8785 (0.7856 to 0.9328)	0.9677 (0.7923 to 0.9954)	0.7558 (0.6071 to 0.8546)	
12 Months	0.9512 (0.8745 to 0.9815)	0.8785 (0.7856 to 0.9328)	0.9677 (0.7923 to 0.9954)	0.7558 (0.6071 to 0.8546)	
14 Months	0.9351 (0.8494 to 0.9728)	0.8785 (0.7856 to 0.9328)	0.9677 (0.7923 to 0.9954)	0.7558 (0.6071 to 0.8546)	
16 Months	0.9351 (0.8494 to 0.9728)	0.8785 (0.7856 to 0.9328)	0.9677 (0.7923 to 0.9954)	0.7558 (0.6071 to 0.8546)	
Number of patients at risk[b]					
2 Months	91	80	44	48	
4 Months	87	77	41	44	
6 Months	77	71	34	40	
8 Months	71	68	28	36	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.1 Treatment emergent adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	67	64	27	29	
12 Months	59	55	22	27	
14 Months	35	38	14	18	
16 Months	16	16	7	5	
Eye disorders (days)					
Number (%) of events	11 (11.7)	8 (9.3)	4 (8.5)	5 (9.3)	0.7167
Number (%) of patients censored	83 (88.3)	78 (90.7)	43 (91.5)	49 (90.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4572		0.9460	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.1 Treatment emergent adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.5456 (0.4590 to 0.6241)	0.3828 (0.3006 to 0.4643)	
Number of patients at risk[b]					
2 Months	1	2	97	75	
4 Months	1	2	83	62	
6 Months	0	2	72	50	
8 Months	0	2	64	47	
10 Months	0	2	61	43	
12 Months	0	2	53	38	
14 Months	0	2	33	25	
16 Months	0	0	19	9	
Cardiac disorders (days)					
Number (%) of events	0 (0.0)	0 (0.0)	6 (4.1)	22 (14.7)	0.9996
Number (%) of patients censored	2 (100.0)	2 (100.0)	141 (95.9)	128 (85.3)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.1 Treatment emergent adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0026	
Hazard ratio (95% CI) vs Pd	-	NC		3.65 (1.48 to 9.01)	
P-value	-			0.0049	
Hazard ratio inverted (95% CI) vs IPd			0.27 (0.11 to 0.68)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9930 (0.9514 to 0.9990)	0.9261 (0.8705 to 0.9584)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9930 (0.9514 to 0.9990)	0.9055 (0.8456 to 0.9429)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.1 Treatment emergent adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9776 (0.9321 to 0.9927)	0.8910 (0.8282 to 0.9318)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9686 (0.9182 to 0.9882)	0.8749 (0.8084 to 0.9194)	
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9589 (0.9033 to 0.9828)	0.8406 (0.7673 to 0.8925)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9589 (0.9033 to 0.9828)	0.8406 (0.7673 to 0.8925)	
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9473 (0.8849 to 0.9763)	0.8406 (0.7673 to 0.8925)	
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9473 (0.8849 to 0.9763)	0.8406 (0.7673 to 0.8925)	
Number of patients at risk[b]					
2 Months	2	2	140	136	
4 Months	2	2	132	127	
6 Months	1	2	114	114	
8 Months	0	2	103	107	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.1 Treatment emergent adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0	2	98	96	
12 Months	0	2	83	85	
14 Months	0	2	51	58	
16 Months	0	0	25	22	
Eye disorders (days)					
Number (%) of events	0 (0.0)	0 (0.0)	15 (10.2)	13 (8.7)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	132 (89.8)	137 (91.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.4971	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5311 (0.4313 to 0.6212)	0.3704 (0.2769 to 0.4638)	0.5844 (0.4062 to 0.7259)	0.4571 (0.2890 to 0.6105)	
Number of patients at risk[b]					
2 Months	71	60	27	17	
4 Months	60	50	24	14	
6 Months	51	39	21	13	
8 Months	47	36	17	13	
10 Months	44	32	17	13	
12 Months	39	28	14	12	
14 Months	24	19	9	8	
16 Months	13	8	6	1	
Cardiac disorders (days)					
Number (%) of events	3 (2.7)	19 (16.2)	3 (7.9)	3 (8.6)	0.0830
Number (%) of patients censored	108 (97.3)	98 (83.8)	35 (92.1)	32 (91.4)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (9.0678 to NC)	NC (9.7248 to NC)	NC (9.8234 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0008		0.9942	
Hazard ratio (95% CI) vs Pd	-	6.14 (1.82 to 20.75)		0.99 (0.20 to 4.93)	
P-value	-	0.0035		0.9942	
Hazard ratio inverted (95% CI) vs IPd	0.16 (0.05 to 0.55)				
Events probability (95% CI)[b]					
2 Months	0.9907 (0.9361 to 0.9987)	0.9137 (0.8455 to 0.9526)	1.0000 (1.0000 to 1.0000)	0.9714 (0.8140 to 0.9959)	
4 Months	0.9907 (0.9361 to 0.9987)	0.8874 (0.8140 to 0.9330)	1.0000 (1.0000 to 1.0000)	0.9714 (0.8140 to 0.9959)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9805 (0.9242 to 0.9951)	0.8690 (0.7921 to 0.9189)	0.9697 (0.8037 to 0.9957)	0.9714 (0.8140 to 0.9959)	
8 Months	0.9805 (0.9242 to 0.9951)	0.8485 (0.7672 to 0.9031)	0.9363 (0.7679 to 0.9837)	0.9714 (0.8140 to 0.9959)	
10 Months	0.9805 (0.9242 to 0.9951)	0.8267 (0.7411 to 0.8861)	0.9002 (0.7206 to 0.9669)	0.9020 (0.7247 to 0.9675)	
12 Months	0.9805 (0.9242 to 0.9951)	0.8267 (0.7411 to 0.8861)	0.9002 (0.7206 to 0.9669)	0.9020 (0.7247 to 0.9675)	
14 Months	0.9645 (0.8899 to 0.9888)	0.8267 (0.7411 to 0.8861)	0.9002 (0.7206 to 0.9669)	0.9020 (0.7247 to 0.9675)	
16 Months	0.9645 (0.8899 to 0.9888)	0.8267 (0.7411 to 0.8861)	0.9002 (0.7206 to 0.9669)	0.9020 (0.7247 to 0.9675)	
Number of patients at risk[b]					
2 Months	105	105	37	33	
4 Months	99	98	35	31	
6 Months	85	87	30	29	
8 Months	77	81	26	28	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	73	72	25	26	
12 Months	61	64	22	23	
14 Months	38	45	13	15	
16 Months	17	18	8	4	
Eye disorders (days)					
Number (%) of events	11 (9.9)	10 (8.5)	4 (10.5)	3 (8.6)	0.9486
Number (%) of patients censored	100 (90.1)	107 (91.5)	34 (89.5)	32 (91.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.1211 to NC)	NC (10.6119 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5746		0.6917	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5682 (0.4793 to 0.6475)	0.3921 (0.3083 to 0.4747)	0.2222 (0.0337 to 0.5131)	0.3810 (0.0612 to 0.7164)	
Number of patients at risk[b]					
2 Months	93	73	5	4	
4 Months	80	60	4	4	
6 Months	69	48	3	4	
8 Months	61	46	3	3	
10 Months	59	43	2	2	
12 Months	51	38	2	2	
14 Months	32	25	1	2	
16 Months	19	9	0	0	
Cardiac disorders (days)					
Number (%) of events	5 (3.6)	20 (13.8)	1 (11.1)	2 (28.6)	0.8534
Number (%) of patients censored	135 (96.4)	125 (86.2)	8 (88.9)	5 (71.4)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.7351 to NC)	9.8234 (1.9384 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.7351 to NC)	NC (1.9384 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.8234 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0036		0.3245	
Hazard ratio (95% CI) vs Pd	-	3.86 (1.45 to 10.28)		3.15 (0.28 to 35.09)	
P-value	-	0.0069		0.3502	
Hazard ratio inverted (95% CI) vs IPd	0.26 (0.10 to 0.69)				
Events probability (95% CI)[b]					
2 Months	0.9926 (0.9490 to 0.9990)	0.9305 (0.8748 to 0.9620)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
4 Months	0.9926 (0.9490 to 0.9990)	0.9092 (0.8488 to 0.9463)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9762 (0.9280 to 0.9923)	0.8942 (0.8306 to 0.9349)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
8 Months	0.9762 (0.9280 to 0.9923)	0.8776 (0.8101 to 0.9222)	0.8889 (0.4330 to 0.9836)	0.8571 (0.3341 to 0.9786)	
10 Months	0.9655 (0.9097 to 0.9871)	0.8515 (0.7786 to 0.9018)	0.8889 (0.4330 to 0.9836)	0.6429 (0.1515 to 0.9017)	
12 Months	0.9655 (0.9097 to 0.9871)	0.8515 (0.7786 to 0.9018)	0.8889 (0.4330 to 0.9836)	0.6429 (0.1515 to 0.9017)	
14 Months	0.9528 (0.8881 to 0.9805)	0.8515 (0.7786 to 0.9018)	0.8889 (0.4330 to 0.9836)	0.6429 (0.1515 to 0.9017)	
16 Months	0.9528 (0.8881 to 0.9805)	0.8515 (0.7786 to 0.9018)	0.8889 (0.4330 to 0.9836)	0.6429 (0.1515 to 0.9017)	
Number of patients at risk[b]					
2 Months	133	132	9	6	
4 Months	125	123	9	6	
6 Months	106	110	9	6	
8 Months	95	105	8	4	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	90	95	8	3	
12 Months	76	84	7	3	
14 Months	47	58	4	2	
16 Months	23	22	2	0	
Eye disorders (days)					
Number (%) of events	14 (10.0)	12 (8.3)	1 (11.1)	1 (14.3)	0.7101
Number (%) of patients censored	126 (90.0)	133 (91.7)	8 (88.9)	6 (85.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.6283 to NC)	NC (10.6119 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.6283 to NC)	NC (10.6119 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.6119 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4521		0.7979	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5745 (0.4615 to 0.6722)	0.4291 (0.3247 to 0.5292)	0.4997 (0.3636 to 0.6214)	0.3400 (0.2153 to 0.4686)	
Number of patients at risk[b]					
2 Months	58	45	40	32	
4 Months	51	37	33	27	
6 Months	46	30	26	22	
8 Months	41	29	23	20	
10 Months	41	28	20	17	
12 Months	35	26	18	14	
14 Months	22	16	11	11	
16 Months	12	5	7	4	
Cardiac disorders (days)					
Number (%) of events	2 (2.3)	10 (11.0)	4 (6.5)	12 (19.7)	0.6183
Number (%) of patients censored	85 (97.7)	81 (89.0)	58 (93.5)	49 (80.3)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.5996 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0237		0.0460	
Hazard ratio (95% CI) vs Pd	-	4.87 (1.07 to 22.21)		2.99 (0.97 to 9.28)	
P-value	-	0.0411		0.0576	
Hazard ratio inverted (95% CI) vs IPd	0.21 (0.05 to 0.94)				
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9446 (0.8719 to 0.9765)	0.9833 (0.8875 to 0.9976)	0.9013 (0.7935 to 0.9544)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9217 (0.8426 to 0.9619)	0.9833 (0.8875 to 0.9976)	0.8846 (0.7732 to 0.9433)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	1.0000 (1.0000 to 1.0000)	0.9217 (0.8426 to 0.9619)	0.9462 (0.8422 to 0.9824)	0.8500 (0.7313 to 0.9190)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9079 (0.8238 to 0.9530)	0.9242 (0.8093 to 0.9711)	0.8315 (0.7090 to 0.9057)	
10 Months	0.9839 (0.8910 to 0.9977)	0.8791 (0.7857 to 0.9335)	0.9242 (0.8093 to 0.9711)	0.7908 (0.6597 to 0.8759)	
12 Months	0.9839 (0.8910 to 0.9977)	0.8791 (0.7857 to 0.9335)	0.9242 (0.8093 to 0.9711)	0.7908 (0.6597 to 0.8759)	
14 Months	0.9650 (0.8664 to 0.9912)	0.8791 (0.7857 to 0.9335)	0.9242 (0.8093 to 0.9711)	0.7908 (0.6597 to 0.8759)	
16 Months	0.9650 (0.8664 to 0.9912)	0.8791 (0.7857 to 0.9335)	0.9242 (0.8093 to 0.9711)	0.7908 (0.6597 to 0.8759)	
Number of patients at risk[b]					
2 Months	83	84	59	54	
4 Months	79	77	55	52	
6 Months	70	69	45	47	
8 Months	62	66	41	43	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	61	61	37	37	
12 Months	52	57	31	30	
14 Months	32	36	19	24	
16 Months	15	12	10	10	
Eye disorders (days)					
Number (%) of events	7 (8.0)	6 (6.6)	8 (12.9)	7 (11.5)	0.9846
Number (%) of patients censored	80 (92.0)	85 (93.4)	54 (87.1)	54 (88.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.3511 to NC)	NC (10.6119 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6114		0.6463	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_llen_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.1 Treatment emergent adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	44	40	33	48	13	21	
4 Months	34	33	28	40	9	17	
6 Months	31	26	24	34	5	16	
8 Months	26	24	21	29	4	15	
10 Months	23	21	19	24	2	12	
12 Months	20	18	15	22	2	9	
14 Months	12	13	10	16	0	7	
16 Months	7	9	5	7	0	2	
Infections and infestations (days)							
Number (%) of events	47 (69.1)	40 (74.1)	30 (56.6)	57 (86.4)	19 (67.9)	26 (81.3)	0.2938
Number (%) of patients censored	21 (30.9)	14 (25.9)	23 (43.4)	9 (13.6)	9 (32.1)	6 (18.8)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	1.4620 (0.8214 to 1.6756)	0.6571 (0.3285 to 1.2485)	1.3470 (0.4928 to 1.9055)	0.6899 (0.4271 to 0.9856)	0.7885 (0.1643 to 1.4127)	0.7228 (0.3614 to 0.8871)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.1 Treatment emergent adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	2.0698 (1.8070 to 3.5154)	2.3984 (1.2485 to 4.0411)	5.3224 (1.8398 to NC)	2.0041 (1.1499 to 3.9097)	1.5113 (0.7885 to 5.2895)	2.2341 (0.7228 to 3.7454)	
75% quantile (95% CI)	NC (6.5051 to NC)	6.2094 (4.0411 to NC)	NC (9.3306 to NC)	5.8809 (3.9097 to 9.7906)	NC (2.5955 to NC)	5.2895 (2.4969 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4070		0.0037		0.6202	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.78 to 1.82)		1.91 (1.22 to 2.99)		1.16 (0.64 to 2.10)	
P-value	-	0.4076		0.0044		0.6206	
Hazard ratio inverted (95% CI) vs IPd			0.52 (0.33 to 0.82)				
Events probability (95% CI)[b]							
2 Months	0.5588 (0.4332 to 0.6671)	0.5741 (0.4319 to 0.6929)	0.6055 (0.4573 to 0.7249)	0.5009 (0.3736 to 0.6155)	0.4845 (0.2895 to 0.6546)	0.5313 (0.3471 to 0.6852)	
4 Months	0.3764 (0.2618 to 0.4905)	0.3809 (0.2518 to 0.5089)	0.5203 (0.3735 to 0.6483)	0.3444 (0.2313 to 0.4602)	0.3634 (0.1879 to 0.5418)	0.2750 (0.1343 to 0.4361)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_age_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.1 Treatment emergent adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.3764 (0.2618 to 0.4905)	0.2566 (0.1464 to 0.3817)	0.4977 (0.3516 to 0.6276)	0.2495 (0.1515 to 0.3601)	0.2768 (0.1218 to 0.4568)	0.2406 (0.1094 to 0.3997)	
8 Months	0.3226 (0.2127 to 0.4375)	0.2352 (0.1295 to 0.3589)	0.4230 (0.2801 to 0.5590)	0.1830 (0.0990 to 0.2872)	0.2768 (0.1218 to 0.4568)	0.2005 (0.0805 to 0.3588)	
10 Months	0.3047 (0.1969 to 0.4194)	0.2352 (0.1295 to 0.3589)	0.3733 (0.2352 to 0.5112)	0.1464 (0.0715 to 0.2467)	0.2768 (0.1218 to 0.4568)	0.2005 (0.0805 to 0.3588)	
12 Months	0.3047 (0.1969 to 0.4194)	0.2352 (0.1295 to 0.3589)	0.3733 (0.2352 to 0.5112)	0.1281 (0.0586 to 0.2257)	0.2768 (0.1218 to 0.4568)	0.1504 (0.0462 to 0.3112)	
14 Months	0.2830 (0.1769 to 0.3985)	0.2352 (0.1295 to 0.3589)	0.3733 (0.2352 to 0.5112)	0.1098 (0.0463 to 0.2042)	0.2768 (0.1218 to 0.4568)	0.1504 (0.0462 to 0.3112)	
16 Months	0.2830 (0.1769 to 0.3985)	0.2352 (0.1295 to 0.3589)	0.3733 (0.2352 to 0.5112)	0.1098 (0.0463 to 0.2042)	0.2768 (0.1218 to 0.4568)	0.1504 (0.0462 to 0.3112)	
Number of patients at risk[b]							
2 Months	37	30	30	32	13	17	
4 Months	24	19	24	22	9	8	
6 Months	21	12	22	15	6	6	
8 Months	18	11	17	11	4	5	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.1 Treatment emergent adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	17	11	15	8	3	4	
12 Months	15	9	12	7	1	3	
14 Months	7	5	9	6	1	2	
16 Months	5	4	3	3	1	1	
Injury, poisoning and procedural complications (days)							
Number (%) of events	5 (7.4)	27 (50.0)	4 (7.5)	29 (43.9)	8 (28.6)	16 (50.0)	0.0629
Number (%) of patients censored	63 (92.6)	27 (50.0)	49 (92.5)	37 (56.1)	20 (71.4)	16 (50.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1643)	NC (NC to NC)	0.1314 (0.0657 to 0.1971)	6.8337 (0.1971 to NC)	0.1478 (0.0657 to 4.7310)	
Median (95% CI)	NC (NC to NC)	14.7187 (0.1643 to NC)	NC (NC to NC)	15.4415 (3.0554 to NC)	NC (6.8337 to NC)	8.5092 (0.1971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.7187 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.1 Treatment emergent adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001		0.0647	
Hazard ratio (95% CI) vs Pd	-	9.67 (3.71 to 25.23)		7.40 (2.60 to 21.07)		2.26 (0.93 to 5.50)	
P-value	-	<.0001		0.0002		0.0724	
Hazard ratio inverted (95% CI) vs IPd	0.10 (0.04 to 0.27)		0.14 (0.05 to 0.39)				
Events probability (95% CI)[b]							
2 Months	0.9851 (0.8987 to 0.9979)	0.5370 (0.3962 to 0.6587)	1.0000 (1.0000 to 1.0000)	0.6364 (0.5083 to 0.7394)	0.8052 (0.5928 to 0.9141)	0.6563 (0.4658 to 0.7927)	
4 Months	0.9697 (0.8841 to 0.9923)	0.5370 (0.3962 to 0.6587)	0.9792 (0.8612 to 0.9970)	0.6208 (0.4925 to 0.7255)	0.7649 (0.5491 to 0.8871)	0.6234 (0.4330 to 0.7659)	
6 Months	0.9530 (0.8610 to 0.9846)	0.5370 (0.3962 to 0.6587)	0.9792 (0.8612 to 0.9970)	0.6208 (0.4925 to 0.7255)	0.7649 (0.5491 to 0.8871)	0.5542 (0.3651 to 0.7077)	
8 Months	0.9530 (0.8610 to 0.9846)	0.5126 (0.3709 to 0.6375)	0.9097 (0.7768 to 0.9652)	0.5864 (0.4569 to 0.6950)	0.7139 (0.4880 to 0.8536)	0.5195 (0.3326 to 0.6774)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_age_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.1 Treatment emergent adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.9106 (0.7960 to 0.9623)	0.5126 (0.3709 to 0.6375)	0.9097 (0.7768 to 0.9652)	0.5864 (0.4569 to 0.6950)	0.7139 (0.4880 to 0.8536)	0.4849 (0.3011 to 0.6463)	
12 Months	0.9106 (0.7960 to 0.9623)	0.5126 (0.3709 to 0.6375)	0.9097 (0.7768 to 0.9652)	0.5646 (0.4333 to 0.6766)	0.7139 (0.4880 to 0.8536)	0.4849 (0.3011 to 0.6463)	
14 Months	0.9106 (0.7960 to 0.9623)	0.5126 (0.3709 to 0.6375)	0.9097 (0.7768 to 0.9652)	0.5646 (0.4333 to 0.6766)	0.7139 (0.4880 to 0.8536)	0.4849 (0.3011 to 0.6463)	
16 Months	0.9106 (0.7960 to 0.9623)	0.4101 (0.2055 to 0.6053)	0.9097 (0.7768 to 0.9652)	0.4941 (0.3189 to 0.6472)	0.7139 (0.4880 to 0.8536)	0.4849 (0.3011 to 0.6463)	
Number of patients at risk[b]							
2 Months	65	29	50	41	20	21	
4 Months	61	27	47	40	19	18	
6 Months	52	23	44	36	15	16	
8 Months	47	19	37	33	12	15	
10 Months	43	18	37	29	11	14	
12 Months	37	15	32	25	7	12	
14 Months	21	7	19	16	6	7	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.1 Treatment emergent adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	11	2	8	6	3	2	
Investigations (days)							
Number (%) of events	5 (7.4)	3 (5.6)	2 (3.8)	9 (13.6)	3 (10.7)	5 (15.6)	0.3304
Number (%) of patients censored	63 (92.6)	51 (94.4)	51 (96.2)	57 (86.4)	25 (89.3)	27 (84.4)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.8747 to NC)	NC (0.8542 to NC)	NC (2.2669 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6780		0.0811		0.4803	
Hazard ratio (95% CI) vs Pd	-	0.74 (0.18 to 3.09)		3.58 (0.77 to 16.57)		1.79 (0.35 to 9.26)	
P-value	-	0.6791		0.1028		0.4867	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.5 Treatment emergent serious adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Injury, poisoning and procedural complications (days)							
Number (%) of events	1 (1.5)	2 (3.7)	0 (0.0)	5 (7.6)	1 (3.6)	4 (12.5)	0.9819
Number (%) of patients censored	67 (98.5)	52 (96.3)	53 (100.0)	61 (92.4)	27 (96.4)	28 (87.5)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.2813 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4299		0.0463		0.2296	
Hazard ratio (95% CI) vs Pd	-	2.54 (0.23 to 28.02)		NC		3.52 (0.39 to 31.51)	
P-value	-	0.4464		0.9945		0.2603	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_age_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.5 Treatment emergent serious adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]							
2 Months	0.9851 (0.8987 to 0.9979)	0.9630 (0.8599 to 0.9906)	1.0000 (1.0000 to 1.0000)	0.9697 (0.8842 to 0.9923)	0.9643 (0.7724 to 0.9949)	0.9063 (0.7369 to 0.9688)	
4 Months	0.9851 (0.8987 to 0.9979)	0.9630 (0.8599 to 0.9906)	1.0000 (1.0000 to 1.0000)	0.9389 (0.8454 to 0.9766)	0.9643 (0.7724 to 0.9949)	0.8739 (0.6979 to 0.9507)	
6 Months	0.9851 (0.8987 to 0.9979)	0.9630 (0.8599 to 0.9906)	1.0000 (1.0000 to 1.0000)	0.9389 (0.8454 to 0.9766)	0.9643 (0.7724 to 0.9949)	0.8739 (0.6979 to 0.9507)	
8 Months	0.9851 (0.8987 to 0.9979)	0.9630 (0.8599 to 0.9906)	1.0000 (1.0000 to 1.0000)	0.9218 (0.8221 to 0.9668)	0.9643 (0.7724 to 0.9949)	0.8739 (0.6979 to 0.9507)	
10 Months	0.9851 (0.8987 to 0.9979)	0.9630 (0.8599 to 0.9906)	1.0000 (1.0000 to 1.0000)	0.9218 (0.8221 to 0.9668)	0.9643 (0.7724 to 0.9949)	0.8739 (0.6979 to 0.9507)	
12 Months	0.9851 (0.8987 to 0.9979)	0.9630 (0.8599 to 0.9906)	1.0000 (1.0000 to 1.0000)	0.9218 (0.8221 to 0.9668)	0.9643 (0.7724 to 0.9949)	0.8739 (0.6979 to 0.9507)	
14 Months	0.9851 (0.8987 to 0.9979)	0.9630 (0.8599 to 0.9906)	1.0000 (1.0000 to 1.0000)	0.9218 (0.8221 to 0.9668)	0.9643 (0.7724 to 0.9949)	0.8739 (0.6979 to 0.9507)	
16 Months	0.9851 (0.8987 to 0.9979)	0.9630 (0.8599 to 0.9906)	1.0000 (1.0000 to 1.0000)	0.9218 (0.8221 to 0.9668)	0.9643 (0.7724 to 0.9949)	0.8739 (0.6979 to 0.9507)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_age_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.5 Treatment emergent serious adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	65	51	50	63	25	29	
4 Months	62	48	48	61	23	25	
6 Months	54	43	45	55	17	23	
8 Months	49	39	41	53	15	23	
10 Months	47	37	40	49	14	22	
12 Months	41	33	35	44	10	19	
14 Months	25	21	21	31	7	13	
16 Months	14	11	8	13	4	3	
Metabolism and nutrition disorders (days)							
Number (%) of events	2 (2.9)	1 (1.9)	3 (5.7)	5 (7.6)	1 (3.6)	2 (6.3)	0.8269
Number (%) of patients censored	66 (97.1)	53 (98.1)	50 (94.3)	61 (92.4)	27 (96.4)	30 (93.8)	
Kaplan-Meier estimates of event in months							

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_age_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.13 Treatment emergent severe adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.6843 (0.5574 to 0.7817)	0.6092 (0.4497 to 0.7354)	0.6683 (0.4708 to 0.8061)	0.5303 (0.3977 to 0.6464)	0.6504 (0.3968 to 0.8185)	0.5212 (0.3241 to 0.6859)	
Number of patients at risk[b]							
2 Months	56	45	43	53	21	25	
4 Months	48	38	37	48	18	23	
6 Months	42	33	34	38	15	20	
8 Months	36	31	31	33	13	20	
10 Months	36	29	31	29	12	18	
12 Months	32	26	26	28	7	12	
14 Months	19	14	16	20	5	10	
16 Months	11	8	5	9	4	2	
Injury, poisoning and procedural complications (days)							
Number (%) of events	0 (0.0)	1 (1.9)	0 (0.0)	3 (4.5)	0 (0.0)	4 (12.5)	1.0000
Number (%) of patients censored	68 (100.0)	53 (98.1)	53 (100.0)	63 (95.5)	28 (100.0)	28 (87.5)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.13 Treatment emergent severe adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.5298 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2653		0.1214		0.0779	
Hazard ratio (95% CI) vs Pd	-	NC		NC		NC	
P-value	-	0.9975		0.9957		0.9951	
Events probability (95% CI)[b]							
2 Months	1.0000 (1.0000 to 1.0000)	0.9815 (0.8757 to 0.9974)	1.0000 (1.0000 to 1.0000)	0.9697 (0.8842 to 0.9923)	1.0000 (1.0000 to 1.0000)	0.9375 (0.7725 to 0.9840)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_age_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.13 Treatment emergent severe adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	1.0000 (1.0000 to 1.0000)	0.9815 (0.8757 to 0.9974)	1.0000 (1.0000 to 1.0000)	0.9543 (0.8650 to 0.9850)	1.0000 (1.0000 to 1.0000)	0.9052 (0.7340 to 0.9684)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9815 (0.8757 to 0.9974)	1.0000 (1.0000 to 1.0000)	0.9543 (0.8650 to 0.9850)	1.0000 (1.0000 to 1.0000)	0.9052 (0.7340 to 0.9684)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9815 (0.8757 to 0.9974)	1.0000 (1.0000 to 1.0000)	0.9543 (0.8650 to 0.9850)	1.0000 (1.0000 to 1.0000)	0.9052 (0.7340 to 0.9684)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9815 (0.8757 to 0.9974)	1.0000 (1.0000 to 1.0000)	0.9543 (0.8650 to 0.9850)	1.0000 (1.0000 to 1.0000)	0.9052 (0.7340 to 0.9684)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9815 (0.8757 to 0.9974)	1.0000 (1.0000 to 1.0000)	0.9543 (0.8650 to 0.9850)	1.0000 (1.0000 to 1.0000)	0.9052 (0.7340 to 0.9684)	
14 Months	1.0000 (1.0000 to 1.0000)	0.9815 (0.8757 to 0.9974)	1.0000 (1.0000 to 1.0000)	0.9543 (0.8650 to 0.9850)	1.0000 (1.0000 to 1.0000)	0.8599 (0.6631 to 0.9461)	
16 Months	1.0000 (1.0000 to 1.0000)	0.9815 (0.8757 to 0.9974)	1.0000 (1.0000 to 1.0000)	0.9543 (0.8650 to 0.9850)	1.0000 (1.0000 to 1.0000)	0.8599 (0.6631 to 0.9461)	
Number of patients at risk[b]							
2 Months	66	52	50	63	26	30	
4 Months	62	49	48	62	24	26	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_age_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.13 Treatment emergent severe adverse event according to SOC by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	54	44	45	56	18	24	
8 Months	49	40	41	55	16	24	
10 Months	47	38	40	51	15	23	
12 Months	41	34	35	46	11	20	
14 Months	25	22	21	32	8	13	
16 Months	14	11	8	14	4	3	
Metabolism and nutrition disorders (days)							
Number (%) of events	4 (5.9)	1 (1.9)	3 (5.7)	7 (10.6)	1 (3.6)	5 (15.6)	0.2171
Number (%) of patients censored	64 (94.1)	53 (98.1)	50 (94.3)	59 (89.4)	27 (96.4)	27 (84.4)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.0370 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.1 Treatment emergent adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Infections and infestations (days)					
Number (%) of events	59 (59.0)	80 (79.2)	37 (75.5)	43 (84.3)	0.2489
Number (%) of patients censored	41 (41.0)	21 (20.8)	12 (24.5)	8 (15.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.9856 (0.7885 to 1.8727)	0.7228 (0.4928 to 0.8542)	1.4127 (0.5914 to 1.5441)	0.5585 (0.3943 to 0.8542)	
Median (95% CI)	4.9610 (2.2669 to 7.5893)	2.2341 (1.4456 to 3.2526)	1.8070 (1.5113 to 2.5955)	2.3984 (0.7556 to 3.3183)	
75% quantile (95% CI)	NC (12.4517 to NC)	6.2094 (3.9097 to NC)	7.4251 (2.0698 to NC)	5.2238 (3.3183 to 12.5832)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0062		0.5598	
Hazard ratio (95% CI) vs Pd	-	1.60 (1.14 to 2.24)		1.14 (0.73 to 1.77)	
P-value	-	0.0067		0.5608	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_plne_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.1 Treatment emergent adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.63 (0.45 to 0.88)				
Events probability (95% CI)[b]					
2 Months	0.6323 (0.5285 to 0.7193)	0.5259 (0.4233 to 0.6186)	0.4174 (0.2778 to 0.5511)	0.5490 (0.4034 to 0.6730)	
4 Months	0.5009 (0.3966 to 0.5963)	0.3405 (0.2487 to 0.4344)	0.2713 (0.1554 to 0.4009)	0.3457 (0.2184 to 0.4763)	
6 Months	0.4645 (0.3607 to 0.5617)	0.2521 (0.1699 to 0.3425)	0.2713 (0.1554 to 0.4009)	0.2440 (0.1359 to 0.3690)	
8 Months	0.3995 (0.2975 to 0.4993)	0.2041 (0.1288 to 0.2916)	0.2467 (0.1352 to 0.3756)	0.2033 (0.1053 to 0.3240)	
10 Months	0.3709 (0.2701 to 0.4718)	0.1905 (0.1172 to 0.2773)	0.2220 (0.1158 to 0.3497)	0.1830 (0.0906 to 0.3009)	
12 Months	0.3709 (0.2701 to 0.4718)	0.1768 (0.1058 to 0.2629)	0.2220 (0.1158 to 0.3497)	0.1601 (0.0740 to 0.2756)	
14 Months	0.3514 (0.2499 to 0.4544)	0.1768 (0.1058 to 0.2629)	0.2220 (0.1158 to 0.3497)	0.1334 (0.0548 to 0.2474)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_plne_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.1 Treatment emergent adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3514 (0.2499 to 0.4544)	0.1768 (0.1058 to 0.2629)	0.2220 (0.1158 to 0.3497)	0.1334 (0.0548 to 0.2474)	
Number of patients at risk[b]					
2 Months	60	52	20	27	
4 Months	44	32	13	17	
6 Months	37	21	12	12	
8 Months	29	17	10	10	
10 Months	26	14	9	9	
12 Months	21	13	7	6	
14 Months	13	9	4	4	
16 Months	6	6	3	2	
Injury, poisoning and procedural complications (days)					
Number (%) of events	10 (10.0)	50 (49.5)	7 (14.3)	22 (43.1)	0.4030
Number (%) of patients censored	90 (90.0)	51 (50.5)	42 (85.7)	29 (56.9)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.1 Treatment emergent adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1643)	NC (6.8337 to NC)	0.1314 (0.1314 to 0.2300)	
Median (95% CI)	NC (NC to NC)	11.4661 (2.5298 to NC)	NC (NC to NC)	NC (0.1971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		0.0005	
Hazard ratio (95% CI) vs Pd	-	6.66 (3.37 to 13.15)		4.33 (1.75 to 10.69)	
P-value	-	<.0001		0.0015	
Hazard ratio inverted (95% CI) vs IPd	0.15 (0.08 to 0.30)		0.23 (0.09 to 0.57)		
Events probability (95% CI)[b]					
2 Months	0.9690 (0.9071 to 0.9899)	0.6036 (0.5013 to 0.6914)	0.9366 (0.8161 to 0.9791)	0.6078 (0.4606 to 0.7263)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.1 Treatment emergent adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	0.9474 (0.8781 to 0.9778)	0.5828 (0.4802 to 0.6721)	0.9148 (0.7887 to 0.9672)	0.6078 (0.4606 to 0.7263)	
6 Months	0.9360 (0.8629 to 0.9708)	0.5604 (0.4573 to 0.6513)	0.9148 (0.7887 to 0.9672)	0.6078 (0.4606 to 0.7263)	
8 Months	0.8984 (0.8131 to 0.9460)	0.5230 (0.4189 to 0.6171)	0.8862 (0.7457 to 0.9515)	0.5869 (0.4396 to 0.7078)	
10 Months	0.8847 (0.7954 to 0.9366)	0.5096 (0.4051 to 0.6048)	0.8534 (0.6973 to 0.9327)	0.5869 (0.4396 to 0.7078)	
12 Months	0.8847 (0.7954 to 0.9366)	0.4951 (0.3899 to 0.5916)	0.8534 (0.6973 to 0.9327)	0.5869 (0.4396 to 0.7078)	
14 Months	0.8847 (0.7954 to 0.9366)	0.4951 (0.3899 to 0.5916)	0.8534 (0.6973 to 0.9327)	0.5869 (0.4396 to 0.7078)	
16 Months	0.8847 (0.7954 to 0.9366)	0.4400 (0.3023 to 0.5694)	0.8534 (0.6973 to 0.9327)	0.5030 (0.3026 to 0.6737)	
Number of patients at risk[b]					
2 Months	91	60	44	31	
4 Months	86	54	41	31	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.1 Treatment emergent adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	IPd (N=101)	Pd (N=49)	IPd (N=51)	p-value of treatment-by-sub group interaction[c]
6 Months	76	46	35	29	
8 Months	67	41	29	26	
10 Months	65	37	26	24	
12 Months	53	32	23	20	
14 Months	32	17	14	13	
16 Months	14	6	8	4	
Investigations (days)					
Number (%) of events	6 (6.0)	11 (10.9)	4 (8.2)	6 (11.8)	0.9621
Number (%) of patients censored	94 (94.0)	90 (89.1)	45 (91.8)	45 (88.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.8747 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.3 Treatment emergent serious adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	84	80	38	44	
4 Months	72	71	32	41	
6 Months	64	60	28	34	
8 Months	57	56	24	32	
10 Months	56	48	23	31	
12 Months	47	43	19	25	
14 Months	30	29	11	16	
16 Months	14	12	6	7	
Injury, poisoning and procedural complications (days)					
Number (%) of events	1 (1.0)	10 (9.9)	1 (2.0)	1 (2.0)	0.1785
Number (%) of patients censored	99 (99.0)	91 (90.1)	48 (98.0)	50 (98.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.3 Treatment emergent serious adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0066		0.9830	
Hazard ratio (95% CI) vs Pd	-	10.02 (1.28 to 78.31)		0.97 (0.06 to 15.51)	
P-value	-	0.0280		0.9830	
Hazard ratio inverted (95% CI) vs IPd	0.10 (0.01 to 0.78)				
Events probability (95% CI)[b]					
2 Months	0.9896 (0.9284 to 0.9985)	0.9405 (0.8723 to 0.9728)	0.9796 (0.8638 to 0.9971)	0.9804 (0.8689 to 0.9972)	
4 Months	0.9896 (0.9284 to 0.9985)	0.9100 (0.8342 to 0.9522)	0.9796 (0.8638 to 0.9971)	0.9804 (0.8689 to 0.9972)	
6 Months	0.9896 (0.9284 to 0.9985)	0.9100 (0.8342 to 0.9522)	0.9796 (0.8638 to 0.9971)	0.9804 (0.8689 to 0.9972)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.3 Treatment emergent serious adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.9896 (0.9284 to 0.9985)	0.8981 (0.8185 to 0.9439)	0.9796 (0.8638 to 0.9971)	0.9804 (0.8689 to 0.9972)	
10 Months	0.9896 (0.9284 to 0.9985)	0.8981 (0.8185 to 0.9439)	0.9796 (0.8638 to 0.9971)	0.9804 (0.8689 to 0.9972)	
12 Months	0.9896 (0.9284 to 0.9985)	0.8981 (0.8185 to 0.9439)	0.9796 (0.8638 to 0.9971)	0.9804 (0.8689 to 0.9972)	
14 Months	0.9896 (0.9284 to 0.9985)	0.8981 (0.8185 to 0.9439)	0.9796 (0.8638 to 0.9971)	0.9804 (0.8689 to 0.9972)	
16 Months	0.9896 (0.9284 to 0.9985)	0.8981 (0.8185 to 0.9439)	0.9796 (0.8638 to 0.9971)	0.9804 (0.8689 to 0.9972)	
Number of patients at risk[b]					
2 Months	93	94	47	49	
4 Months	89	85	44	49	
6 Months	79	77	37	44	
8 Months	73	74	32	41	
10 Months	72	69	29	39	
12 Months	60	63	26	33	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.3 Treatment emergent serious adverse event according to SOC by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	37	43	16	22	
16 Months	16	19	10	8	
Metabolism and nutrition disorders (days)					
Number (%) of events	4 (4.0)	7 (6.9)	2 (4.1)	1 (2.0)	0.3372
Number (%) of patients censored	96 (96.0)	94 (93.1)	47 (95.9)	50 (98.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3746		0.4744	
Hazard ratio (95% CI) vs Pd	-	1.73 (0.51 to 5.92)		0.43 (0.04 to 4.72)	
P-value	-	0.3806		0.4875	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.1 Treatment emergent adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Infections and infestations (days)					
Number (%) of events	42 (61.8)	76 (86.4)	54 (66.7)	47 (73.4)	0.0580
Number (%) of patients censored	26 (38.2)	12 (13.6)	27 (33.3)	17 (26.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.1828 (0.5257 to 1.9055)	0.6571 (0.4600 to 0.7885)	1.2813 (0.7885 to 1.5113)	0.7228 (0.4600 to 1.3142)	
Median (95% CI)	3.1211 (1.9384 to 9.3306)	1.9713 (0.9856 to 2.8912)	2.3326 (1.6756 to 4.9610)	2.7598 (1.3799 to 4.4353)	
75% quantile (95% CI)	NC (12.4517 to NC)	4.5339 (3.6797 to 6.3409)	NC (7.3265 to NC)	12.5832 (5.2895 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0019		0.7271	
Hazard ratio (95% CI) vs Pd	-	1.81 (1.24 to 2.64)		1.07 (0.72 to 1.59)	
P-value	-	0.0022		0.7262	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.1 Treatment emergent adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.55 (0.38 to 0.81)				
Events probability (95% CI)[b]					
2 Months	0.5980 (0.4710 to 0.7040)	0.4936 (0.3848 to 0.5934)	0.5289 (0.4129 to 0.6322)	0.5873 (0.4560 to 0.6972)	
4 Months	0.4436 (0.3218 to 0.5584)	0.3056 (0.2119 to 0.4042)	0.4056 (0.2952 to 0.5130)	0.3928 (0.2722 to 0.5111)	
6 Months	0.4266 (0.3057 to 0.5420)	0.1979 (0.1211 to 0.2886)	0.3765 (0.2682 to 0.4843)	0.3218 (0.2088 to 0.4401)	
8 Months	0.3895 (0.2705 to 0.5066)	0.1237 (0.0640 to 0.2042)	0.3116 (0.2085 to 0.4202)	0.3218 (0.2088 to 0.4401)	
10 Months	0.3700 (0.2522 to 0.4879)	0.1237 (0.0640 to 0.2042)	0.2770 (0.1775 to 0.3855)	0.2815 (0.1734 to 0.3998)	
12 Months	0.3700 (0.2522 to 0.4879)	0.1100 (0.0539 to 0.1885)	0.2770 (0.1775 to 0.3855)	0.2599 (0.1545 to 0.3782)	
14 Months	0.3415 (0.2226 to 0.4638)	0.1100 (0.0539 to 0.1885)	0.2770 (0.1775 to 0.3855)	0.2382 (0.1363 to 0.3561)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.1 Treatment emergent adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3415 (0.2226 to 0.4638)	0.1100 (0.0539 to 0.1885)	0.2770 (0.1775 to 0.3855)	0.2382 (0.1363 to 0.3561)	
Number of patients at risk[b]					
2 Months	40	42	40	37	
4 Months	28	26	29	23	
6 Months	24	16	25	17	
8 Months	21	10	18	17	
10 Months	19	9	16	14	
12 Months	14	7	14	12	
14 Months	9	6	8	7	
16 Months	5	4	4	4	
Injury, poisoning and procedural complications (days)					
Number (%) of events	5 (7.4)	39 (44.3)	12 (14.8)	33 (51.6)	0.4360
Number (%) of patients censored	63 (92.6)	49 (55.7)	69 (85.2)	31 (48.4)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.1 Treatment emergent adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0986 to 0.5585)	NC (6.8337 to NC)	0.0986 (0.0657 to 0.1643)	
Median (95% CI)	NC (NC to NC)	14.7187 (6.1766 to NC)	NC (NC to NC)	8.5092 (0.1643 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Pd	-	7.99 (3.14 to 20.33)		5.03 (2.54 to 9.97)	
P-value	-	<.0001		<.0001	
Hazard ratio inverted (95% CI) vs IPd	0.13 (0.05 to 0.32)		0.20 (0.10 to 0.39)		
Events probability (95% CI)[b]					
2 Months	0.9846 (0.8958 to 0.9978)	0.6471 (0.5376 to 0.7370)	0.9360 (0.8530 to 0.9729)	0.5469 (0.4176 to 0.6590)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.1 Treatment emergent adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	0.9846 (0.8958 to 0.9978)	0.6232 (0.5129 to 0.7153)	0.8955 (0.8017 to 0.9464)	0.5469 (0.4176 to 0.6590)	
6 Months	0.9846 (0.8958 to 0.9978)	0.6107 (0.5000 to 0.7041)	0.8815 (0.7844 to 0.9366)	0.5303 (0.4013 to 0.6436)	
8 Months	0.9478 (0.8461 to 0.9829)	0.5691 (0.4566 to 0.6667)	0.8485 (0.7420 to 0.9136)	0.5126 (0.3838 to 0.6273)	
10 Months	0.9075 (0.7908 to 0.9606)	0.5691 (0.4566 to 0.6667)	0.8485 (0.7420 to 0.9136)	0.4943 (0.3658 to 0.6104)	
12 Months	0.9075 (0.7908 to 0.9606)	0.5513 (0.4371 to 0.6515)	0.8485 (0.7420 to 0.9136)	0.4943 (0.3658 to 0.6104)	
14 Months	0.9075 (0.7908 to 0.9606)	0.5513 (0.4371 to 0.6515)	0.8485 (0.7420 to 0.9136)	0.4943 (0.3658 to 0.6104)	
16 Months	0.9075 (0.7908 to 0.9606)	0.4824 (0.3192 to 0.6279)	0.8485 (0.7420 to 0.9136)	0.4325 (0.2748 to 0.5806)	
Number of patients at risk[b]					
2 Months	64	56	71	35	
4 Months	61	51	66	34	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_sex_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.1 Treatment emergent adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	54	44	57	31	
8 Months	50	39	46	28	
10 Months	45	34	46	27	
12 Months	36	28	40	24	
14 Months	23	13	23	17	
16 Months	13	4	9	6	
Investigations (days)					
Number (%) of events	6 (8.8)	14 (15.9)	4 (4.9)	3 (4.7)	0.3311
Number (%) of patients censored	62 (91.2)	74 (84.1)	77 (95.1)	61 (95.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (10.8747 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.5 Treatment emergent serious adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	56	71	66	53	
4 Months	48	66	56	46	
6 Months	44	54	48	40	
8 Months	40	49	41	39	
10 Months	39	44	40	35	
12 Months	32	37	34	31	
14 Months	22	22	19	23	
16 Months	11	11	9	8	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	5 (5.7)	2 (2.5)	6 (9.4)	0.9909
Number (%) of patients censored	68 (100.0)	83 (94.3)	79 (97.5)	58 (90.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.5 Treatment emergent serious adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0485		0.0758	
Hazard ratio (95% CI) vs Pd	-	NC		3.84 (0.78 to 19.04)	
P-value	-	0.9945		0.0993	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9773 (0.9122 to 0.9943)	0.9748 (0.9030 to 0.9936)	0.9219 (0.8224 to 0.9667)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9537 (0.8814 to 0.9824)	0.9748 (0.9030 to 0.9936)	0.9063 (0.8032 to 0.9568)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9537 (0.8814 to 0.9824)	0.9748 (0.9030 to 0.9936)	0.9063 (0.8032 to 0.9568)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9399 (0.8612 to 0.9746)	0.9748 (0.9030 to 0.9936)	0.9063 (0.8032 to 0.9568)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9399 (0.8612 to 0.9746)	0.9748 (0.9030 to 0.9936)	0.9063 (0.8032 to 0.9568)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.5 Treatment emergent serious adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
12 Months	1.0000 (1.0000 to 1.0000)	0.9399 (0.8612 to 0.9746)	0.9748 (0.9030 to 0.9936)	0.9063 (0.8032 to 0.9568)	
14 Months	1.0000 (1.0000 to 1.0000)	0.9399 (0.8612 to 0.9746)	0.9748 (0.9030 to 0.9936)	0.9063 (0.8032 to 0.9568)	
16 Months	1.0000 (1.0000 to 1.0000)	0.9399 (0.8612 to 0.9746)	0.9748 (0.9030 to 0.9936)	0.9063 (0.8032 to 0.9568)	
Number of patients at risk[b]					
2 Months	65	84	75	59	
4 Months	62	78	71	56	
6 Months	55	70	61	51	
8 Months	53	66	52	49	
10 Months	50	61	51	47	
12 Months	41	54	45	42	
14 Months	27	33	26	32	
16 Months	15	15	11	12	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.13 Treatment emergent severe adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	45	54	46	37	
8 Months	41	48	39	36	
10 Months	40	43	39	33	
12 Months	32	37	33	29	
14 Months	22	22	18	22	
16 Months	11	10	9	9	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	3 (3.4)	0 (0.0)	5 (7.8)	0.9999
Number (%) of patients censored	68 (100.0)	85 (96.6)	81 (100.0)	59 (92.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.13 Treatment emergent severe adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Log-Rank test p-value[a] vs Pd	-	0.1358		0.0110	
Hazard ratio (95% CI) vs Pd	-	NC		NC	
P-value	-	0.9958		0.9943	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9219 (0.8224 to 0.9667)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9765 (0.9092 to 0.9941)	1.0000 (1.0000 to 1.0000)	0.9219 (0.8224 to 0.9667)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9765 (0.9092 to 0.9941)	1.0000 (1.0000 to 1.0000)	0.9219 (0.8224 to 0.9667)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9765 (0.9092 to 0.9941)	1.0000 (1.0000 to 1.0000)	0.9219 (0.8224 to 0.9667)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9765 (0.9092 to 0.9941)	1.0000 (1.0000 to 1.0000)	0.9219 (0.8224 to 0.9667)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9765 (0.9092 to 0.9941)	1.0000 (1.0000 to 1.0000)	0.9219 (0.8224 to 0.9667)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.13 Treatment emergent severe adverse event according to SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	1.0000 (1.0000 to 1.0000)	0.9590 (0.8756 to 0.9869)	1.0000 (1.0000 to 1.0000)	0.9219 (0.8224 to 0.9667)	
16 Months	1.0000 (1.0000 to 1.0000)	0.9590 (0.8756 to 0.9869)	1.0000 (1.0000 to 1.0000)	0.9219 (0.8224 to 0.9667)	
Number of patients at risk[b]					
2 Months	65	86	77	59	
4 Months	62	80	72	57	
6 Months	55	72	62	52	
8 Months	53	69	53	50	
10 Months	50	64	52	48	
12 Months	41	57	46	43	
14 Months	27	35	27	32	
16 Months	15	16	11	12	
Metabolism and nutrition disorders (days)					
Number (%) of events	3 (4.4)	7 (8.0)	5 (6.2)	6 (9.4)	0.8090

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.1 Treatment emergent adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	11	18	0	0	
Infections and infestations (days)					
Number (%) of events	82 (67.2)	97 (83.6)	10 (52.6)	19 (79.2)	0.1117
Number (%) of patients censored	40 (32.8)	19 (16.4)	9 (47.4)	5 (20.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.9528 (0.7556 to 1.4784)	0.6571 (0.4928 to 0.8214)	1.7741 (0.5257 to 7.5893)	0.6899 (0.1643 to 0.9856)	
Median (95% CI)	2.2998 (1.8398 to 3.5154)	2.2669 (1.3799 to 3.2854)	9.3306 (1.7741 to NC)	1.9055 (0.7228 to 4.1068)	
75% quantile (95% CI)	NC (6.7351 to NC)	5.9138 (4.0411 to 11.2690)	NC (9.3306 to NC)	4.1725 (2.0370 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0699		0.0181	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.1 Treatment emergent adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	1.31 (0.98 to 1.76)		2.49 (1.14 to 5.42)	
P-value	-	0.0703		0.0220	
Hazard ratio inverted (95% CI) vs IPd			0.40 (0.18 to 0.88)		
Events probability (95% CI)[b]					
2 Months	0.5404 (0.4469 to 0.6248)	0.5391 (0.4439 to 0.6250)	0.6316 (0.3790 to 0.8044)	0.4936 (0.2831 to 0.6736)	
4 Months	0.3809 (0.2930 to 0.4682)	0.3361 (0.2511 to 0.4230)	0.6316 (0.3790 to 0.8044)	0.3141 (0.1416 to 0.5036)	
6 Months	0.3519 (0.2657 to 0.4391)	0.2431 (0.1681 to 0.3258)	0.6316 (0.3790 to 0.8044)	0.1795 (0.0566 to 0.3579)	
8 Months	0.3091 (0.2255 to 0.3964)	0.1945 (0.1265 to 0.2735)	0.5263 (0.2872 to 0.7188)	0.1795 (0.0566 to 0.3579)	
10 Months	0.2854 (0.2031 to 0.3728)	0.1740 (0.1093 to 0.2512)	0.4737 (0.2444 to 0.6728)	0.1795 (0.0566 to 0.3579)	
12 Months	0.2854 (0.2031 to 0.3728)	0.1523 (0.0914 to 0.2275)	0.4737 (0.2444 to 0.6728)	0.1795 (0.0566 to 0.3579)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.1 Treatment emergent adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0.2854 (0.2031 to 0.3728)	0.1406 (0.0818 to 0.2149)	0.4737 (0.2444 to 0.6728)	0.1795 (0.0566 to 0.3579)	
16 Months	0.2854 (0.2031 to 0.3728)	0.1406 (0.0818 to 0.2149)	0.4737 (0.2444 to 0.6728)	0.1795 (0.0566 to 0.3579)	
Number of patients at risk[b]					
2 Months	63	62	12	11	
4 Months	42	37	12	7	
6 Months	35	25	12	4	
8 Months	27	20	10	4	
10 Months	24	17	9	3	
12 Months	20	13	7	3	
14 Months	17	9	0	2	
16 Months	9	6	0	1	
Injury, poisoning and procedural complications (days)					
Number (%) of events	16 (13.1)	51 (44.0)	1 (5.3)	16 (66.7)	0.1831

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.1 Treatment emergent adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of patients censored	106 (86.9)	65 (56.0)	18 (94.7)	8 (33.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1150 (0.0657 to 0.1971)	NC (3.6797 to NC)	0.1314 (0.0657 to 0.1643)	
Median (95% CI)	NC (NC to NC)	15.4415 (6.5051 to NC)	NC (NC to NC)	1.3799 (0.1314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.0554 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Pd	-	4.53 (2.55 to 8.07)		19.67 (2.60 to 149.13)	
P-value	-	<.0001		0.0039	
Hazard ratio inverted (95% CI) vs IPd	0.22 (0.12 to 0.39)		0.05 (0.01 to 0.39)		
Events probability (95% CI)[b]					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_race_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.1 Treatment emergent adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9490 (0.8899 to 0.9767)	0.6293 (0.5346 to 0.7100)	1.0000 (1.0000 to 1.0000)	0.5000 (0.2910 to 0.6776)	
4 Months	0.9311 (0.8669 to 0.9650)	0.6293 (0.5346 to 0.7100)	0.9474 (0.6812 to 0.9924)	0.4167 (0.2224 to 0.6006)	
6 Months	0.9218 (0.8550 to 0.9586)	0.6202 (0.5253 to 0.7015)	0.9474 (0.6812 to 0.9924)	0.3750 (0.1900 to 0.5603)	
8 Months	0.8788 (0.7995 to 0.9281)	0.5903 (0.4942 to 0.6742)	0.9474 (0.6812 to 0.9924)	0.3333 (0.1590 to 0.5187)	
10 Months	0.8544 (0.7685 to 0.9102)	0.5796 (0.4830 to 0.6645)	0.9474 (0.6812 to 0.9924)	0.3333 (0.1590 to 0.5187)	
12 Months	0.8544 (0.7685 to 0.9102)	0.5673 (0.4698 to 0.6535)	0.9474 (0.6812 to 0.9924)	0.3333 (0.1590 to 0.5187)	
14 Months	0.8544 (0.7685 to 0.9102)	0.5673 (0.4698 to 0.6535)	0.9474 (0.6812 to 0.9924)	0.3333 (0.1590 to 0.5187)	
16 Months	0.8544 (0.7685 to 0.9102)	0.4727 (0.3264 to 0.6057)	0.9474 (0.6812 to 0.9924)	0.3333 (0.1590 to 0.5187)	

Number of patients at risk[b]

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.1 Treatment emergent adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	109	73	19	12	
4 Months	103	71	18	10	
6 Months	89	63	18	9	
8 Months	75	57	17	7	
10 Months	70	51	17	7	
12 Months	61	43	13	6	
14 Months	41	24	3	4	
16 Months	19	7	1	2	
Investigations (days)					
Number (%) of events	9 (7.4)	13 (11.2)	1 (5.3)	3 (12.5)	0.7191
Number (%) of patients censored	113 (92.6)	103 (88.8)	18 (94.7)	21 (87.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.0041 to NC)	NC (0.8871 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_race_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.4 Treatment emergent serious adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	99	93	16	22	
4 Months	83	82	15	22	
6 Months	74	71	14	18	
8 Months	64	66	13	17	
10 Months	63	59	13	15	
12 Months	55	49	10	14	
14 Months	39	31	1	10	
16 Months	19	13	0	5	
Injury, poisoning and procedural complications (days)					
Number (%) of events	2 (1.6)	9 (7.8)	0 (0.0)	1 (4.2)	0.9925
Number (%) of patients censored	120 (98.4)	107 (92.2)	19 (100.0)	23 (95.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.5298 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.4 Treatment emergent serious adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0291		0.3634	
Hazard ratio (95% CI) vs Pd	-	4.70 (1.02 to 21.75)		NC	
P-value	-	0.0478		0.9984	
Hazard ratio inverted (95% CI) vs IPd	0.21 (0.05 to 0.98)				
Events probability (95% CI)[b]					
2 Months	0.9833 (0.9350 to 0.9958)	0.9483 (0.8885 to 0.9764)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9833 (0.9350 to 0.9958)	0.9310 (0.8667 to 0.9649)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
6 Months	0.9833 (0.9350 to 0.9958)	0.9310 (0.8667 to 0.9649)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.4 Treatment emergent serious adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.9833 (0.9350 to 0.9958)	0.9209 (0.8534 to 0.9581)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
10 Months	0.9833 (0.9350 to 0.9958)	0.9209 (0.8534 to 0.9581)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
12 Months	0.9833 (0.9350 to 0.9958)	0.9209 (0.8534 to 0.9581)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
14 Months	0.9833 (0.9350 to 0.9958)	0.9209 (0.8534 to 0.9581)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
16 Months	0.9833 (0.9350 to 0.9958)	0.9209 (0.8534 to 0.9581)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
Number of patients at risk[b]					
2 Months	114	110	19	23	
4 Months	108	104	19	22	
6 Months	93	94	19	22	
8 Months	83	90	18	20	
10 Months	80	84	17	19	
12 Months	71	74	13	17	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.4 Treatment emergent serious adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	48	48	3	13	
16 Months	23	21	1	5	
Metabolism and nutrition disorders (days)					
Number (%) of events	4 (3.3)	4 (3.4)	2 (10.5)	3 (12.5)	0.8553
Number (%) of patients censored	118 (96.7)	112 (96.6)	17 (89.5)	21 (87.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.2957 to NC)	NC (0.1314 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9715		0.7843	
Hazard ratio (95% CI) vs Pd	-	1.03 (0.26 to 4.10)		1.28 (0.21 to 7.68)	
P-value	-	0.9715		0.7849	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_race_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.11 Treatment emergent severe adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	73	69	14	17	
8 Months	63	63	13	16	
10 Months	62	57	13	14	
12 Months	53	48	10	13	
14 Months	37	30	1	10	
16 Months	18	13	0	5	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	6 (5.2)	0 (0.0)	1 (4.2)	1.0000
Number (%) of patients censored	122 (100.0)	110 (94.8)	19 (100.0)	23 (95.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.5298 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.11 Treatment emergent severe adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Log-Rank test p-value[a] vs Pd	-	0.0134		0.3634	
Hazard ratio (95% CI) vs Pd	-	NC		NC	
P-value	-	0.9938		0.9984	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9655 (0.9107 to 0.9869)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9569 (0.8995 to 0.9818)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9569 (0.8995 to 0.9818)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9569 (0.8995 to 0.9818)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9569 (0.8995 to 0.9818)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9569 (0.8995 to 0.9818)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.11 Treatment emergent severe adverse event according to SOC by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	1.0000 (1.0000 to 1.0000)	0.9445 (0.8793 to 0.9749)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
16 Months	1.0000 (1.0000 to 1.0000)	0.9445 (0.8793 to 0.9749)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
Number of patients at risk[b]					
2 Months	116	112	19	23	
4 Months	109	107	19	22	
6 Months	94	97	19	22	
8 Months	84	94	18	20	
10 Months	81	88	17	19	
12 Months	72	78	13	17	
14 Months	49	50	3	13	
16 Months	23	22	1	5	
Metabolism and nutrition disorders (days)					
Number (%) of events	4 (3.3)	8 (6.9)	3 (15.8)	4 (16.7)	0.5301

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.1 Treatment emergent adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Infections and infestations (days)					
Number (%) of events	2 (66.7)	4 (100.0)	83 (63.8)	104 (81.3)	0.6245
Number (%) of patients censored	1 (33.3)	0 (0.0)	47 (36.2)	24 (18.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.4271 (0.4271 to 2.0370)	0.4928 (0.1971 to 1.3142)	1.2813 (0.8542 to 1.5113)	0.6571 (0.4928 to 0.7556)	
Median (95% CI)	1.2320 (0.4271 to 2.0370)	1.0513 (0.1971 to 5.9138)	2.3655 (1.8398 to 4.9610)	2.2341 (1.3142 to 3.2526)	
75% quantile (95% CI)	2.0370 (0.4271 to 2.0370)	3.6140 (0.1971 to 5.9138)	NC (9.3306 to NC)	6.2752 (4.1068 to 11.8275)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9344		0.0125	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.15 to 5.71)		1.44 (1.08 to 1.93)	
P-value	-	0.9344		0.0130	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.1 Treatment emergent adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.69 (0.52 to 0.93)		
Events probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	0.2500 (0.0089 to 0.6653)	0.5486 (0.4585 to 0.6299)	0.5307 (0.4406 to 0.6128)	
4 Months	0.5000 (0.0060 to 0.9104)	0.2500 (0.0089 to 0.6653)	0.4178 (0.3310 to 0.5021)	0.3461 (0.2643 to 0.4291)	
6 Months	0.5000 (0.0060 to 0.9104)	0.2500 (0.0089 to 0.6653)	0.4002 (0.3141 to 0.4847)	0.2542 (0.1812 to 0.3334)	
8 Months	0.5000 (0.0060 to 0.9104)	0.2500 (0.0089 to 0.6653)	0.3520 (0.2679 to 0.4371)	0.2103 (0.1430 to 0.2866)	
10 Months	0.5000 (0.0060 to 0.9104)	0.2500 (0.0089 to 0.6653)	0.3313 (0.2482 to 0.4166)	0.1912 (0.1264 to 0.2663)	
12 Months	0.5000 (0.0060 to 0.9104)	0.2500 (0.0089 to 0.6653)	0.3313 (0.2482 to 0.4166)	0.1711 (0.1092 to 0.2448)	
14 Months	0.5000 (0.0060 to 0.9104)	0.2500 (0.0089 to 0.6653)	0.3313 (0.2482 to 0.4166)	0.1604 (0.1001 to 0.2334)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_ethn_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.1 Treatment emergent adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5000 (0.0060 to 0.9104)	0.2500 (0.0089 to 0.6653)	0.3313 (0.2482 to 0.4166)	0.1604 (0.1001 to 0.2334)	
Number of patients at risk[b]					
2 Months	1	1	69	67	
4 Months	0	1	50	42	
6 Months	0	0	44	29	
8 Months	0	0	35	24	
10 Months	0	0	32	20	
12 Months	0	0	26	16	
14 Months	0	0	16	11	
16 Months	0	0	8	7	
Injury, poisoning and procedural complications (days)					
Number (%) of events	1 (33.3)	2 (50.0)	15 (11.5)	61 (47.7)	0.3298
Number (%) of patients censored	2 (66.7)	2 (50.0)	115 (88.5)	67 (52.3)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.1 Treatment emergent adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.1971 (0.1971 to NC)	0.0821 (0.0657 to NC)	NC (NC to NC)	0.1314 (0.0986 to 0.1643)	
Median (95% CI)	NC (0.1971 to NC)	NC (0.0657 to NC)	NC (NC to NC)	14.7187 (5.2238 to NC)	
75% quantile (95% CI)	NC (0.1971 to NC)	NC (0.0657 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5375		<.0001	
Hazard ratio (95% CI) vs Pd	-	2.11 (0.19 to 23.75)		5.42 (3.07 to 9.54)	
P-value	-	0.5464		<.0001	
Hazard ratio inverted (95% CI) vs IPd			0.18 (0.10 to 0.33)		
Events probability (95% CI)[b]					
2 Months	0.6667 (0.0541 to 0.9452)	0.5000 (0.0578 to 0.8449)	0.9605 (0.9078 to 0.9834)	0.6172 (0.5272 to 0.6951)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.1 Treatment emergent adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	0.6667 (0.0541 to 0.9452)	0.5000 (0.0578 to 0.8449)	0.9360 (0.8760 to 0.9675)	0.6014 (0.5111 to 0.6802)	
6 Months	0.6667 (0.0541 to 0.9452)	0.5000 (0.0578 to 0.8449)	0.9275 (0.8652 to 0.9616)	0.5846 (0.4941 to 0.6646)	
8 Months	0.6667 (0.0541 to 0.9452)	0.5000 (0.0578 to 0.8449)	0.8884 (0.8149 to 0.9339)	0.5488 (0.4574 to 0.6311)	
10 Months	0.6667 (0.0541 to 0.9452)	0.5000 (0.0578 to 0.8449)	0.8665 (0.7871 to 0.9178)	0.5390 (0.4473 to 0.6220)	
12 Months	0.6667 (0.0541 to 0.9452)	0.5000 (0.0578 to 0.8449)	0.8665 (0.7871 to 0.9178)	0.5278 (0.4355 to 0.6118)	
14 Months	0.6667 (0.0541 to 0.9452)	0.5000 (0.0578 to 0.8449)	0.8665 (0.7871 to 0.9178)	0.5278 (0.4355 to 0.6118)	
16 Months	0.6667 (0.0541 to 0.9452)	0.5000 (0.0578 to 0.8449)	0.8665 (0.7871 to 0.9178)	0.4515 (0.3251 to 0.5697)	
Number of patients at risk[b]					
2 Months	1	2	120	79	
4 Months	1	2	113	75	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.1 Treatment emergent adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	1	2	99	66	
8 Months	1	2	84	58	
10 Months	1	2	79	52	
12 Months	0	2	66	43	
14 Months	0	2	40	26	
16 Months	0	1	19	8	
Investigations (days)					
Number (%) of events	0 (0.0)	1 (25.0)	8 (6.2)	15 (11.7)	0.9906
Number (%) of patients censored	3 (100.0)	3 (75.0)	122 (93.8)	113 (88.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.9856 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (0.9856 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.9856 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.4 Treatment emergent serious adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1	1	106	107	
4 Months	1	1	91	97	
6 Months	1	1	82	83	
8 Months	1	1	71	77	
10 Months	1	1	70	68	
12 Months	0	1	59	57	
14 Months	0	1	37	39	
16 Months	0	1	18	17	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	2 (50.0)	2 (1.5)	7 (5.5)	0.9930
Number (%) of patients censored	3 (100.0)	2 (50.0)	128 (98.5)	121 (94.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	1.2977 (0.0657 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (0.0657 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.0657 to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.4 Treatment emergent serious adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2341		0.0948	
Hazard ratio (95% CI) vs Pd	-	NC		3.51 (0.73 to 16.89)	
P-value	-	0.9978		0.1174	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9844 (0.9392 to 0.9961)	0.9688 (0.9189 to 0.9882)	
4 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.9844 (0.9392 to 0.9961)	0.9529 (0.8982 to 0.9786)	
6 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.9844 (0.9392 to 0.9961)	0.9529 (0.8982 to 0.9786)	
8 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.9844 (0.9392 to 0.9961)	0.9439 (0.8857 to 0.9729)	
10 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.9844 (0.9392 to 0.9961)	0.9439 (0.8857 to 0.9729)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.4 Treatment emergent serious adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
12 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.9844 (0.9392 to 0.9961)	0.9439 (0.8857 to 0.9729)	
14 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.9844 (0.9392 to 0.9961)	0.9439 (0.8857 to 0.9729)	
16 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.9844 (0.9392 to 0.9961)	0.9439 (0.8857 to 0.9729)	
Number of patients at risk[b]					
2 Months	2	3	123	123	
4 Months	2	2	118	117	
6 Months	1	2	104	107	
8 Months	1	2	93	101	
10 Months	1	2	89	94	
12 Months	0	2	76	82	
14 Months	0	2	47	56	
16 Months	0	1	23	24	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.10 Treatment emergent severe adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	1	2	70	65	
12 Months	0	2	58	55	
14 Months	0	2	35	38	
16 Months	0	1	17	17	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	1 (25.0)	0 (0.0)	5 (3.9)	0.9999
Number (%) of patients censored	3 (100.0)	3 (75.0)	130 (100.0)	123 (96.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (2.5298 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (2.5298 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (2.5298 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.0270	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.10 Treatment emergent severe adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	NC		NC	
P-value	-	0.9985		0.9944	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9766 (0.9291 to 0.9924)	
4 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	1.0000 (1.0000 to 1.0000)	0.9687 (0.9187 to 0.9881)	
6 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	1.0000 (1.0000 to 1.0000)	0.9687 (0.9187 to 0.9881)	
8 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	1.0000 (1.0000 to 1.0000)	0.9687 (0.9187 to 0.9881)	
10 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	1.0000 (1.0000 to 1.0000)	0.9687 (0.9187 to 0.9881)	
12 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	1.0000 (1.0000 to 1.0000)	0.9687 (0.9187 to 0.9881)	
14 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	1.0000 (1.0000 to 1.0000)	0.9572 (0.8987 to 0.9822)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.10 Treatment emergent severe adverse event according to SOC by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	1.0000 (1.0000 to 1.0000)	0.9572 (0.8987 to 0.9822)	
Number of patients at risk[b]					
2 Months	2	4	125	124	
4 Months	2	3	119	119	
6 Months	1	3	105	109	
8 Months	1	3	94	104	
10 Months	1	3	90	97	
12 Months	0	3	77	85	
14 Months	0	3	48	57	
16 Months	0	1	23	25	
Metabolism and nutrition disorders (days)					
Number (%) of events	0 (0.0)	0 (0.0)	7 (5.4)	11 (8.6)	0.9999
Number (%) of patients censored	3 (100.0)	4 (100.0)	123 (94.6)	117 (91.4)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Number of patients at risk[b]											
2 Months	43	37	10	21	3	3	9	12	25	36	
4 Months	35	30	9	16	1	3	8	9	18	32	
6 Months	30	26	7	13	1	2	8	8	14	27	
8 Months	23	21	7	12	1	2	8	7	12	26	
10 Months	22	17	6	10	1	1	5	7	10	22	
12 Months	19	14	4	8	1	1	4	5	9	21	
14 Months	13	10	3	5	0	0	0	3	6	18	
16 Months	6	5	1	3	0	0	0	0	5	10	
Infections and infestations (days)											
Number (%) of events	44 (59.5)	39 (70.9)	16 (80.0)	25 (89.3)	5 (100.0)	5 (71.4)	6 (40.0)	17 (81.0)	25 (71.4)	37 (90.2)	0.0928

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_greg_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Number (%) of patients censored	30 (40.5)	16 (29.1)	4 (20.0)	3 (10.7)	0 (0.0)	2 (28.6)	9 (60.0)	4 (19.0)	10 (28.6)	4 (9.8)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	1.4127 (0.8214 to 1.8398)	0.7885 (0.4600 to 1.8070)	0.8214 (0.0986 to 1.4127)	0.5749 (0.2628 to 1.2813)	0.2957 (0.1971 to 2.0370)	0.7228 (0.4928 to 2.0041)	1.7741 (0.5257 to NC)	0.7228 (0.1643 to 0.9856)	1.2813 (0.2628 to 1.6756)	0.5585 (0.3943 to 0.8214)	
Median (95% CI)	3.1211 (1.9055 to 8.9692)	2.6612 (1.8070 to 5.0595)	1.4949 (0.7885 to 3.6140)	1.3799 (0.7228 to 3.3183)	0.9528 (0.1971 to 7.5893)	2.0041 (0.4928 to NC)	NC (1.5770 to NC)	1.9055 (0.7228 to 4.1068)	2.0370 (1.4784 to 3.9425)	2.7598 (0.6571 to 3.9097)	
75% quantile (95% CI)	NC (9.1663 to NC)	11.8275 (5.0595 to NC)	5.4702 (1.5113 to NC)	4.0575 (1.9713 to NC)	2.0370 (0.1971 to 7.5893)	NC (0.7885 to NC)	NC (NC to NC)	4.1725 (1.9055 to NC)	7.1622 (3.3183 to NC)	5.5524 (3.2854 to 11.2690)	
Comparison vs. Pd											

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Log-Rank test p-value[a] vs Pd	-	0.2479		0.6457		0.3292		0.0045		0.4303	
Hazard ratio (95% CI) vs Pd	-	1.29 (0.84 to 1.98)		1.16 (0.62 to 2.18)		0.54 (0.16 to 1.89)		3.68 (1.42 to 9.54)		1.23 (0.74 to 2.05)	
P-value	-	0.2492		0.6460		0.3365		0.0074		0.4311	
Hazard ratio inverted (95% CI) vs IPd							0.27 (0.10 to 0.71)				
Events probability (95% CI)[b]											
2 Months	0.6034 (0.4794 to 0.7067)	0.5756 (0.4335 to 0.6942)	0.3500 (0.1566 to 0.5519)	0.4286 (0.2457 to 0.5996)	0.4000 (0.0520 to 0.7528)	0.5714 (0.1719 to 0.8371)	0.7333 (0.4362 to 0.8905)	0.4675 (0.2469 to 0.6615)	0.5429 (0.3661 to 0.6898)	0.5750 (0.4084 to 0.7104)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
4 Months	0.4658 (0.3443 to 0.5784)	0.4247 (0.2914 to 0.5516)	0.2500 (0.0910 to 0.4485)	0.2500 (0.1106 to 0.4178)	0.2000 (0.0084 to 0.5819)	0.2857 (0.0411 to 0.6115)	0.7333 (0.4362 to 0.8905)	0.3117 (0.1296 to 0.5143)	0.3317 (0.1825 to 0.4889)	0.3250 (0.1878 to 0.4698)	
6 Months	0.4146 (0.2954 to 0.5296)	0.3415 (0.2169 to 0.4699)	0.2500 (0.0910 to 0.4485)	0.1786 (0.0651 to 0.3375)	0.2000 (0.0084 to 0.5819)	0.2857 (0.0411 to 0.6115)	0.7333 (0.4362 to 0.8905)	0.1558 (0.0391 to 0.3444)	0.3317 (0.1825 to 0.4889)	0.2250 (0.1115 to 0.3626)	
8 Months	0.3966 (0.2783 to 0.5123)	0.2927 (0.1737 to 0.4222)	0.2000 (0.0624 to 0.3931)	0.1429 (0.0450 to 0.2950)	0.2000 (0.0084 to 0.5819)	0.2857 (0.0411 to 0.6115)	0.6667 (0.3753 to 0.8456)	0.1558 (0.0391 to 0.3444)	0.2370 (0.1011 to 0.4047)	0.1500 (0.0609 to 0.2764)	
10 Months	0.3569 (0.2408 to 0.4745)	0.2661 (0.1507 to 0.3962)	0.2000 (0.0624 to 0.3931)	0.1071 (0.0272 to 0.2506)	0.2000 (0.0084 to 0.5819)	0.2857 (0.0411 to 0.6115)	0.6000 (0.3176 to 0.7965)	0.1558 (0.0391 to 0.3444)	0.2370 (0.1011 to 0.4047)	0.1500 (0.0609 to 0.2764)	
12 Months	0.3569 (0.2408 to 0.4745)	0.2366 (0.1253 to 0.3677)	0.2000 (0.0624 to 0.3931)	0.1071 (0.0272 to 0.2506)	0.2000 (0.0084 to 0.5819)	0.2857 (0.0411 to 0.6115)	0.6000 (0.3176 to 0.7965)	0.1558 (0.0391 to 0.3444)	0.2370 (0.1011 to 0.4047)	0.1250 (0.0458 to 0.2461)	

SOC are presented if at least 10 events in a arm
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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
14 Months	0.3314 (0.2154 to 0.4518)	0.2366 (0.1253 to 0.3677)	0.2000 (0.0624 to 0.3931)	0.1071 (0.0272 to 0.2506)	0.2000 (0.0084 to 0.5819)	0.2857 (0.0411 to 0.6115)	0.6000 (0.3176 to 0.7965)	0.1558 (0.0391 to 0.3444)	0.2370 (0.1011 to 0.4047)	0.1000 (0.0318 to 0.2149)	
16 Months	0.3314 (0.2154 to 0.4518)	0.2366 (0.1253 to 0.3677)	0.2000 (0.0624 to 0.3931)	0.1071 (0.0272 to 0.2506)	0.2000 (0.0084 to 0.5819)	0.2857 (0.0411 to 0.6115)	0.6000 (0.3176 to 0.7965)	0.1558 (0.0391 to 0.3444)	0.2370 (0.1011 to 0.4047)	0.1000 (0.0318 to 0.2149)	
Number of patients at risk[b]											
2 Months	42	31	7	12	2	4	11	9	18	23	
4 Months	29	21	5	7	1	2	11	6	11	13	
6 Months	24	14	5	5	1	2	11	3	8	9	
8 Months	20	12	4	4	0	2	10	3	5	6	
10 Months	18	10	3	3	0	1	9	3	5	6	
12 Months	15	7	2	3	0	1	7	3	4	5	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
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16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
14 Months	13	4	1	2	0	1	0	2	3	4	
16 Months	6	2	0	1	0	1	0	1	3	3	
Injury, poisoning and procedural complications (days)											
Number (%) of events	9 (12.2)	27 (49.1)	3 (15.0)	7 (25.0)	0 (0.0)	4 (57.1)	1 (6.7)	15 (71.4)	4 (11.4)	19 (46.3)	0.4322
Number (%) of patients censored	65 (87.8)	28 (50.9)	17 (85.0)	21 (75.0)	5 (100.0)	3 (42.9)	14 (93.3)	6 (28.6)	31 (88.6)	22 (53.7)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1643)	NC (0.1971 to NC)	15.4415 (0.0329 to NC)	NC (NC to NC)	0.0986 (0.0986 to 5.2238)	NC (3.6797 to NC)	0.1314 (0.0657 to 0.1643)	NC (9.1006 to NC)	0.1314 (0.0657 to 0.5585)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Median (95% CI)	NC (NC to NC)	11.4661 (0.1643 to NC)	NC (NC to NC)	NC (15.4415 to NC)	NC (NC to NC)	5.2238 (0.0986 to NC)	NC (NC to NC)	0.1643 (0.1314 to 6.7680)	NC (NC to NC)	14.7187 (0.1971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.1971 to NC)	NC (NC to NC)	NC (0.2300 to NC)	NC (NC to NC)	NC (14.7187 to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	<.0001		0.3452		0.0568		0.0002		0.0006	
Hazard ratio (95% CI) vs Pd	-	5.48 (2.57 to 11.68)		1.90 (0.49 to 7.35)		NC		17.82 (2.33 to 136.09)		6.37 (1.88 to 21.56)	
P-value	-	<.0001		0.3535		0.9968		0.0055		0.0029	
Hazard ratio inverted (95% CI) vs IPd	0.18 (0.09 to 0.39)						0.06 (0.01 to 0.43)		0.16 (0.05 to 0.53)		

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
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16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Events probability (95% CI)[b]											
2 Months	0.9432 (0.8555 to 0.9783)	0.5807 (0.4394 to 0.6982)	0.8972 (0.6475 to 0.9733)	0.7857 (0.5840 to 0.8975)	1.0000 (1.0000 to 1.0000)	0.5714 (0.1719 to 0.8371)	1.0000 (1.0000 to 1.0000)	0.4286 (0.2192 to 0.6231)	1.0000 (1.0000 to 1.0000)	0.6098 (0.4442 to 0.7397)	
4 Months	0.9135 (0.8173 to 0.9602)	0.5807 (0.4394 to 0.6982)	0.8972 (0.6475 to 0.9733)	0.7857 (0.5840 to 0.8975)	1.0000 (1.0000 to 1.0000)	0.5714 (0.1719 to 0.8371)	0.9333 (0.6126 to 0.9903)	0.3333 (0.1488 to 0.5307)	1.0000 (1.0000 to 1.0000)	0.6098 (0.4442 to 0.7397)	
6 Months	0.9135 (0.8173 to 0.9602)	0.5600 (0.4184 to 0.6798)	0.8972 (0.6475 to 0.9733)	0.7857 (0.5840 to 0.8975)	1.0000 (1.0000 to 1.0000)	0.4286 (0.0978 to 0.7344)	0.9333 (0.6126 to 0.9903)	0.3333 (0.1488 to 0.5307)	0.9677 (0.7923 to 0.9954)	0.6098 (0.4442 to 0.7397)	
8 Months	0.8620 (0.7505 to 0.9260)	0.5123 (0.3692 to 0.6382)	0.8331 (0.5631 to 0.9436)	0.7857 (0.5840 to 0.8975)	1.0000 (1.0000 to 1.0000)	0.4286 (0.0978 to 0.7344)	0.9333 (0.6126 to 0.9903)	0.2857 (0.1166 to 0.4818)	0.9677 (0.7923 to 0.9954)	0.5832 (0.4176 to 0.7168)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
10 Months	0.8620 (0.7505 to 0.9260)	0.5123 (0.3692 to 0.6382)	0.8331 (0.5631 to 0.9436)	0.7857 (0.5840 to 0.8975)	1.0000 (1.0000 to 1.0000)	0.4286 (0.0978 to 0.7344)	0.9333 (0.6126 to 0.9903)	0.2857 (0.1166 to 0.4818)	0.8602 (0.6169 to 0.9541)	0.5541 (0.3881 to 0.6919)	
12 Months	0.8620 (0.7505 to 0.9260)	0.4866 (0.3432 to 0.6157)	0.8331 (0.5631 to 0.9436)	0.7857 (0.5840 to 0.8975)	1.0000 (1.0000 to 1.0000)	0.4286 (0.0978 to 0.7344)	0.9333 (0.6126 to 0.9903)	0.2857 (0.1166 to 0.4818)	0.8602 (0.6169 to 0.9541)	0.5541 (0.3881 to 0.6919)	
14 Months	0.8620 (0.7505 to 0.9260)	0.4866 (0.3432 to 0.6157)	0.8331 (0.5631 to 0.9436)	0.7857 (0.5840 to 0.8975)	1.0000 (1.0000 to 1.0000)	0.4286 (0.0978 to 0.7344)	0.9333 (0.6126 to 0.9903)	0.2857 (0.1166 to 0.4818)	0.8602 (0.6169 to 0.9541)	0.5541 (0.3881 to 0.6919)	
16 Months	0.8620 (0.7505 to 0.9260)	0.4866 (0.3432 to 0.6157)	0.8331 (0.5631 to 0.9436)	0.6286 (0.2718 to 0.8475)	1.0000 (1.0000 to 1.0000)	0.4286 (0.0978 to 0.7344)	0.9333 (0.6126 to 0.9903)	0.2857 (0.1166 to 0.4818)	0.8602 (0.6169 to 0.9541)	0.4617 (0.2491 to 0.6507)	
Number of patients at risk[b]											
2 Months	65	31	17	22	5	4	15	9	33	25	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_greg_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.1 Treatment emergent adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
4 Months	59	29	17	21	5	4	14	7	32	24	
6 Months	56	24	14	19	5	2	14	7	22	23	
8 Months	44	21	13	17	5	2	14	6	20	21	
10 Months	44	20	12	16	5	2	14	6	16	17	
12 Months	38	17	11	14	3	2	11	5	13	14	
14 Months	28	8	7	8	1	0	2	3	8	11	
16 Months	12	2	3	3	0	0	1	2	6	3	
Investigations (days)											
Number (%) of events	4 (5.4)	4 (7.3)	1 (5.0)	5 (17.9)	0 (0.0)	1 (14.3)	1 (6.7)	2 (9.5)	4 (11.4)	5 (12.2)	0.9507
Number (%) of patients censored	70 (94.6)	51 (92.7)	19 (95.0)	23 (82.1)	5 (100.0)	6 (85.7)	14 (93.3)	19 (90.5)	31 (88.6)	36 (87.8)	
Kaplan-Meier estimates of event in months											

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_greg_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.3 Treatment emergent serious adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
4 Months	52	39	13	21	3	4	12	19	24	29	
6 Months	46	32	13	19	3	4	12	16	18	23	
8 Months	38	30	13	19	3	4	12	15	15	20	
10 Months	37	27	12	18	3	2	12	14	15	18	
12 Months	32	24	10	13	1	2	10	13	13	16	
14 Months	24	14	7	7	0	1	1	9	9	14	
16 Months	11	4	3	2	0	1	0	5	6	7	
Injury, poisoning and procedural complications (days)											
Number (%) of events	1 (1.4)	5 (9.1)	1 (5.0)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)	1 (4.8)	0 (0.0)	4 (9.8)	1.0000
Number (%) of patients censored	73 (98.6)	50 (90.9)	19 (95.0)	28 (100.0)	5 (100.0)	6 (85.7)	15 (100.0)	20 (95.2)	35 (100.0)	37 (90.2)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_greg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.3 Treatment emergent serious adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.1971 to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.5298 to NC)	NC (NC to NC)	NC (2.5298 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.5298 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.0405		0.2367		0.3980		0.3865		0.0741	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_greg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.3 Treatment emergent serious adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Hazard ratio (95% CI) vs Pd	-	6.89 (0.81 to 58.98)		NC		NC		NC		NC	
P-value	-	0.0781		0.9984		0.9984		0.9984		0.9951	
Events probability (95% CI)[b]											
2 Months	0.9857 (0.9029 to 0.9980)	0.9087 (0.7945 to 0.9610)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9512 (0.8187 to 0.9876)	
4 Months	0.9857 (0.9029 to 0.9980)	0.9087 (0.7945 to 0.9610)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	0.9262 (0.7883 to 0.9756)	
6 Months	0.9857 (0.9029 to 0.9980)	0.9087 (0.7945 to 0.9610)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	0.9262 (0.7883 to 0.9756)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_greg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.3 Treatment emergent serious adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
8 Months	0.9857 (0.9029 to 0.9980)	0.9087 (0.7945 to 0.9610)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	0.8989 (0.7523 to 0.9609)	
10 Months	0.9857 (0.9029 to 0.9980)	0.9087 (0.7945 to 0.9610)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	0.8989 (0.7523 to 0.9609)	
12 Months	0.9857 (0.9029 to 0.9980)	0.9087 (0.7945 to 0.9610)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	0.8989 (0.7523 to 0.9609)	
14 Months	0.9857 (0.9029 to 0.9980)	0.9087 (0.7945 to 0.9610)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	0.8989 (0.7523 to 0.9609)	
16 Months	0.9857 (0.9029 to 0.9980)	0.9087 (0.7945 to 0.9610)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	0.8989 (0.7523 to 0.9609)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_greg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.9 Treatment emergent severe adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Injury, poisoning and procedural complications (days)											
Number (%) of events	0 (0.0)	4 (7.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)	1 (4.8)	0 (0.0)	2 (4.9)	1.0000
Number (%) of patients censored	74 (100.0)	51 (92.7)	20 (100.0)	28 (100.0)	5 (100.0)	6 (85.7)	15 (100.0)	20 (95.2)	35 (100.0)	39 (95.1)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.5298 to NC)	NC (NC to NC)	NC (2.5298 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.5298 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_greg_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.9 Treatment emergent severe adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.0194				0.3980		0.3865		0.2376	
Hazard ratio (95% CI) vs Pd	-	NC		NC		NC		NC		NC	
P-value	-	0.9950				0.9984		0.9984		0.9966	
Events probability (95% CI)[b]											
2 Months	1.0000 (1.0000 to 1.0000)	0.9269 (0.8169 to 0.9719)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9756 (0.8392 to 0.9965)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9269 (0.8169 to 0.9719)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	0.9756 (0.8392 to 0.9965)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_greg_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.9 Treatment emergent severe adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
6 Months	1.0000 (1.0000 to 1.0000)	0.9269 (0.8169 to 0.9719)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	0.9756 (0.8392 to 0.9965)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9269 (0.8169 to 0.9719)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	0.9756 (0.8392 to 0.9965)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9269 (0.8169 to 0.9719)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	0.9756 (0.8392 to 0.9965)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9269 (0.8169 to 0.9719)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	0.9756 (0.8392 to 0.9965)	
14 Months	1.0000 (1.0000 to 1.0000)	0.9269 (0.8169 to 0.9719)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	0.9420 (0.7834 to 0.9855)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_greg_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.9 Treatment emergent severe adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
16 Months	1.0000 (1.0000 to 1.0000)	0.9269 (0.8169 to 0.9719)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	0.9420 (0.7834 to 0.9855)	
Number of patients at risk[b]											
2 Months	69	50	19	28	5	7	15	20	34	40	
4 Months	63	46	19	27	5	6	15	19	32	39	
6 Months	59	40	15	24	5	5	15	19	23	36	
8 Months	50	39	15	22	5	5	15	18	21	35	
10 Months	50	37	14	21	5	4	14	18	19	32	
12 Months	44	33	13	18	3	4	11	16	16	29	
14 Months	31	20	9	12	1	1	2	12	11	22	
16 Months	14	7	3	4	0	1	1	5	8	11	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_greg_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.1 Treatment emergent adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0.3513 (0.2476 to 0.4565)	0.3991 (0.2842 to 0.5114)	0.3893 (0.2552 to 0.5212)	0.5283 (0.4085 to 0.6345)	
16 Months	0.3513 (0.2476 to 0.4565)	0.3079 (0.1737 to 0.4526)	0.3893 (0.2552 to 0.5212)	0.4876 (0.3529 to 0.6094)	
Number of patients at risk[b]					
2 Months	55	51	35	58	
4 Months	42	42	29	48	
6 Months	37	35	23	41	
8 Months	29	29	22	39	
10 Months	26	23	18	34	
12 Months	23	19	14	30	
14 Months	14	14	8	22	
16 Months	7	7	5	11	
Infections and infestations (days)					
Number (%) of events	62 (66.0)	59 (76.6)	34 (61.8)	64 (85.3)	0.1587

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.1 Treatment emergent adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of patients censored	32 (34.0)	18 (23.4)	21 (38.2)	11 (14.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.1828 (0.7556 to 1.6756)	0.7556 (0.4928 to 1.1499)	1.2813 (0.6571 to 1.5770)	0.6571 (0.4271 to 0.7556)	
Median (95% CI)	2.2998 (1.8398 to 3.6468)	2.6283 (1.8070 to 3.9097)	3.6140 (1.5770 to 9.3306)	1.9713 (0.9856 to 3.0883)	
75% quantile (95% CI)	NC (6.7351 to NC)	9.7906 (4.4353 to NC)	NC (9.3306 to NC)	4.5667 (3.6797 to 6.7351)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3248		0.0057	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.84 to 1.71)		1.79 (1.18 to 2.73)	
P-value	-	0.3255		0.0064	
Hazard ratio inverted (95% CI) vs IPd			0.56 (0.37 to 0.85)		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.1 Treatment emergent adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.5483 (0.4402 to 0.6440)	0.5667 (0.4481 to 0.6691)	0.5818 (0.4408 to 0.6990)	0.4990 (0.3806 to 0.6064)	
4 Months	0.3953 (0.2931 to 0.4956)	0.3792 (0.2707 to 0.4870)	0.4692 (0.3330 to 0.5941)	0.3049 (0.2038 to 0.4119)	
6 Months	0.3561 (0.2565 to 0.4568)	0.3078 (0.2068 to 0.4144)	0.4692 (0.3330 to 0.5941)	0.1940 (0.1127 to 0.2918)	
8 Months	0.3270 (0.2293 to 0.4282)	0.2592 (0.1640 to 0.3648)	0.3839 (0.2536 to 0.5127)	0.1525 (0.0812 to 0.2443)	
10 Months	0.2959 (0.2004 to 0.3975)	0.2407 (0.1477 to 0.3463)	0.3613 (0.2331 to 0.4909)	0.1386 (0.0712 to 0.2281)	
12 Months	0.2959 (0.2004 to 0.3975)	0.2006 (0.1130 to 0.3060)	0.3613 (0.2331 to 0.4909)	0.1386 (0.0712 to 0.2281)	
14 Months	0.2762 (0.1813 to 0.3793)	0.1755 (0.0912 to 0.2824)	0.3613 (0.2331 to 0.4909)	0.1386 (0.0712 to 0.2281)	
16 Months	0.2762 (0.1813 to 0.3793)	0.1755 (0.0912 to 0.2824)	0.3613 (0.2331 to 0.4909)	0.1386 (0.0712 to 0.2281)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.1 Treatment emergent adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	49	43	31	36	
4 Months	32	27	25	22	
6 Months	27	19	22	14	
8 Months	21	16	18	11	
10 Months	19	13	16	10	
12 Months	16	9	12	10	
14 Months	13	5	4	8	
16 Months	6	3	3	5	
Injury, poisoning and procedural complications (days)					
Number (%) of events	11 (11.7)	37 (48.1)	6 (10.9)	35 (46.7)	0.9057
Number (%) of patients censored	83 (88.3)	40 (51.9)	49 (89.1)	40 (53.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1971)	NC (9.4620 to NC)	0.1314 (0.0657 to 0.1643)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.1 Treatment emergent adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	14.7187 (0.5585 to NC)	NC (NC to NC)	15.4415 (0.2300 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Pd	-	6.00 (2.98 to 12.08)		5.55 (2.33 to 13.21)	
P-value	-	<.0001		0.0001	
Hazard ratio inverted (95% CI) vs IPd	0.17 (0.08 to 0.34)		0.18 (0.08 to 0.43)		
Events probability (95% CI)[b]					
2 Months	0.9553 (0.8851 to 0.9830)	0.5966 (0.4783 to 0.6965)	0.9633 (0.8611 to 0.9907)	0.6133 (0.4936 to 0.7129)	
4 Months	0.9321 (0.8550 to 0.9689)	0.5966 (0.4783 to 0.6965)	0.9440 (0.8363 to 0.9816)	0.5860 (0.4662 to 0.6879)	
6 Months	0.9321 (0.8550 to 0.9689)	0.5675 (0.4486 to 0.6700)	0.9239 (0.8096 to 0.9708)	0.5860 (0.4662 to 0.6879)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.1 Treatment emergent adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.8911 (0.8003 to 0.9421)	0.5355 (0.4157 to 0.6411)	0.9003 (0.7755 to 0.9575)	0.5560 (0.4357 to 0.6605)	
10 Months	0.8752 (0.7789 to 0.9313)	0.5355 (0.4157 to 0.6411)	0.8759 (0.7425 to 0.9428)	0.5396 (0.4189 to 0.6458)	
12 Months	0.8752 (0.7789 to 0.9313)	0.5170 (0.3963 to 0.6248)	0.8759 (0.7425 to 0.9428)	0.5396 (0.4189 to 0.6458)	
14 Months	0.8752 (0.7789 to 0.9313)	0.5170 (0.3963 to 0.6248)	0.8759 (0.7425 to 0.9428)	0.5396 (0.4189 to 0.6458)	
16 Months	0.8752 (0.7789 to 0.9313)	0.4596 (0.3087 to 0.5979)	0.8759 (0.7425 to 0.9428)	0.4722 (0.3085 to 0.6195)	
Number of patients at risk[b]					
2 Months	84	45	51	46	
4 Months	78	43	49	42	
6 Months	72	36	39	39	
8 Months	58	32	38	35	
10 Months	55	31	36	30	
12 Months	47	26	29	26	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.1 Treatment emergent adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	32	14	14	16	
16 Months	13	4	9	6	
Investigations (days)					
Number (%) of events	5 (5.3)	6 (7.8)	5 (9.1)	11 (14.7)	0.7132
Number (%) of patients censored	89 (94.7)	71 (92.2)	50 (90.9)	64 (85.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.3532 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5547		0.2500	
Hazard ratio (95% CI) vs Pd	-	1.43 (0.44 to 4.68)		1.93 (0.62 to 6.08)	
P-value	-	0.5567		0.2585	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.3 Treatment emergent serious adverse event according to SOC by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Number of patients at risk[b]											
2 Months	68	49	18	28	5	7	15	20	34	39	
4 Months	63	45	18	27	5	6	15	19	32	37	
6 Months	59	39	14	24	5	5	15	19	23	34	
8 Months	50	38	14	22	5	5	15	18	21	32	
10 Months	50	36	13	21	5	4	14	18	19	29	
12 Months	44	32	12	18	3	4	11	16	16	26	
14 Months	31	19	8	12	1	1	2	12	11	21	
16 Months	14	7	3	4	0	1	1	5	8	10	
Metabolism and nutrition disorders (days)											
Number (%) of events	4 (5.4)	3 (5.5)	0 (0.0)	0 (0.0)	1 (20.0)	0 (0.0)	1 (6.7)	3 (14.3)	0 (0.0)	2 (4.9)	0.9832

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.10 Treatment emergent severe adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	46	37	33	39	
12 Months	38	33	27	33	
14 Months	27	21	13	23	
16 Months	13	8	7	11	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	6 (7.8)	0 (0.0)	2 (2.7)	0.9998
Number (%) of patients censored	94 (100.0)	71 (92.2)	55 (100.0)	73 (97.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0071		0.2292	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.10 Treatment emergent severe adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	NC		NC	
P-value	-	0.9938		0.9966	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9479 (0.8670 to 0.9801)	1.0000 (1.0000 to 1.0000)	0.9867 (0.9091 to 0.9981)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9345 (0.8498 to 0.9722)	1.0000 (1.0000 to 1.0000)	0.9732 (0.8969 to 0.9932)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9345 (0.8498 to 0.9722)	1.0000 (1.0000 to 1.0000)	0.9732 (0.8969 to 0.9932)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9345 (0.8498 to 0.9722)	1.0000 (1.0000 to 1.0000)	0.9732 (0.8969 to 0.9932)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9345 (0.8498 to 0.9722)	1.0000 (1.0000 to 1.0000)	0.9732 (0.8969 to 0.9932)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9345 (0.8498 to 0.9722)	1.0000 (1.0000 to 1.0000)	0.9732 (0.8969 to 0.9932)	
14 Months	1.0000 (1.0000 to 1.0000)	0.9146 (0.8172 to 0.9613)	1.0000 (1.0000 to 1.0000)	0.9732 (0.8969 to 0.9932)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.10 Treatment emergent severe adverse event according to SOC by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.9146 (0.8172 to 0.9613)	1.0000 (1.0000 to 1.0000)	0.9732 (0.8969 to 0.9932)	
Number of patients at risk[b]					
2 Months	89	72	53	73	
4 Months	82	67	52	70	
6 Months	75	59	42	65	
8 Months	64	57	42	62	
10 Months	62	54	40	58	
12 Months	54	48	33	52	
14 Months	36	29	18	38	
16 Months	16	11	10	17	
Metabolism and nutrition disorders (days)					
Number (%) of events	5 (5.3)	5 (6.5)	3 (5.5)	8 (10.7)	0.6051
Number (%) of patients censored	89 (94.7)	72 (93.5)	52 (94.5)	67 (89.3)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.1 Treatment emergent adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Infections and infestations (days)					
Number (%) of events	85 (63.0)	110 (80.9)	11 (78.6)	13 (81.3)	0.8931
Number (%) of patients censored	50 (37.0)	26 (19.1)	3 (21.4)	3 (18.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.4127 (0.9528 to 1.6099)	0.7228 (0.4928 to 0.8542)	0.4271 (0.1643 to 0.8542)	0.3614 (0.1643 to 0.7228)	
Median (95% CI)	2.8255 (1.9384 to 5.3224)	2.3655 (1.8070 to 3.2526)	1.3142 (0.2628 to 7.4251)	0.7885 (0.2957 to 3.9097)	
75% quantile (95% CI)	NC (9.3306 to NC)	6.2752 (4.3696 to 12.5832)	7.4251 (0.8542 to NC)	3.9097 (0.7228 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0133		0.4404	
Hazard ratio (95% CI) vs Pd	-	1.43 (1.08 to 1.90)		1.39 (0.60 to 3.24)	
P-value	-	0.0138		0.4424	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.1 Treatment emergent adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.70 (0.53 to 0.93)				
Events probability (95% CI)[b]					
2 Months	0.5746 (0.4854 to 0.6539)	0.5508 (0.4633 to 0.6299)	0.4286 (0.1773 to 0.6604)	0.3667 (0.1357 to 0.6041)	
4 Months	0.4382 (0.3512 to 0.5217)	0.3559 (0.2759 to 0.4365)	0.2857 (0.0883 to 0.5237)	0.1956 (0.0372 to 0.4451)	
6 Months	0.4117 (0.3255 to 0.4957)	0.2634 (0.1918 to 0.3404)	0.2857 (0.0883 to 0.5237)	0.0978 (0.0065 to 0.3419)	
8 Months	0.3635 (0.2789 to 0.4484)	0.2155 (0.1497 to 0.2894)	0.2143 (0.0521 to 0.4479)	0.0978 (0.0065 to 0.3419)	
10 Months	0.3324 (0.2491 to 0.4177)	0.1983 (0.1347 to 0.2710)	0.2143 (0.0521 to 0.4479)	0.0978 (0.0065 to 0.3419)	
12 Months	0.3324 (0.2491 to 0.4177)	0.1803 (0.1191 to 0.2517)	0.2143 (0.0521 to 0.4479)	0.0978 (0.0065 to 0.3419)	
14 Months	0.3191 (0.2358 to 0.4053)	0.1703 (0.1104 to 0.2412)	0.2143 (0.0521 to 0.4479)	0.0978 (0.0065 to 0.3419)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.1 Treatment emergent adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3191 (0.2358 to 0.4053)	0.1703 (0.1104 to 0.2412)	0.2143 (0.0521 to 0.4479)	0.0978 (0.0065 to 0.3419)	
Number of patients at risk[b]					
2 Months	74	74	6	5	
4 Months	53	47	4	2	
6 Months	45	33	4	0	
8 Months	36	27	3	0	
10 Months	32	23	3	0	
12 Months	27	19	1	0	
14 Months	16	13	1	0	
16 Months	9	8	0	0	
Injury, poisoning and procedural complications (days)					
Number (%) of events	13 (9.6)	62 (45.6)	4 (28.6)	10 (62.5)	0.6997
Number (%) of patients censored	122 (90.4)	74 (54.4)	10 (71.4)	6 (37.5)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.1 Treatment emergent adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0986 to 0.1971)	NC (0.1971 to NC)	0.0657 (0.0329 to 0.1643)	
Median (95% CI)	NC (NC to NC)	15.4415 (6.1766 to NC)	NC (3.6797 to NC)	1.3470 (0.0657 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.1643 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		0.0165	
Hazard ratio (95% CI) vs Pd	-	6.10 (3.35 to 11.11)		4.35 (1.18 to 16.03)	
P-value	-	<.0001		0.0271	
Hazard ratio inverted (95% CI) vs IPd	0.16 (0.09 to 0.30)		0.23 (0.06 to 0.85)		
Events probability (95% CI)[b]					
2 Months	0.9694 (0.9205 to 0.9884)	0.6176 (0.5305 to 0.6934)	0.8462 (0.5122 to 0.9591)	0.5000 (0.2452 to 0.7105)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.1 Treatment emergent adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	0.9534 (0.8992 to 0.9788)	0.6101 (0.5228 to 0.6863)	0.7692 (0.4421 to 0.9191)	0.4167 (0.1736 to 0.6455)	
6 Months	0.9451 (0.8881 to 0.9734)	0.5944 (0.5067 to 0.6716)	0.7692 (0.4421 to 0.9191)	0.4167 (0.1736 to 0.6455)	
8 Months	0.9071 (0.8380 to 0.9477)	0.5610 (0.4725 to 0.6404)	0.7692 (0.4421 to 0.9191)	0.4167 (0.1736 to 0.6455)	
10 Months	0.8861 (0.8108 to 0.9326)	0.5519 (0.4632 to 0.6320)	0.7692 (0.4421 to 0.9191)	0.4167 (0.1736 to 0.6455)	
12 Months	0.8861 (0.8108 to 0.9326)	0.5519 (0.4632 to 0.6320)	0.7692 (0.4421 to 0.9191)	0.2778 (0.0605 to 0.5572)	
14 Months	0.8861 (0.8108 to 0.9326)	0.5519 (0.4632 to 0.6320)	0.7692 (0.4421 to 0.9191)	0.2778 (0.0605 to 0.5572)	
16 Months	0.8861 (0.8108 to 0.9326)	0.4865 (0.3693 to 0.5938)	0.7692 (0.4421 to 0.9191)	0.2778 (0.0605 to 0.5572)	
Number of patients at risk[b]					
2 Months	124	84	11	7	
4 Months	117	80	10	5	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.1 Treatment emergent adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	103	72	8	3	
8 Months	89	64	7	3	
10 Months	84	58	7	3	
12 Months	71	50	5	2	
14 Months	43	30	3	0	
16 Months	20	10	2	0	
Investigations (days)					
Number (%) of events	10 (7.4)	13 (9.6)	0 (0.0)	4 (25.0)	0.9891
Number (%) of patients censored	125 (92.6)	123 (90.4)	14 (100.0)	12 (75.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	2.2669 (0.0657 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.2669 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.3 Treatment emergent serious adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	111	117	11	7	
4 Months	95	107	9	5	
6 Months	84	91	8	3	
8 Months	74	86	7	2	
10 Months	72	78	7	1	
12 Months	61	67	5	1	
14 Months	37	45	4	0	
16 Months	17	19	3	0	
Injury, poisoning and procedural complications (days)					
Number (%) of events	2 (1.5)	5 (3.7)	0 (0.0)	6 (37.5)	0.9924
Number (%) of patients censored	133 (98.5)	131 (96.3)	14 (100.0)	10 (62.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	1.3470 (0.0657 to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.3 Treatment emergent serious adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.1643 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2786		0.0113	
Hazard ratio (95% CI) vs Pd	-	2.41 (0.47 to 12.40)		NC	
P-value	-	0.2940		0.9960	
Events probability (95% CI)[b]					
2 Months	0.9849 (0.9409 to 0.9962)	0.9779 (0.9332 to 0.9928)	1.0000 (1.0000 to 1.0000)	0.7500 (0.4634 to 0.8980)	
4 Months	0.9849 (0.9409 to 0.9962)	0.9705 (0.9232 to 0.9888)	1.0000 (1.0000 to 1.0000)	0.6000 (0.3130 to 0.7988)	
6 Months	0.9849 (0.9409 to 0.9962)	0.9705 (0.9232 to 0.9888)	1.0000 (1.0000 to 1.0000)	0.6000 (0.3130 to 0.7988)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.3 Treatment emergent serious adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.9849 (0.9409 to 0.9962)	0.9620 (0.9109 to 0.9840)	1.0000 (1.0000 to 1.0000)	0.6000 (0.3130 to 0.7988)	
10 Months	0.9849 (0.9409 to 0.9962)	0.9620 (0.9109 to 0.9840)	1.0000 (1.0000 to 1.0000)	0.6000 (0.3130 to 0.7988)	
12 Months	0.9849 (0.9409 to 0.9962)	0.9620 (0.9109 to 0.9840)	1.0000 (1.0000 to 1.0000)	0.6000 (0.3130 to 0.7988)	
14 Months	0.9849 (0.9409 to 0.9962)	0.9620 (0.9109 to 0.9840)	1.0000 (1.0000 to 1.0000)	0.6000 (0.3130 to 0.7988)	
16 Months	0.9849 (0.9409 to 0.9962)	0.9620 (0.9109 to 0.9840)	1.0000 (1.0000 to 1.0000)	0.6000 (0.3130 to 0.7988)	
Number of patients at risk[b]					
2 Months	126	132	14	11	
4 Months	120	126	13	8	
6 Months	106	116	10	5	
8 Months	96	110	9	5	
10 Months	93	103	8	5	
12 Months	80	91	6	5	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.3 Treatment emergent serious adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	49	63	4	2	
16 Months	23	25	3	2	
Metabolism and nutrition disorders (days)					
Number (%) of events	5 (3.7)	6 (4.4)	1 (7.1)	2 (12.5)	0.6597
Number (%) of patients censored	130 (96.3)	130 (95.6)	13 (92.9)	14 (87.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.2053 to NC)	NC (0.0657 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8247		0.5668	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.35 to 3.75)		1.99 (0.18 to 22.08)	
P-value	-	0.8254		0.5744	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_ecog_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.10 Treatment emergent severe adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	73	73	6	3	
12 Months	61	63	4	3	
14 Months	37	42	3	2	
16 Months	18	18	2	1	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	3 (2.2)	0 (0.0)	5 (31.3)	0.9997
Number (%) of patients censored	135 (100.0)	133 (97.8)	14 (100.0)	11 (68.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	2.5298 (0.0657 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.5298 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0951		0.0219	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_ecog_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.10 Treatment emergent severe adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	NC		NC	
P-value	-	0.9957		0.9964	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9853 (0.9425 to 0.9963)	1.0000 (1.0000 to 1.0000)	0.8125 (0.5246 to 0.9354)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9853 (0.9425 to 0.9963)	1.0000 (1.0000 to 1.0000)	0.6648 (0.3688 to 0.8461)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9853 (0.9425 to 0.9963)	1.0000 (1.0000 to 1.0000)	0.6648 (0.3688 to 0.8461)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9853 (0.9425 to 0.9963)	1.0000 (1.0000 to 1.0000)	0.6648 (0.3688 to 0.8461)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9853 (0.9425 to 0.9963)	1.0000 (1.0000 to 1.0000)	0.6648 (0.3688 to 0.8461)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9853 (0.9425 to 0.9963)	1.0000 (1.0000 to 1.0000)	0.6648 (0.3688 to 0.8461)	
14 Months	1.0000 (1.0000 to 1.0000)	0.9746 (0.9217 to 0.9919)	1.0000 (1.0000 to 1.0000)	0.6648 (0.3688 to 0.8461)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_ecog_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.10 Treatment emergent severe adverse event according to SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.9746 (0.9217 to 0.9919)	1.0000 (1.0000 to 1.0000)	0.6648 (0.3688 to 0.8461)	
Number of patients at risk[b]					
2 Months	128	133	14	12	
4 Months	121	128	13	9	
6 Months	107	118	10	6	
8 Months	97	113	9	6	
10 Months	94	106	8	6	
12 Months	81	94	6	6	
14 Months	50	64	4	3	
16 Months	23	26	3	2	
Metabolism and nutrition disorders (days)					
Number (%) of events	7 (5.2)	10 (7.4)	1 (7.1)	3 (18.8)	0.4928
Number (%) of patients censored	128 (94.8)	126 (92.6)	13 (92.9)	13 (81.3)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.1 Treatment emergent adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	22	28	16	16	5	13	
12 Months	19	24	13	13	4	12	
14 Months	12	16	8	10	2	10	
16 Months	8	9	4	5	0	4	
Infections and infestations (days)							
Number (%) of events	34 (66.7)	49 (77.8)	34 (61.8)	42 (79.2)	25 (62.5)	29 (87.9)	0.9163
Number (%) of patients censored	17 (33.3)	14 (22.2)	21 (38.2)	11 (20.8)	15 (37.5)	4 (12.1)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	1.7084 (0.9528 to 1.9055)	0.6899 (0.3943 to 1.2485)	0.8542 (0.4928 to 1.5113)	0.7228 (0.3943 to 1.3142)	1.1828 (0.4271 to 1.4127)	0.5585 (0.4271 to 0.8214)	
Median (95% CI)	2.3984 (1.8727 to 7.5893)	2.0041 (1.2485 to 3.6797)	2.5955 (1.5113 to 8.9692)	2.6612 (1.3142 to 4.1068)	3.3183 (1.3470 to 7.3265)	2.2341 (0.6571 to 3.3183)	
75% quantile (95% CI)	NC (7.5893 to NC)	11.8275 (3.7454 to NC)	NC (7.1622 to NC)	6.6694 (4.1068 to NC)	9.1663 (5.3224 to NC)	3.9754 (2.6283 to 7.7536)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.1 Treatment emergent adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1100		0.1727		0.0650	
Hazard ratio (95% CI) vs Pd	-	1.43 (0.92 to 2.22)		1.37 (0.87 to 2.16)		1.65 (0.96 to 2.82)	
P-value	-	0.1118		0.1747		0.0678	
Events probability (95% CI)[b]							
2 Months	0.6078 (0.4606 to 0.7263)	0.5000 (0.3706 to 0.6163)	0.5717 (0.4287 to 0.6914)	0.5843 (0.4403 to 0.7033)	0.5034 (0.3371 to 0.6483)	0.5010 (0.3199 to 0.6577)	
4 Months	0.4305 (0.2933 to 0.5604)	0.3548 (0.2387 to 0.4727)	0.4193 (0.2860 to 0.5468)	0.3877 (0.2565 to 0.5169)	0.4363 (0.2724 to 0.5891)	0.2411 (0.1096 to 0.4004)	
6 Months	0.4100 (0.2748 to 0.5403)	0.2696 (0.1657 to 0.3846)	0.3983 (0.2668 to 0.5265)	0.3061 (0.1864 to 0.4341)	0.3966 (0.2341 to 0.5548)	0.1378 (0.0443 to 0.2835)	
8 Months	0.3690 (0.2387 to 0.4996)	0.2517 (0.1508 to 0.3657)	0.3762 (0.2466 to 0.5052)	0.2186 (0.1159 to 0.3421)	0.2974 (0.1418 to 0.4711)	0.1033 (0.0267 to 0.2411)	
10 Months	0.3473 (0.2197 to 0.4780)	0.2517 (0.1508 to 0.3657)	0.3527 (0.2252 to 0.4825)	0.1640 (0.0735 to 0.2859)	0.2380 (0.0926 to 0.4205)	0.1033 (0.0267 to 0.2411)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_seiss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.1 Treatment emergent adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
12 Months	0.3473 (0.2197 to 0.4780)	0.2323 (0.1347 to 0.3455)	0.3527 (0.2252 to 0.4825)	0.1640 (0.0735 to 0.2859)	0.2380 (0.0926 to 0.4205)	0.0689 (0.0123 to 0.1963)	
14 Months	0.3206 (0.1953 to 0.4527)	0.2091 (0.1149 to 0.3224)	0.3527 (0.2252 to 0.4825)	0.1640 (0.0735 to 0.2859)	0.2380 (0.0926 to 0.4205)	0.0689 (0.0123 to 0.1963)	
16 Months	0.3206 (0.1953 to 0.4527)	0.2091 (0.1149 to 0.3224)	0.3527 (0.2252 to 0.4825)	0.1640 (0.0735 to 0.2859)	0.2380 (0.0926 to 0.4205)	0.0689 (0.0123 to 0.1963)	
Number of patients at risk[b]							
2 Months	31	31	30	30	18	16	
4 Months	21	22	22	19	13	7	
6 Months	20	15	18	14	10	4	
8 Months	17	14	16	10	6	3	
10 Months	16	14	15	6	4	3	
12 Months	14	11	10	6	4	2	
14 Months	7	7	7	4	3	2	
16 Months	5	5	2	1	2	2	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.1 Treatment emergent adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Injury, poisoning and procedural complications (days)							
Number (%) of events	7 (13.7)	33 (52.4)	4 (7.3)	27 (50.9)	5 (12.5)	11 (33.3)	0.3030
Number (%) of patients censored	44 (86.3)	30 (47.6)	51 (92.7)	26 (49.1)	35 (87.5)	22 (66.7)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (9.1006 to NC)	0.0986 (0.0657 to 0.1643)	NC (NC to NC)	0.0986 (0.0657 to 0.1643)	NC (6.0780 to NC)	2.5298 (0.0657 to NC)	
Median (95% CI)	NC (NC to NC)	6.7680 (0.1971 to NC)	NC (NC to NC)	11.4661 (0.1643 to NC)	NC (NC to NC)	NC (6.1766 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.4415 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001		0.0539	
Hazard ratio (95% CI) vs Pd	-	5.59 (2.46 to 12.70)		9.15 (3.20 to 26.20)		2.72 (0.94 to 7.85)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.1 Treatment emergent adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
P-value	-	<.0001		<.0001		0.0643	
Hazard ratio inverted (95% CI) vs IPd	0.18 (0.08 to 0.41)		0.11 (0.04 to 0.31)				
Events probability (95% CI)[b]							
2 Months	0.9804 (0.8689 to 0.9972)	0.5397 (0.4095 to 0.6530)	0.9441 (0.8364 to 0.9816)	0.5849 (0.4410 to 0.7037)	0.9471 (0.8043 to 0.9866)	0.7576 (0.5733 to 0.8706)	
4 Months	0.9216 (0.8044 to 0.9698)	0.5233 (0.3937 to 0.6377)	0.9441 (0.8364 to 0.9816)	0.5849 (0.4410 to 0.7037)	0.9471 (0.8043 to 0.9866)	0.7246 (0.5371 to 0.8463)	
6 Months	0.9020 (0.7804 to 0.9580)	0.5233 (0.3937 to 0.6377)	0.9441 (0.8364 to 0.9816)	0.5446 (0.4012 to 0.6673)	0.9471 (0.8043 to 0.9866)	0.7246 (0.5371 to 0.8463)	
8 Months	0.8819 (0.7559 to 0.9451)	0.4859 (0.3567 to 0.6034)	0.9210 (0.8020 to 0.9698)	0.5236 (0.3807 to 0.6483)	0.8469 (0.6246 to 0.9430)	0.6865 (0.4936 to 0.8184)	
10 Months	0.8609 (0.7301 to 0.9312)	0.4859 (0.3567 to 0.6034)	0.9210 (0.8020 to 0.9698)	0.5236 (0.3807 to 0.6483)	0.7864 (0.5405 to 0.9104)	0.6407 (0.4398 to 0.7857)	
12 Months	0.8609 (0.7301 to 0.9312)	0.4859 (0.3567 to 0.6034)	0.9210 (0.8020 to 0.9698)	0.4974 (0.3536 to 0.6256)	0.7864 (0.5405 to 0.9104)	0.6407 (0.4398 to 0.7857)	
14 Months	0.8609 (0.7301 to 0.9312)	0.4859 (0.3567 to 0.6034)	0.9210 (0.8020 to 0.9698)	0.4974 (0.3536 to 0.6256)	0.7864 (0.5405 to 0.9104)	0.6407 (0.4398 to 0.7857)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.1 Treatment emergent adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.8609 (0.7301 to 0.9312)	0.4165 (0.2520 to 0.5732)	0.9210 (0.8020 to 0.9698)	0.4145 (0.2292 to 0.5907)	0.7864 (0.5405 to 0.9104)	0.6407 (0.4398 to 0.7857)	
Number of patients at risk[b]							
2 Months	50	34	50	31	33	24	
4 Months	47	32	50	29	28	22	
6 Months	46	28	43	26	20	19	
8 Months	42	26	37	24	15	15	
10 Months	41	24	35	22	13	13	
12 Months	37	21	26	18	11	11	
14 Months	23	11	16	11	7	6	
16 Months	12	5	6	2	4	3	
Investigations (days)							
Number (%) of events	4 (7.8)	6 (9.5)	3 (5.5)	2 (3.8)	3 (7.5)	8 (24.2)	0.5548
Number (%) of patients censored	47 (92.2)	57 (90.5)	52 (94.5)	51 (96.2)	37 (92.5)	25 (75.8)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.3 Treatment emergent serious adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	12	12	5	4	3	3	
Injury, poisoning and procedural complications (days)							
Number (%) of events	1 (2.0)	5 (7.9)	1 (1.8)	3 (5.7)	0 (0.0)	3 (9.1)	0.9835
Number (%) of patients censored	50 (98.0)	58 (92.1)	54 (98.2)	50 (94.3)	40 (100.0)	30 (90.9)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.5298 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1504		0.2906		0.0610	
Hazard ratio (95% CI) vs Pd	-	4.25 (0.50 to 36.38)		3.17 (0.33 to 30.52)		NC	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_seiss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.3 Treatment emergent serious adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
P-value	-	0.1868		0.3171		0.9956	
Events probability (95% CI)[b]							
2 Months	0.9804 (0.8689 to 0.9972)	0.9683 (0.8790 to 0.9920)	0.9818 (0.8779 to 0.9974)	0.9434 (0.8347 to 0.9814)	1.0000 (1.0000 to 1.0000)	0.9384 (0.7754 to 0.9842)	
4 Months	0.9804 (0.8689 to 0.9972)	0.9362 (0.8390 to 0.9756)	0.9818 (0.8779 to 0.9974)	0.9434 (0.8347 to 0.9814)	1.0000 (1.0000 to 1.0000)	0.9061 (0.7361 to 0.9687)	
6 Months	0.9804 (0.8689 to 0.9972)	0.9362 (0.8390 to 0.9756)	0.9818 (0.8779 to 0.9974)	0.9434 (0.8347 to 0.9814)	1.0000 (1.0000 to 1.0000)	0.9061 (0.7361 to 0.9687)	
8 Months	0.9804 (0.8689 to 0.9972)	0.9179 (0.8135 to 0.9651)	0.9818 (0.8779 to 0.9974)	0.9434 (0.8347 to 0.9814)	1.0000 (1.0000 to 1.0000)	0.9061 (0.7361 to 0.9687)	
10 Months	0.9804 (0.8689 to 0.9972)	0.9179 (0.8135 to 0.9651)	0.9818 (0.8779 to 0.9974)	0.9434 (0.8347 to 0.9814)	1.0000 (1.0000 to 1.0000)	0.9061 (0.7361 to 0.9687)	
12 Months	0.9804 (0.8689 to 0.9972)	0.9179 (0.8135 to 0.9651)	0.9818 (0.8779 to 0.9974)	0.9434 (0.8347 to 0.9814)	1.0000 (1.0000 to 1.0000)	0.9061 (0.7361 to 0.9687)	
14 Months	0.9804 (0.8689 to 0.9972)	0.9179 (0.8135 to 0.9651)	0.9818 (0.8779 to 0.9974)	0.9434 (0.8347 to 0.9814)	1.0000 (1.0000 to 1.0000)	0.9061 (0.7361 to 0.9687)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_seiss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.3 Treatment emergent serious adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.9804 (0.8689 to 0.9972)	0.9179 (0.8135 to 0.9651)	0.9818 (0.8779 to 0.9974)	0.9434 (0.8347 to 0.9814)	1.0000 (1.0000 to 1.0000)	0.9061 (0.7361 to 0.9687)	
Number of patients at risk[b]							
2 Months	50	61	52	49	35	30	
4 Months	50	58	52	47	29	26	
6 Months	50	52	44	44	20	22	
8 Months	47	50	39	43	17	19	
10 Months	46	48	37	39	16	18	
12 Months	42	43	28	34	14	16	
14 Months	26	28	17	24	10	10	
16 Months	15	14	7	8	4	5	
Metabolism and nutrition disorders (days)							
Number (%) of events	2 (3.9)	4 (6.3)	1 (1.8)	1 (1.9)	3 (7.5)	3 (9.1)	0.9263
Number (%) of patients censored	49 (96.1)	59 (93.7)	54 (98.2)	52 (98.1)	37 (92.5)	30 (90.9)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_seiss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.9 Treatment emergent severe adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.7361 (0.5678 to 0.8471)	0.6749 (0.5374 to 0.7796)	0.6496 (0.4994 to 0.7649)	0.5035 (0.3495 to 0.6389)	0.6600 (0.4746 to 0.7932)	0.4452 (0.2645 to 0.6112)	
Number of patients at risk[b]							
2 Months	48	53	42	43	28	24	
4 Months	43	51	37	37	22	18	
6 Months	40	44	33	32	17	14	
8 Months	36	42	29	27	14	14	
10 Months	36	38	29	23	13	14	
12 Months	33	32	20	22	11	11	
14 Months	20	21	12	14	8	8	
16 Months	12	12	4	3	4	4	
Injury, poisoning and procedural complications (days)							
Number (%) of events	0 (0.0)	2 (3.2)	0 (0.0)	3 (5.7)	0 (0.0)	3 (9.1)	1.0000
Number (%) of patients censored	51 (100.0)	61 (96.8)	55 (100.0)	50 (94.3)	40 (100.0)	30 (90.9)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_seiss_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.9 Treatment emergent severe adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.3532 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2014		0.0748		0.0848	
Hazard ratio (95% CI) vs Pd	-	NC		NC		NC	
P-value	-	0.9965		0.9956		0.9972	
Events probability (95% CI)[b]							
2 Months	1.0000 (1.0000 to 1.0000)	0.9841 (0.8926 to 0.9977)	1.0000 (1.0000 to 1.0000)	0.9434 (0.8347 to 0.9814)	1.0000 (1.0000 to 1.0000)	0.9688 (0.7982 to 0.9955)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_seiss_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.9 Treatment emergent severe adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	1.0000 (1.0000 to 1.0000)	0.9683 (0.8790 to 0.9920)	1.0000 (1.0000 to 1.0000)	0.9434 (0.8347 to 0.9814)	1.0000 (1.0000 to 1.0000)	0.9365 (0.7690 to 0.9837)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9683 (0.8790 to 0.9920)	1.0000 (1.0000 to 1.0000)	0.9434 (0.8347 to 0.9814)	1.0000 (1.0000 to 1.0000)	0.9365 (0.7690 to 0.9837)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9683 (0.8790 to 0.9920)	1.0000 (1.0000 to 1.0000)	0.9434 (0.8347 to 0.9814)	1.0000 (1.0000 to 1.0000)	0.9365 (0.7690 to 0.9837)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9683 (0.8790 to 0.9920)	1.0000 (1.0000 to 1.0000)	0.9434 (0.8347 to 0.9814)	1.0000 (1.0000 to 1.0000)	0.9365 (0.7690 to 0.9837)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9683 (0.8790 to 0.9920)	1.0000 (1.0000 to 1.0000)	0.9434 (0.8347 to 0.9814)	1.0000 (1.0000 to 1.0000)	0.9365 (0.7690 to 0.9837)	
14 Months	1.0000 (1.0000 to 1.0000)	0.9683 (0.8790 to 0.9920)	1.0000 (1.0000 to 1.0000)	0.9434 (0.8347 to 0.9814)	1.0000 (1.0000 to 1.0000)	0.8814 (0.6615 to 0.9621)	
16 Months	1.0000 (1.0000 to 1.0000)	0.9683 (0.8790 to 0.9920)	1.0000 (1.0000 to 1.0000)	0.9434 (0.8347 to 0.9814)	1.0000 (1.0000 to 1.0000)	0.8814 (0.6615 to 0.9621)	
Number of patients at risk[b]							
2 Months	51	62	53	49	35	31	
4 Months	50	60	53	47	29	27	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_seiss_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.9 Treatment emergent severe adverse event according to SOC by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	50	54	45	44	20	23	
8 Months	47	53	40	43	17	20	
10 Months	46	51	38	39	16	19	
12 Months	42	46	29	34	14	17	
14 Months	26	30	18	24	10	10	
16 Months	15	15	7	8	4	5	
Metabolism and nutrition disorders (days)							
Number (%) of events	3 (5.9)	6 (9.5)	2 (3.6)	4 (7.5)	3 (7.5)	3 (9.1)	0.8522
Number (%) of patients censored	48 (94.1)	57 (90.5)	53 (96.4)	49 (92.5)	37 (92.5)	30 (90.9)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.0678 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_seiss_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.1 Treatment emergent adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	25	32	57	68	8	9	
4 Months	22	27	42	56	7	7	
6 Months	22	23	34	46	4	7	
8 Months	18	21	29	42	4	5	
10 Months	17	21	25	32	2	4	
12 Months	15	19	20	26	2	4	
14 Months	9	12	12	20	1	4	
16 Months	6	7	6	9	0	2	
Infections and infestations (days)							
Number (%) of events	19 (61.3)	30 (76.9)	61 (62.9)	81 (82.7)	16 (76.2)	12 (80.0)	0.3859
Number (%) of patients censored	12 (38.7)	9 (23.1)	36 (37.1)	17 (17.3)	5 (23.8)	3 (20.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	1.7084 (0.8542 to 1.9055)	0.7885 (0.3943 to 1.7741)	1.4127 (0.7556 to 1.6756)	0.6571 (0.4271 to 0.7885)	0.7885 (0.1314 to 1.2813)	0.4928 (0.2957 to 1.1499)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_seriss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.1 Treatment emergent adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	2.3326 (1.8727 to NC)	2.3984 (1.3142 to 4.5339)	3.4497 (2.0370 to 7.1622)	2.2669 (1.2813 to 3.2854)	1.4127 (0.7885 to 5.3224)	2.2341 (0.4928 to 3.9754)	
75% quantile (95% CI)	NC (7.4251 to NC)	9.4620 (3.6797 to NC)	NC (9.3306 to NC)	5.9138 (4.0411 to 11.2690)	5.3224 (1.4127 to NC)	3.9754 (1.1499 to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1746		0.0086		0.7867	
Hazard ratio (95% CI) vs Pd	-	1.49 (0.84 to 2.65)		1.56 (1.12 to 2.18)		0.90 (0.42 to 1.93)	
P-value	-	0.1773		0.0091		0.7868	
Hazard ratio inverted (95% CI) vs IPd			0.64 (0.46 to 0.90)				
Events probability (95% CI)[b]							
2 Months	0.5806 (0.3896 to 0.7309)	0.5128 (0.3479 to 0.6555)	0.6094 (0.5035 to 0.6995)	0.5460 (0.4418 to 0.6388)	0.3048 (0.1251 to 0.5069)	0.5026 (0.2305 to 0.7243)	
4 Months	0.4516 (0.2739 to 0.6139)	0.3846 (0.2351 to 0.5322)	0.4457 (0.3431 to 0.5432)	0.3453 (0.2519 to 0.4404)	0.3048 (0.1251 to 0.5069)	0.1795 (0.0313 to 0.4267)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_seriss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.1 Treatment emergent adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.4516 (0.2739 to 0.6139)	0.2778 (0.1483 to 0.4233)	0.4216 (0.3199 to 0.5197)	0.2472 (0.1655 to 0.3377)	0.2032 (0.0469 to 0.4361)	0.1795 (0.0313 to 0.4267)	
8 Months	0.3871 (0.2201 to 0.5515)	0.2500 (0.1271 to 0.3939)	0.3807 (0.2803 to 0.4804)	0.2001 (0.1256 to 0.2873)	0.1016 (0.0076 to 0.3423)	0.0897 (0.0057 to 0.3245)	
10 Months	0.3871 (0.2201 to 0.5515)	0.2500 (0.1271 to 0.3939)	0.3368 (0.2384 to 0.4378)	0.1735 (0.1032 to 0.2590)	0.1016 (0.0076 to 0.3423)	0.0897 (0.0057 to 0.3245)	
12 Months	0.3871 (0.2201 to 0.5515)	0.2500 (0.1271 to 0.3939)	0.3368 (0.2384 to 0.4378)	0.1468 (0.0818 to 0.2298)	0.1016 (0.0076 to 0.3423)	0.0897 (0.0057 to 0.3245)	
14 Months	0.3871 (0.2201 to 0.5515)	0.2143 (0.0986 to 0.3591)	0.3143 (0.2148 to 0.4186)	0.1468 (0.0818 to 0.2298)	0.1016 (0.0076 to 0.3423)	0.0897 (0.0057 to 0.3245)	
16 Months	0.3871 (0.2201 to 0.5515)	0.2143 (0.0986 to 0.3591)	0.3143 (0.2148 to 0.4186)	0.1468 (0.0818 to 0.2298)	0.1016 (0.0076 to 0.3423)	0.0897 (0.0057 to 0.3245)	
Number of patients at risk[b]							
2 Months	18	20	57	52	5	7	
4 Months	14	15	40	32	3	2	
6 Months	14	10	33	21	2	2	
8 Months	11	9	27	17	1	1	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_seriss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.1 Treatment emergent adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	11	9	23	13	1	1	
12 Months	10	8	17	10	1	1	
14 Months	6	4	10	8	1	1	
16 Months	4	2	5	5	0	1	
Injury, poisoning and procedural complications (days)							
Number (%) of events	5 (16.1)	22 (56.4)	9 (9.3)	41 (41.8)	3 (14.3)	9 (60.0)	0.9487
Number (%) of patients censored	26 (83.9)	17 (43.6)	88 (90.7)	57 (58.2)	18 (85.7)	6 (40.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (4.4353 to NC)	0.0986 (0.0657 to 0.1643)	NC (NC to NC)	0.1314 (0.0657 to 0.2300)	NC (0.1971 to NC)	0.0657 (0.0329 to 2.5298)	
Median (95% CI)	NC (NC to NC)	3.0554 (0.1314 to NC)	NC (NC to NC)	NC (6.7680 to NC)	NC (6.0780 to NC)	6.1766 (0.0657 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.7187 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.1766 to NC)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.1 Treatment emergent adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0002		<.0001		0.0097	
Hazard ratio (95% CI) vs Pd	-	5.35 (2.01 to 14.23)		6.32 (2.96 to 13.50)		4.82 (1.30 to 17.92)	
P-value	-	0.0008		<.0001		0.0189	
Hazard ratio inverted (95% CI) vs IPd	0.19 (0.07 to 0.50)		0.16 (0.07 to 0.34)		0.21 (0.06 to 0.77)		
Events probability (95% CI)[b]							
2 Months	1.0000 (1.0000 to 1.0000)	0.5128 (0.3479 to 0.6555)	0.9573 (0.8902 to 0.9838)	0.6429 (0.5395 to 0.7288)	0.8964 (0.6433 to 0.9732)	0.6000 (0.3176 to 0.7965)	
4 Months	0.9355 (0.7659 to 0.9835)	0.4858 (0.3229 to 0.6306)	0.9464 (0.8761 to 0.9774)	0.6429 (0.5395 to 0.7288)	0.8964 (0.6433 to 0.9732)	0.5250 (0.2524 to 0.7397)	
6 Months	0.9032 (0.7293 to 0.9677)	0.4858 (0.3229 to 0.6306)	0.9464 (0.8761 to 0.9774)	0.6207 (0.5165 to 0.7087)	0.8964 (0.6433 to 0.9732)	0.5250 (0.2524 to 0.7397)	
8 Months	0.8710 (0.6919 to 0.9495)	0.4573 (0.2964 to 0.6043)	0.9200 (0.8386 to 0.9612)	0.5968 (0.4916 to 0.6871)	0.7683 (0.3856 to 0.9297)	0.4375 (0.1789 to 0.6723)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.1 Treatment emergent adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.8375 (0.6525 to 0.9290)	0.4573 (0.2964 to 0.6043)	0.9051 (0.8178 to 0.9518)	0.5968 (0.4916 to 0.6871)	0.7683 (0.3856 to 0.9297)	0.2917 (0.0619 to 0.5795)	
12 Months	0.8375 (0.6525 to 0.9290)	0.4573 (0.2964 to 0.6043)	0.9051 (0.8178 to 0.9518)	0.5822 (0.4758 to 0.6745)	0.7683 (0.3856 to 0.9297)	0.2917 (0.0619 to 0.5795)	
14 Months	0.8375 (0.6525 to 0.9290)	0.4573 (0.2964 to 0.6043)	0.9051 (0.8178 to 0.9518)	0.5822 (0.4758 to 0.6745)	0.7683 (0.3856 to 0.9297)	0.2917 (0.0619 to 0.5795)	
16 Months	0.8375 (0.6525 to 0.9290)	0.3429 (0.1370 to 0.5620)	0.9051 (0.8178 to 0.9518)	0.5337 (0.3973 to 0.6524)	0.7683 (0.3856 to 0.9297)	0.2917 (0.0619 to 0.5795)	
Number of patients at risk[b]							
2 Months	31	20	89	63	15	8	
4 Months	29	18	87	60	11	7	
6 Months	28	17	76	52	7	6	
8 Months	26	16	65	48	5	3	
10 Months	25	16	61	44	5	1	
12 Months	23	14	49	37	4	1	
14 Months	13	5	30	24	3	1	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.1 Treatment emergent adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	7	3	14	7	1	0	
Investigations (days)							
Number (%) of events	4 (12.9)	4 (10.3)	4 (4.1)	12 (12.2)	2 (9.5)	1 (6.7)	0.1708
Number (%) of patients censored	27 (87.1)	35 (89.7)	93 (95.9)	86 (87.8)	19 (90.5)	14 (93.3)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (5.6181 to NC)	NC (4.5667 to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.0041 to NC)	NC (0.0657 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.4353 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7974		0.0241		0.6464	
Hazard ratio (95% CI) vs Pd	-	0.83 (0.21 to 3.34)		3.86 (1.09 to 13.69)		0.57 (0.05 to 6.38)	
P-value	-	0.7977		0.0363		0.6506	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.5 Treatment emergent serious adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	8	8	12	10	0	1	
Injury, poisoning and procedural complications (days)							
Number (%) of events	0 (0.0)	4 (10.3)	2 (2.1)	5 (5.1)	0 (0.0)	2 (13.3)	1.0000
Number (%) of patients censored	31 (100.0)	35 (89.7)	95 (97.9)	93 (94.9)	21 (100.0)	13 (86.7)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (6.4394 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.2813 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0649		0.2535		0.1185	
Hazard ratio (95% CI) vs Pd	-	NC		2.52 (0.49 to 12.97)		NC	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_seriss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.5 Treatment emergent serious adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
P-value	-	0.9950		0.2703		0.9977	
Events probability (95% CI)[b]							
2 Months	1.0000 (1.0000 to 1.0000)	0.9744 (0.8316 to 0.9963)	0.9790 (0.9188 to 0.9947)	0.9490 (0.8818 to 0.9784)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9224 (0.7782 to 0.9743)	0.9790 (0.9188 to 0.9947)	0.9490 (0.8818 to 0.9784)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9224 (0.7782 to 0.9743)	0.9790 (0.9188 to 0.9947)	0.9490 (0.8818 to 0.9784)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
8 Months	1.0000 (1.0000 to 1.0000)	0.8944 (0.7423 to 0.9591)	0.9790 (0.9188 to 0.9947)	0.9490 (0.8818 to 0.9784)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
10 Months	1.0000 (1.0000 to 1.0000)	0.8944 (0.7423 to 0.9591)	0.9790 (0.9188 to 0.9947)	0.9490 (0.8818 to 0.9784)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
12 Months	1.0000 (1.0000 to 1.0000)	0.8944 (0.7423 to 0.9591)	0.9790 (0.9188 to 0.9947)	0.9490 (0.8818 to 0.9784)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
14 Months	1.0000 (1.0000 to 1.0000)	0.8944 (0.7423 to 0.9591)	0.9790 (0.9188 to 0.9947)	0.9490 (0.8818 to 0.9784)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.5 Treatment emergent serious adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.8944 (0.7423 to 0.9591)	0.9790 (0.9188 to 0.9947)	0.9490 (0.8818 to 0.9784)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
Number of patients at risk[b]							
2 Months	31	38	92	92	17	13	
4 Months	31	35	90	89	12	10	
6 Months	31	33	78	80	7	8	
8 Months	30	32	69	77	6	6	
10 Months	30	32	65	71	6	5	
12 Months	28	29	53	62	5	5	
14 Months	16	17	33	43	4	5	
16 Months	10	10	15	15	1	2	
Metabolism and nutrition disorders (days)							
Number (%) of events	0 (0.0)	1 (2.6)	3 (3.1)	6 (6.1)	3 (14.3)	1 (6.7)	0.5157
Number (%) of patients censored	31 (100.0)	38 (97.4)	94 (96.9)	92 (93.9)	18 (85.7)	14 (93.3)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.8 Treatment emergent severe adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.8710 (0.6919 to 0.9495)	0.7356 (0.5638 to 0.8483)	0.6560 (0.5315 to 0.7549)	0.4938 (0.3821 to 0.5960)	0.4317 (0.1889 to 0.6549)	0.4821 (0.2081 to 0.7125)	
Number of patients at risk[b]							
2 Months	30	35	79	79	11	9	
4 Months	28	34	68	69	7	6	
6 Months	28	30	58	56	5	5	
8 Months	26	29	50	50	4	5	
10 Months	26	27	49	44	4	5	
12 Months	24	24	38	37	3	5	
14 Months	14	15	23	24	3	5	
16 Months	8	8	11	9	1	2	
Injury, poisoning and procedural complications (days)							
Number (%) of events	0 (0.0)	1 (2.6)	0 (0.0)	5 (5.1)	0 (0.0)	2 (13.3)	1.0000
Number (%) of patients censored	31 (100.0)	38 (97.4)	97 (100.0)	93 (94.9)	21 (100.0)	13 (86.7)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.8 Treatment emergent severe adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.2813 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.3726		0.0283		0.1185	
Hazard ratio (95% CI) vs Pd	-	NC		NC		NC	
P-value	-	0.9975		0.9944		0.9977	
Events probability (95% CI)[b]							
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9592 (0.8949 to 0.9845)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_seriss_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.8 Treatment emergent severe adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	1.0000 (1.0000 to 1.0000)	0.9744 (0.8316 to 0.9963)	1.0000 (1.0000 to 1.0000)	0.9592 (0.8949 to 0.9845)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9744 (0.8316 to 0.9963)	1.0000 (1.0000 to 1.0000)	0.9592 (0.8949 to 0.9845)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9744 (0.8316 to 0.9963)	1.0000 (1.0000 to 1.0000)	0.9592 (0.8949 to 0.9845)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9744 (0.8316 to 0.9963)	1.0000 (1.0000 to 1.0000)	0.9592 (0.8949 to 0.9845)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9744 (0.8316 to 0.9963)	1.0000 (1.0000 to 1.0000)	0.9592 (0.8949 to 0.9845)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
14 Months	1.0000 (1.0000 to 1.0000)	0.9744 (0.8316 to 0.9963)	1.0000 (1.0000 to 1.0000)	0.9437 (0.8679 to 0.9766)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
16 Months	1.0000 (1.0000 to 1.0000)	0.9744 (0.8316 to 0.9963)	1.0000 (1.0000 to 1.0000)	0.9437 (0.8679 to 0.9766)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
Number of patients at risk[b]							
2 Months	31	39	94	93	17	13	
4 Months	31	37	91	90	12	10	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.8 Treatment emergent severe adverse event according to SOC by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	31	35	79	81	7	8	
8 Months	30	35	70	78	6	6	
10 Months	30	35	66	72	6	5	
12 Months	28	32	54	63	5	5	
14 Months	16	19	34	43	4	5	
16 Months	10	11	15	15	1	2	
Metabolism and nutrition disorders (days)							
Number (%) of events	0 (0.0)	2 (5.1)	5 (5.2)	10 (10.2)	3 (14.3)	1 (6.7)	0.4553
Number (%) of patients censored	31 (100.0)	37 (94.9)	92 (94.8)	88 (89.8)	18 (85.7)	14 (93.3)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.5585 to NC)	NC (0.1314 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Infections and infestations (days)					
Number (%) of events	15 (71.4)	11 (78.6)	57 (61.3)	95 (81.9)	0.8450
Number (%) of patients censored	6 (28.6)	3 (21.4)	36 (38.7)	21 (18.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.7556 (0.0986 to 1.5441)	0.4928 (0.1643 to 0.7556)	1.4784 (0.7885 to 1.8398)	0.7228 (0.4928 to 0.8542)	
Median (95% CI)	3.4497 (0.7556 to 6.7351)	0.7556 (0.4600 to 3.3183)	2.9569 (1.9055 to 7.4251)	2.3655 (1.7741 to 3.2854)	
75% quantile (95% CI)	12.4517 (3.4497 to NC)	3.3183 (0.7556 to NC)	NC (NC to NC)	6.2752 (4.1068 to 11.8275)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2425		0.0113	
Hazard ratio (95% CI) vs Pd	-	1.60 (0.72 to 3.53)		1.53 (1.10 to 2.12)	
P-value	-	0.2464		0.0120	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.66 (0.47 to 0.91)		
Events probability (95% CI)[b]					
2 Months	0.5714 (0.3380 to 0.7492)	0.3117 (0.0967 to 0.5590)	0.5848 (0.4769 to 0.6779)	0.5391 (0.4439 to 0.6250)	
4 Months	0.4000 (0.1885 to 0.6047)	0.2338 (0.0568 to 0.4789)	0.4488 (0.3442 to 0.5478)	0.3463 (0.2607 to 0.4334)	
6 Months	0.3333 (0.1360 to 0.5461)	0.2338 (0.0568 to 0.4789)	0.4232 (0.3194 to 0.5231)	0.2554 (0.1791 to 0.3385)	
8 Months	0.2667 (0.0907 to 0.4830)	0.1169 (0.0087 to 0.3786)	0.3959 (0.2931 to 0.4967)	0.2063 (0.1365 to 0.2863)	
10 Months	0.2667 (0.0907 to 0.4830)	0.1169 (0.0087 to 0.3786)	0.3519 (0.2511 to 0.4541)	0.1846 (0.1178 to 0.2632)	
12 Months	0.2667 (0.0907 to 0.4830)	0.1169 (0.0087 to 0.3786)	0.3519 (0.2511 to 0.4541)	0.1615 (0.0983 to 0.2386)	
14 Months	0.2000 (0.0528 to 0.4145)	0.1169 (0.0087 to 0.3786)	0.3519 (0.2511 to 0.4541)	0.1615 (0.0983 to 0.2386)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.2000 (0.0528 to 0.4145)	0.1169 (0.0087 to 0.3786)	0.3519 (0.2511 to 0.4541)	0.1615 (0.0983 to 0.2386)	
Number of patients at risk[b]					
2 Months	11	4	53	62	
4 Months	7	2	38	39	
6 Months	5	2	32	26	
8 Months	4	1	28	21	
10 Months	4	1	24	17	
12 Months	4	1	18	13	
14 Months	2	1	13	10	
16 Months	1	1	7	6	
Injury, poisoning and procedural complications (days)					
Number (%) of events	3 (14.3)	8 (57.1)	9 (9.7)	50 (43.1)	0.8185
Number (%) of patients censored	18 (85.7)	6 (42.9)	84 (90.3)	66 (56.9)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (0.1971 to NC)	0.1314 (0.0657 to 0.1643)	NC (NC to NC)	0.1314 (0.0657 to 0.1971)	
Median (95% CI)	NC (NC to NC)	1.3470 (0.0986 to NC)	NC (NC to NC)	NC (6.7680 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0035		<.0001	
Hazard ratio (95% CI) vs Pd	-	5.83 (1.53 to 22.12)		6.32 (2.99 to 13.36)	
P-value	-	0.0096		<.0001	
Hazard ratio inverted (95% CI) vs IPd	0.17 (0.05 to 0.65)		0.16 (0.07 to 0.33)		
Events probability (95% CI)[b]					
2 Months	0.8433 (0.5871 to 0.9469)	0.5000 (0.2286 to 0.7221)	0.9778 (0.9141 to 0.9944)	0.6466 (0.5523 to 0.7259)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	0.8433 (0.5871 to 0.9469)	0.4167 (0.1642 to 0.6543)	0.9665 (0.8998 to 0.9891)	0.6376 (0.5430 to 0.7177)	
6 Months	0.8433 (0.5871 to 0.9469)	0.4167 (0.1642 to 0.6543)	0.9665 (0.8998 to 0.9891)	0.6281 (0.5331 to 0.7090)	
8 Months	0.8433 (0.5871 to 0.9469)	0.4167 (0.1642 to 0.6543)	0.9262 (0.8424 to 0.9663)	0.5882 (0.4916 to 0.6725)	
10 Months	0.8433 (0.5871 to 0.9469)	0.4167 (0.1642 to 0.6543)	0.8964 (0.8022 to 0.9471)	0.5775 (0.4805 to 0.6628)	
12 Months	0.8433 (0.5871 to 0.9469)	0.4167 (0.1642 to 0.6543)	0.8964 (0.8022 to 0.9471)	0.5655 (0.4677 to 0.6520)	
14 Months	0.8433 (0.5871 to 0.9469)	0.4167 (0.1642 to 0.6543)	0.8964 (0.8022 to 0.9471)	0.5655 (0.4677 to 0.6520)	
16 Months	0.8433 (0.5871 to 0.9469)	0.4167 (0.1642 to 0.6543)	0.8964 (0.8022 to 0.9471)	0.5251 (0.4045 to 0.6322)	
Number of patients at risk[b]					
2 Months	15	6	88	75	
4 Months	13	5	85	70	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	9	5	75	63	
8 Months	9	4	65	57	
10 Months	9	3	60	52	
12 Months	9	3	49	43	
14 Months	8	2	32	25	
16 Months	3	0	16	9	
Investigations (days)					
Number (%) of events	2 (9.5)	1 (7.1)	6 (6.5)	12 (10.3)	0.9575
Number (%) of patients censored	19 (90.5)	13 (92.9)	87 (93.5)	104 (89.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (4.4353 to NC)	NC (0.0657 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (4.4353 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.3 Treatment emergent serious adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	12	7	82	97	
4 Months	9	6	69	87	
6 Months	7	6	59	75	
8 Months	6	5	53	71	
10 Months	6	4	52	64	
12 Months	6	4	43	54	
14 Months	5	3	30	36	
16 Months	3	1	14	15	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	3 (21.4)	1 (1.1)	7 (6.0)	0.9930
Number (%) of patients censored	21 (100.0)	11 (78.6)	92 (98.9)	109 (94.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.0657 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (2.5298 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.3 Treatment emergent serious adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0309		0.0694	
Hazard ratio (95% CI) vs Pd	-	NC		5.59 (0.69 to 45.43)	
P-value	-	0.9972		0.1075	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	0.9890 (0.9246 to 0.9984)	0.9655 (0.9107 to 0.9869)	
4 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	0.9890 (0.9246 to 0.9984)	0.9480 (0.8880 to 0.9763)	
6 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	0.9890 (0.9246 to 0.9984)	0.9480 (0.8880 to 0.9763)	
8 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	0.9890 (0.9246 to 0.9984)	0.9383 (0.8747 to 0.9701)	
10 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	0.9890 (0.9246 to 0.9984)	0.9383 (0.8747 to 0.9701)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_cyto_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.3 Treatment emergent serious adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
12 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	0.9890 (0.9246 to 0.9984)	0.9383 (0.8747 to 0.9701)	
14 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	0.9890 (0.9246 to 0.9984)	0.9383 (0.8747 to 0.9701)	
16 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	0.9890 (0.9246 to 0.9984)	0.9383 (0.8747 to 0.9701)	
Number of patients at risk[b]					
2 Months	18	11	90	112	
4 Months	15	9	87	105	
6 Months	10	7	76	97	
8 Months	10	6	69	94	
10 Months	10	5	66	88	
12 Months	10	5	55	77	
14 Months	9	4	37	53	
16 Months	4	1	18	22	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.9 Treatment emergent severe adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	6	4	50	61	
12 Months	6	4	41	52	
14 Months	5	3	28	36	
16 Months	3	1	13	16	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	3 (21.4)	0 (0.0)	4 (3.4)	0.9998
Number (%) of patients censored	21 (100.0)	11 (78.6)	93 (100.0)	112 (96.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.0657 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (2.5298 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0309		0.0814	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.9 Treatment emergent severe adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	NC		NC	
P-value	-	0.9972		0.9951	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	1.0000 (1.0000 to 1.0000)	0.9828 (0.9328 to 0.9957)	
4 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	1.0000 (1.0000 to 1.0000)	0.9741 (0.9217 to 0.9916)	
6 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	1.0000 (1.0000 to 1.0000)	0.9741 (0.9217 to 0.9916)	
8 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	1.0000 (1.0000 to 1.0000)	0.9741 (0.9217 to 0.9916)	
10 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	1.0000 (1.0000 to 1.0000)	0.9741 (0.9217 to 0.9916)	
12 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	1.0000 (1.0000 to 1.0000)	0.9741 (0.9217 to 0.9916)	
14 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	1.0000 (1.0000 to 1.0000)	0.9620 (0.9008 to 0.9858)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.9 Treatment emergent severe adverse event according to SOC by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	1.0000 (1.0000 to 1.0000)	0.9620 (0.9008 to 0.9858)	
Number of patients at risk[b]					
2 Months	18	11	91	114	
4 Months	15	9	87	108	
6 Months	10	7	76	100	
8 Months	10	6	69	98	
10 Months	10	5	66	92	
12 Months	10	5	55	81	
14 Months	9	4	37	55	
16 Months	4	1	18	23	
Metabolism and nutrition disorders (days)					
Number (%) of events	2 (9.5)	2 (14.3)	4 (4.3)	10 (8.6)	0.8471
Number (%) of patients censored	19 (90.5)	12 (85.7)	89 (95.7)	106 (91.4)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0.3270 (0.1528 to 0.5143)	0.1325 (0.0249 to 0.3307)	0.3790 (0.2657 to 0.4915)	0.5263 (0.4242 to 0.6186)	
16 Months	0.3270 (0.1528 to 0.5143)	0.1325 (0.0249 to 0.3307)	0.3790 (0.2657 to 0.4915)	0.4380 (0.3140 to 0.5553)	
Number of patients at risk[b]					
2 Months	17	10	48	81	
4 Months	13	6	38	69	
6 Months	9	5	34	58	
8 Months	8	4	31	53	
10 Months	8	2	26	45	
12 Months	8	1	19	39	
14 Months	5	1	13	30	
16 Months	3	0	7	15	
Infections and infestations (days)					
Number (%) of events	23 (67.6)	18 (78.3)	47 (61.8)	85 (82.5)	0.6742

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of patients censored	11 (32.4)	5 (21.7)	29 (38.2)	18 (17.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.7885 (0.1314 to 1.8398)	0.4928 (0.1643 to 0.7556)	1.4784 (0.7885 to 1.8398)	0.7228 (0.4928 to 0.8542)	
Median (95% CI)	2.5955 (1.1828 to 6.7351)	1.2485 (0.4928 to 6.2094)	3.3183 (1.9055 to 8.9692)	2.3326 (1.3799 to 3.3183)	
75% quantile (95% CI)	NC (3.9425 to NC)	6.2752 (1.2485 to NC)	NC (9.3306 to NC)	5.8809 (4.0411 to 9.7906)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3619		0.0106	
Hazard ratio (95% CI) vs Pd	-	1.33 (0.72 to 2.47)		1.59 (1.11 to 2.28)	
P-value	-	0.3635		0.0113	
Hazard ratio inverted (95% CI) vs IPd			0.63 (0.44 to 0.90)		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.5882 (0.4060 to 0.7317)	0.4565 (0.2459 to 0.6451)	0.5701 (0.4499 to 0.6735)	0.5294 (0.4283 to 0.6206)	
4 Months	0.3871 (0.2211 to 0.5506)	0.3196 (0.1426 to 0.5127)	0.4601 (0.3437 to 0.5687)	0.3413 (0.2509 to 0.4335)	
6 Months	0.3484 (0.1878 to 0.5144)	0.3196 (0.1426 to 0.5127)	0.4304 (0.3156 to 0.5400)	0.2380 (0.1597 to 0.3253)	
8 Months	0.3049 (0.1509 to 0.4742)	0.2130 (0.0707 to 0.4055)	0.3985 (0.2854 to 0.5092)	0.1927 (0.1212 to 0.2768)	
10 Months	0.3049 (0.1509 to 0.4742)	0.2130 (0.0707 to 0.4055)	0.3465 (0.2366 to 0.4588)	0.1670 (0.0996 to 0.2495)	
12 Months	0.3049 (0.1509 to 0.4742)	0.1598 (0.0418 to 0.3467)	0.3465 (0.2366 to 0.4588)	0.1531 (0.0880 to 0.2348)	
14 Months	0.2541 (0.1091 to 0.4284)	0.1598 (0.0418 to 0.3467)	0.3465 (0.2366 to 0.4588)	0.1531 (0.0880 to 0.2348)	
16 Months	0.2541 (0.1091 to 0.4284)	0.1598 (0.0418 to 0.3467)	0.3465 (0.2366 to 0.4588)	0.1531 (0.0880 to 0.2348)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	19	10	42	54	
4 Months	11	6	33	34	
6 Months	8	6	28	21	
8 Months	7	4	24	17	
10 Months	7	4	20	13	
12 Months	6	3	15	10	
14 Months	4	2	10	8	
16 Months	3	2	5	4	
Injury, poisoning and procedural complications (days)					
Number (%) of events	4 (11.8)	10 (43.5)	6 (7.9)	46 (44.7)	0.4905
Number (%) of patients censored	30 (88.2)	13 (56.5)	70 (92.1)	57 (55.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (1.4784 to NC)	0.1314 (0.0657 to 2.5298)	NC (NC to NC)	0.0986 (0.0657 to 0.1971)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (0.1643 to NC)	NC (NC to NC)	14.7187 (6.4394 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0034		<.0001	
Hazard ratio (95% CI) vs Pd	-	4.83 (1.51 to 15.44)		7.35 (3.13 to 17.23)	
P-value	-	0.0080		<.0001	
Hazard ratio inverted (95% CI) vs IPd	0.21 (0.06 to 0.66)		0.14 (0.06 to 0.32)		
Events probability (95% CI)[b]					
2 Months	0.8765 (0.7031 to 0.9518)	0.6087 (0.3827 to 0.7737)	0.9865 (0.9079 to 0.9981)	0.6408 (0.5401 to 0.7250)	
4 Months	0.8765 (0.7031 to 0.9518)	0.5619 (0.3387 to 0.7357)	0.9728 (0.8955 to 0.9931)	0.6306 (0.5297 to 0.7157)	
6 Months	0.8765 (0.7031 to 0.9518)	0.5619 (0.3387 to 0.7357)	0.9728 (0.8955 to 0.9931)	0.6197 (0.5183 to 0.7058)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.8765 (0.7031 to 0.9518)	0.5619 (0.3387 to 0.7357)	0.9406 (0.8487 to 0.9774)	0.5738 (0.4706 to 0.6641)	
10 Months	0.8765 (0.7031 to 0.9518)	0.5619 (0.3387 to 0.7357)	0.9037 (0.7966 to 0.9559)	0.5616 (0.4580 to 0.6530)	
12 Months	0.8765 (0.7031 to 0.9518)	0.5619 (0.3387 to 0.7357)	0.9037 (0.7966 to 0.9559)	0.5479 (0.4434 to 0.6408)	
14 Months	0.8765 (0.7031 to 0.9518)	0.5619 (0.3387 to 0.7357)	0.9037 (0.7966 to 0.9559)	0.5479 (0.4434 to 0.6408)	
16 Months	0.8765 (0.7031 to 0.9518)	0.5619 (0.3387 to 0.7357)	0.9037 (0.7966 to 0.9559)	0.4981 (0.3633 to 0.6190)	
Number of patients at risk[b]					
2 Months	27	13	73	66	
4 Months	25	12	71	61	
6 Months	19	12	63	54	
8 Months	19	10	54	49	
10 Months	19	9	49	44	
12 Months	16	7	41	37	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.1 Treatment emergent adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	12	5	27	21	
16 Months	6	1	13	8	
Investigations (days)					
Number (%) of events	2 (5.9)	1 (4.3)	6 (7.9)	12 (11.7)	0.9882
Number (%) of patients censored	32 (94.1)	22 (95.7)	70 (92.1)	91 (88.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (4.4353 to NC)	NC (0.0657 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8422		0.4818	
Hazard ratio (95% CI) vs Pd	-	1.32 (0.08 to 21.22)		1.42 (0.53 to 3.78)	
P-value	-	0.8427		0.4840	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.5 Treatment emergent serious adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	25	13	65	87	
4 Months	20	12	56	77	
6 Months	16	12	48	66	
8 Months	15	10	42	63	
10 Months	15	8	41	57	
12 Months	12	8	35	48	
14 Months	9	6	25	31	
16 Months	6	2	11	13	
Injury, poisoning and procedural complications (days)					
Number (%) of events	1 (2.9)	4 (17.4)	0 (0.0)	6 (5.8)	0.9941
Number (%) of patients censored	33 (97.1)	19 (82.6)	76 (100.0)	97 (94.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.0657 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.5 Treatment emergent serious adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0619		0.0350	
Hazard ratio (95% CI) vs Pd	-	6.20 (0.69 to 55.47)		NC	
P-value	-	0.1028		0.9940	
Events probability (95% CI)[b]					
2 Months	0.9697 (0.8037 to 0.9957)	0.8674 (0.6427 to 0.9552)	1.0000 (1.0000 to 1.0000)	0.9709 (0.9124 to 0.9905)	
4 Months	0.9697 (0.8037 to 0.9957)	0.8217 (0.5917 to 0.9292)	1.0000 (1.0000 to 1.0000)	0.9512 (0.8866 to 0.9794)	
6 Months	0.9697 (0.8037 to 0.9957)	0.8217 (0.5917 to 0.9292)	1.0000 (1.0000 to 1.0000)	0.9512 (0.8866 to 0.9794)	
8 Months	0.9697 (0.8037 to 0.9957)	0.8217 (0.5917 to 0.9292)	1.0000 (1.0000 to 1.0000)	0.9400 (0.8710 to 0.9726)	
10 Months	0.9697 (0.8037 to 0.9957)	0.8217 (0.5917 to 0.9292)	1.0000 (1.0000 to 1.0000)	0.9400 (0.8710 to 0.9726)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.5 Treatment emergent serious adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
12 Months	0.9697 (0.8037 to 0.9957)	0.8217 (0.5917 to 0.9292)	1.0000 (1.0000 to 1.0000)	0.9400 (0.8710 to 0.9726)	
14 Months	0.9697 (0.8037 to 0.9957)	0.8217 (0.5917 to 0.9292)	1.0000 (1.0000 to 1.0000)	0.9400 (0.8710 to 0.9726)	
16 Months	0.9697 (0.8037 to 0.9957)	0.8217 (0.5917 to 0.9292)	1.0000 (1.0000 to 1.0000)	0.9400 (0.8710 to 0.9726)	
Number of patients at risk[b]					
2 Months	30	19	74	100	
4 Months	27	17	73	93	
6 Months	20	15	64	85	
8 Months	20	13	57	83	
10 Months	20	12	54	77	
12 Months	17	10	46	68	
14 Months	13	7	32	47	
16 Months	7	2	15	20	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.13 Treatment emergent severe adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	15	8	39	54	
12 Months	12	8	33	46	
14 Months	9	6	23	31	
16 Months	6	2	10	14	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	4 (17.4)	0 (0.0)	3 (2.9)	0.9997
Number (%) of patients censored	34 (100.0)	19 (82.6)	76 (100.0)	100 (97.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.0657 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0128		0.1479	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.13 Treatment emergent severe adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	NC		NC	
P-value	-	0.9968		0.9958	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.8674 (0.6427 to 0.9552)	1.0000 (1.0000 to 1.0000)	0.9903 (0.9331 to 0.9986)	
4 Months	1.0000 (1.0000 to 1.0000)	0.8217 (0.5917 to 0.9292)	1.0000 (1.0000 to 1.0000)	0.9805 (0.9242 to 0.9951)	
6 Months	1.0000 (1.0000 to 1.0000)	0.8217 (0.5917 to 0.9292)	1.0000 (1.0000 to 1.0000)	0.9805 (0.9242 to 0.9951)	
8 Months	1.0000 (1.0000 to 1.0000)	0.8217 (0.5917 to 0.9292)	1.0000 (1.0000 to 1.0000)	0.9805 (0.9242 to 0.9951)	
10 Months	1.0000 (1.0000 to 1.0000)	0.8217 (0.5917 to 0.9292)	1.0000 (1.0000 to 1.0000)	0.9805 (0.9242 to 0.9951)	
12 Months	1.0000 (1.0000 to 1.0000)	0.8217 (0.5917 to 0.9292)	1.0000 (1.0000 to 1.0000)	0.9805 (0.9242 to 0.9951)	
14 Months	1.0000 (1.0000 to 1.0000)	0.8217 (0.5917 to 0.9292)	1.0000 (1.0000 to 1.0000)	0.9669 (0.8992 to 0.9894)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.13 Treatment emergent severe adverse event according to SOC by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.8217 (0.5917 to 0.9292)	1.0000 (1.0000 to 1.0000)	0.9669 (0.8992 to 0.9894)	
Number of patients at risk[b]					
2 Months	31	19	74	102	
4 Months	27	17	73	96	
6 Months	20	15	64	88	
8 Months	20	13	57	87	
10 Months	20	12	54	81	
12 Months	17	10	46	72	
14 Months	13	7	32	49	
16 Months	7	2	15	21	
Metabolism and nutrition disorders (days)					
Number (%) of events	2 (5.9)	3 (13.0)	4 (5.3)	8 (7.8)	0.6896
Number (%) of patients censored	32 (94.1)	20 (87.0)	72 (94.7)	95 (92.2)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.1 Treatment emergent adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0.3516 (0.2490 to 0.4558)	0.4652 (0.3503 to 0.5720)	0.3842 (0.2487 to 0.5181)	0.4671 (0.3457 to 0.5795)	
16 Months	0.3516 (0.2490 to 0.4558)	0.3817 (0.2435 to 0.5186)	0.3842 (0.2487 to 0.5181)	0.4246 (0.2902 to 0.5526)	
Number of patients at risk[b]					
2 Months	53	62	37	47	
4 Months	42	51	29	39	
6 Months	37	42	23	34	
8 Months	31	36	20	32	
10 Months	28	30	16	27	
12 Months	24	26	13	23	
14 Months	14	18	8	18	
16 Months	8	9	4	9	
Infections and infestations (days)					
Number (%) of events	61 (69.3)	65 (80.2)	35 (57.4)	58 (81.7)	0.6173

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.1 Treatment emergent adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of patients censored	27 (30.7)	16 (19.8)	26 (42.6)	13 (18.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.3470 (0.8214 to 1.6756)	0.5585 (0.3943 to 0.8542)	0.9528 (0.5257 to 1.5113)	0.6899 (0.4928 to 0.8542)	
Median (95% CI)	2.3326 (1.9055 to 3.6468)	2.0370 (1.3142 to 3.6797)	3.3183 (1.5113 to NC)	2.3984 (0.9856 to 3.2526)	
75% quantile (95% CI)	NC (7.3265 to NC)	5.9138 (4.1068 to NC)	NC (NC to NC)	6.3409 (3.7454 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0919		0.0380	
Hazard ratio (95% CI) vs Pd	-	1.35 (0.95 to 1.92)		1.56 (1.02 to 2.37)	
P-value	-	0.0931		0.0395	
Hazard ratio inverted (95% CI) vs IPd			0.64 (0.42 to 0.98)		
Events probability (95% CI)[b]					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.1 Treatment emergent adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.5647 (0.4542 to 0.6611)	0.5062 (0.3913 to 0.6101)	0.5549 (0.4186 to 0.6714)	0.5634 (0.4405 to 0.6693)	
4 Months	0.3974 (0.2937 to 0.4990)	0.3748 (0.2683 to 0.4809)	0.4629 (0.3303 to 0.5854)	0.3076 (0.2045 to 0.4166)	
6 Months	0.3841 (0.2813 to 0.4859)	0.2384 (0.1495 to 0.3389)	0.4242 (0.2941 to 0.5483)	0.2628 (0.1664 to 0.3696)	
8 Months	0.3272 (0.2282 to 0.4297)	0.2103 (0.1266 to 0.3085)	0.3816 (0.2542 to 0.5077)	0.1971 (0.1121 to 0.2997)	
10 Months	0.2845 (0.1900 to 0.3863)	0.2103 (0.1266 to 0.3085)	0.3816 (0.2542 to 0.5077)	0.1613 (0.0839 to 0.2610)	
12 Months	0.2845 (0.1900 to 0.3863)	0.1780 (0.1001 to 0.2741)	0.3816 (0.2542 to 0.5077)	0.1613 (0.0839 to 0.2610)	
14 Months	0.2668 (0.1735 to 0.3690)	0.1582 (0.0836 to 0.2542)	0.3816 (0.2542 to 0.5077)	0.1613 (0.0839 to 0.2610)	
16 Months	0.2668 (0.1735 to 0.3690)	0.1582 (0.0836 to 0.2542)	0.3816 (0.2542 to 0.5077)	0.1613 (0.0839 to 0.2610)	

Number of patients at risk[b]

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.1 Treatment emergent adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	48	39	32	40	
4 Months	32	28	25	21	
6 Months	28	17	21	16	
8 Months	23	15	16	12	
10 Months	20	14	15	9	
12 Months	17	10	11	9	
14 Months	11	5	6	8	
16 Months	6	3	3	5	
Injury, poisoning and procedural complications (days)					
Number (%) of events	8 (9.1)	35 (43.2)	9 (14.8)	37 (52.1)	0.7237
Number (%) of patients censored	80 (90.9)	46 (56.8)	52 (85.2)	34 (47.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0657 to 0.1971)	NC (9.1006 to NC)	0.1314 (0.0657 to 0.1971)	
Median (95% CI)	NC (NC to NC)	15.4415 (0.5585 to NC)	NC (NC to NC)	6.7680 (0.1971 to NC)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.1 Treatment emergent adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Pd	-	6.28 (2.91 to 13.58)		5.15 (2.40 to 11.08)	
P-value	-	<.0001		<.0001	
Hazard ratio inverted (95% CI) vs IPd	0.16 (0.07 to 0.34)		0.19 (0.09 to 0.42)		
Events probability (95% CI)[b]					
2 Months	0.9655 (0.8969 to 0.9887)	0.6044 (0.4894 to 0.7014)	0.9469 (0.8442 to 0.9826)	0.6056 (0.4823 to 0.7083)	
4 Months	0.9418 (0.8658 to 0.9754)	0.6044 (0.4894 to 0.7014)	0.9283 (0.8200 to 0.9725)	0.5764 (0.4531 to 0.6816)	
6 Months	0.9291 (0.8488 to 0.9675)	0.6044 (0.4894 to 0.7014)	0.9283 (0.8200 to 0.9725)	0.5457 (0.4223 to 0.6534)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.1 Treatment emergent adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.9000 (0.8090 to 0.9490)	0.5897 (0.4739 to 0.6883)	0.8861 (0.7630 to 0.9474)	0.4961 (0.3729 to 0.6076)	
10 Months	0.9000 (0.8090 to 0.9490)	0.5897 (0.4739 to 0.6883)	0.8369 (0.6974 to 0.9158)	0.4795 (0.3568 to 0.5921)	
12 Months	0.9000 (0.8090 to 0.9490)	0.5897 (0.4739 to 0.6883)	0.8369 (0.6974 to 0.9158)	0.4618 (0.3393 to 0.5756)	
14 Months	0.9000 (0.8090 to 0.9490)	0.5897 (0.4739 to 0.6883)	0.8369 (0.6974 to 0.9158)	0.4618 (0.3393 to 0.5756)	
16 Months	0.9000 (0.8090 to 0.9490)	0.4587 (0.2746 to 0.6250)	0.8369 (0.6974 to 0.9158)	0.4618 (0.3393 to 0.5756)	
Number of patients at risk[b]					
2 Months	83	48	52	43	
4 Months	77	46	50	39	
6 Months	66	42	45	33	
8 Months	59	37	37	30	
10 Months	57	34	34	27	
12 Months	49	28	27	24	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.1 Treatment emergent adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	30	16	16	14	
16 Months	14	5	8	5	
Investigations (days)					
Number (%) of events	6 (6.8)	8 (9.9)	4 (6.6)	9 (12.7)	0.5884
Number (%) of patients censored	82 (93.2)	73 (90.1)	57 (93.4)	62 (87.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4807		0.1969	
Hazard ratio (95% CI) vs Pd	-	1.46 (0.51 to 4.21)		2.31 (0.62 to 8.54)	
P-value	-	0.4833		0.2099	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.4 Treatment emergent serious adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	72	65	50	59	
4 Months	63	60	41	52	
6 Months	55	51	37	43	
8 Months	49	48	32	40	
10 Months	49	42	30	37	
12 Months	41	37	25	31	
14 Months	28	22	13	23	
16 Months	15	9	5	10	
Injury, poisoning and procedural complications (days)					
Number (%) of events	2 (2.3)	5 (6.2)	0 (0.0)	6 (8.5)	0.9908
Number (%) of patients censored	86 (97.7)	76 (93.8)	61 (100.0)	65 (91.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.4 Treatment emergent serious adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2047		0.0258	
Hazard ratio (95% CI) vs Pd	-	2.76 (0.54 to 14.25)		NC	
P-value	-	0.2242		0.9939	
Events probability (95% CI)[b]					
2 Months	0.9771 (0.9117 to 0.9942)	0.9506 (0.8738 to 0.9812)	1.0000 (1.0000 to 1.0000)	0.9577 (0.8747 to 0.9862)	
4 Months	0.9771 (0.9117 to 0.9942)	0.9379 (0.8573 to 0.9737)	1.0000 (1.0000 to 1.0000)	0.9292 (0.8381 to 0.9699)	
6 Months	0.9771 (0.9117 to 0.9942)	0.9379 (0.8573 to 0.9737)	1.0000 (1.0000 to 1.0000)	0.9292 (0.8381 to 0.9699)	
8 Months	0.9771 (0.9117 to 0.9942)	0.9379 (0.8573 to 0.9737)	1.0000 (1.0000 to 1.0000)	0.9129 (0.8159 to 0.9600)	
10 Months	0.9771 (0.9117 to 0.9942)	0.9379 (0.8573 to 0.9737)	1.0000 (1.0000 to 1.0000)	0.9129 (0.8159 to 0.9600)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.4 Treatment emergent serious adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
12 Months	0.9771 (0.9117 to 0.9942)	0.9379 (0.8573 to 0.9737)	1.0000 (1.0000 to 1.0000)	0.9129 (0.8159 to 0.9600)	
14 Months	0.9771 (0.9117 to 0.9942)	0.9379 (0.8573 to 0.9737)	1.0000 (1.0000 to 1.0000)	0.9129 (0.8159 to 0.9600)	
16 Months	0.9771 (0.9117 to 0.9942)	0.9379 (0.8573 to 0.9737)	1.0000 (1.0000 to 1.0000)	0.9129 (0.8159 to 0.9600)	
Number of patients at risk[b]					
2 Months	84	75	56	68	
4 Months	80	70	53	64	
6 Months	70	64	46	57	
8 Months	65	59	40	56	
10 Months	63	55	38	53	
12 Months	55	48	31	48	
14 Months	34	32	19	33	
16 Months	17	13	9	14	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.11 Treatment emergent severe adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	49	42	30	34	
12 Months	41	37	24	29	
14 Months	27	23	13	21	
16 Months	15	10	5	9	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	3 (3.7)	0 (0.0)	5 (7.0)	0.9999
Number (%) of patients censored	88 (100.0)	78 (96.3)	61 (100.0)	66 (93.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0698		0.0408	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.11 Treatment emergent severe adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	NC		NC	
P-value	-	0.9956		0.9944	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9753 (0.9049 to 0.9938)	1.0000 (1.0000 to 1.0000)	0.9577 (0.8747 to 0.9862)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9753 (0.9049 to 0.9938)	1.0000 (1.0000 to 1.0000)	0.9292 (0.8381 to 0.9699)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9753 (0.9049 to 0.9938)	1.0000 (1.0000 to 1.0000)	0.9292 (0.8381 to 0.9699)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9753 (0.9049 to 0.9938)	1.0000 (1.0000 to 1.0000)	0.9292 (0.8381 to 0.9699)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9753 (0.9049 to 0.9938)	1.0000 (1.0000 to 1.0000)	0.9292 (0.8381 to 0.9699)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9753 (0.9049 to 0.9938)	1.0000 (1.0000 to 1.0000)	0.9292 (0.8381 to 0.9699)	
14 Months	1.0000 (1.0000 to 1.0000)	0.9554 (0.8637 to 0.9859)	1.0000 (1.0000 to 1.0000)	0.9292 (0.8381 to 0.9699)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.11 Treatment emergent severe adverse event according to SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.9554 (0.8637 to 0.9859)	1.0000 (1.0000 to 1.0000)	0.9292 (0.8381 to 0.9699)	
Number of patients at risk[b]					
2 Months	86	77	56	68	
4 Months	81	73	53	64	
6 Months	71	67	46	57	
8 Months	66	62	40	57	
10 Months	64	58	38	54	
12 Months	56	51	31	49	
14 Months	35	33	19	34	
16 Months	17	13	9	15	
Metabolism and nutrition disorders (days)					
Number (%) of events	5 (5.7)	4 (4.9)	3 (4.9)	9 (12.7)	0.2573
Number (%) of patients censored	83 (94.3)	77 (95.1)	58 (95.1)	62 (87.3)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.1 Treatment emergent adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Infections and infestations (days)					
Number (%) of events	2 (100.0)	2 (100.0)	94 (63.9)	121 (80.7)	0.2740
Number (%) of patients censored	0 (0.0)	0 (0.0)	53 (36.1)	29 (19.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.2628 (0.2628 to 1.7084)	0.1643 (0.1643 to 0.3943)	1.3142 (0.8542 to 1.5441)	0.7228 (0.4928 to 0.8214)	
Median (95% CI)	0.9856 (0.2628 to 1.7084)	0.2793 (0.1643 to 0.3943)	2.5955 (1.9055 to 5.2895)	2.2669 (1.7741 to 3.2197)	
75% quantile (95% CI)	1.7084 (0.2628 to 1.7084)	0.3943 (0.1643 to 0.3943)	NC (9.3306 to NC)	6.2094 (4.3696 to 11.8275)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4328		0.0099	
Hazard ratio (95% CI) vs Pd	-	2.56 (0.23 to 29.12)		1.42 (1.09 to 1.87)	
P-value	-	0.4482		0.0103	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.1 Treatment emergent adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.70 (0.54 to 0.92)		
Events probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.5686 (0.4835 to 0.6450)	0.5404 (0.4568 to 0.6168)	
4 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.4293 (0.3466 to 0.5094)	0.3469 (0.2708 to 0.4241)	
6 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.4053 (0.3233 to 0.4857)	0.2532 (0.1853 to 0.3266)	
8 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3531 (0.2730 to 0.4341)	0.2072 (0.1445 to 0.2777)	
10 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3253 (0.2464 to 0.4064)	0.1906 (0.1300 to 0.2601)	
12 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3253 (0.2464 to 0.4064)	0.1733 (0.1150 to 0.2416)	
14 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3128 (0.2338 to 0.3947)	0.1637 (0.1065 to 0.2316)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.1 Treatment emergent adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3128 (0.2338 to 0.3947)	0.1637 (0.1065 to 0.2316)	
Number of patients at risk[b]					
2 Months	0	0	80	79	
4 Months	0	0	57	49	
6 Months	0	0	49	33	
8 Months	0	0	39	27	
10 Months	0	0	35	23	
12 Months	0	0	28	19	
14 Months	0	0	17	13	
16 Months	0	0	9	8	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	1 (50.0)	17 (11.6)	71 (47.3)	0.9839
Number (%) of patients censored	2 (100.0)	1 (50.0)	130 (88.4)	79 (52.7)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.1 Treatment emergent adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1643 (0.1643 to NC)	NC (NC to NC)	0.1314 (0.0657 to 0.1643)	
Median (95% CI)	NC (NC to NC)	NC (0.1643 to NC)	NC (NC to NC)	14.7187 (5.2238 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		<.0001	
Hazard ratio (95% CI) vs Pd	-	NC		5.68 (3.30 to 9.78)	
P-value	-	0.9990		<.0001	
Hazard ratio inverted (95% CI) vs IPd			0.18 (0.10 to 0.30)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9577 (0.9083 to 0.9808)	0.6065 (0.5235 to 0.6795)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.1 Treatment emergent adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9356 (0.8798 to 0.9660)	0.5927 (0.5095 to 0.6664)	
6 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9279 (0.8701 to 0.9606)	0.5779 (0.4944 to 0.6526)	
8 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.8926 (0.8247 to 0.9352)	0.5464 (0.4620 to 0.6230)	
10 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.8732 (0.8002 to 0.9208)	0.5378 (0.4532 to 0.6150)	
12 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.8732 (0.8002 to 0.9208)	0.5284 (0.4433 to 0.6064)	
14 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.8732 (0.8002 to 0.9208)	0.5284 (0.4433 to 0.6064)	
16 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.8732 (0.8002 to 0.9208)	0.4658 (0.3541 to 0.5699)	
Number of patients at risk[b]					
2 Months	2	1	133	90	
4 Months	2	1	125	84	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.1 Treatment emergent adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	2	1	109	74	
8 Months	2	1	94	66	
10 Months	1	1	90	60	
12 Months	1	0	75	52	
14 Months	1	0	45	30	
16 Months	0	0	22	10	
Investigations (days)					
Number (%) of events	1 (50.0)	0 (0.0)	9 (6.1)	17 (11.3)	0.9874
Number (%) of patients censored	1 (50.0)	2 (100.0)	138 (93.9)	133 (88.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.4456 (1.4456 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (1.4456 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (1.4456 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.4 Treatment emergent serious adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1	2	121	122	
4 Months	1	2	103	110	
6 Months	1	2	91	92	
8 Months	1	2	80	86	
10 Months	1	1	78	78	
12 Months	1	1	65	67	
14 Months	1	0	40	45	
16 Months	0	0	20	19	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	0 (0.0)	2 (1.4)	11 (7.3)	0.9996
Number (%) of patients censored	2 (100.0)	2 (100.0)	145 (98.6)	139 (92.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.4 Treatment emergent serious adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0138	
Hazard ratio (95% CI) vs Pd	-	NC		5.40 (1.20 to 24.36)	
P-value	-			0.0282	
Hazard ratio inverted (95% CI) vs IPd			0.19 (0.04 to 0.84)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9862 (0.9458 to 0.9965)	0.9533 (0.9045 to 0.9775)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9862 (0.9458 to 0.9965)	0.9328 (0.8787 to 0.9633)	
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9862 (0.9458 to 0.9965)	0.9328 (0.8787 to 0.9633)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9862 (0.9458 to 0.9965)	0.9248 (0.8682 to 0.9577)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.4 Treatment emergent serious adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9862 (0.9458 to 0.9965)	0.9248 (0.8682 to 0.9577)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9862 (0.9458 to 0.9965)	0.9248 (0.8682 to 0.9577)	
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9862 (0.9458 to 0.9965)	0.9248 (0.8682 to 0.9577)	
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9862 (0.9458 to 0.9965)	0.9248 (0.8682 to 0.9577)	
Number of patients at risk[b]					
2 Months	2	2	138	141	
4 Months	2	2	131	132	
6 Months	2	2	114	119	
8 Months	2	2	103	113	
10 Months	1	2	100	106	
12 Months	1	1	85	95	
14 Months	1	0	52	65	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.4 Treatment emergent serious adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0	0	26	27	
Metabolism and nutrition disorders (days)					
Number (%) of events	0 (0.0)	0 (0.0)	6 (4.1)	8 (5.3)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	141 (95.9)	142 (94.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.6403	
Hazard ratio (95% CI) vs Pd	-	NC		1.29 (0.45 to 3.71)	
P-value	-			0.6411	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.11 Treatment emergent severe adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	1	1	90	90	
8 Months	1	1	79	83	
10 Months	1	0	78	76	
12 Months	1	0	64	66	
14 Months	1	0	39	44	
16 Months	0	0	20	19	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	0 (0.0)	0 (0.0)	8 (5.3)	0.9994
Number (%) of patients censored	2 (100.0)	2 (100.0)	147 (100.0)	142 (94.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.11 Treatment emergent severe adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Log-Rank test p-value[a] vs Pd	-			0.0055	
Hazard ratio (95% CI) vs Pd	-	NC		NC	
P-value	-			0.9929	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9666 (0.9217 to 0.9860)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9530 (0.9039 to 0.9773)	
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9530 (0.9039 to 0.9773)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9530 (0.9039 to 0.9773)	
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9530 (0.9039 to 0.9773)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9530 (0.9039 to 0.9773)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.11 Treatment emergent severe adverse event according to SOC by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9432 (0.8887 to 0.9714)	
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9432 (0.8887 to 0.9714)	
Number of patients at risk[b]					
2 Months	2	2	140	143	
4 Months	2	2	132	135	
6 Months	2	2	115	122	
8 Months	2	2	104	117	
10 Months	1	2	101	110	
12 Months	1	1	86	99	
14 Months	1	0	53	67	
16 Months	0	0	26	28	
Metabolism and nutrition disorders (days)					
Number (%) of events	0 (0.0)	0 (0.0)	8 (5.4)	13 (8.7)	0.9999

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Infections and infestations (days)					
Number (%) of events	72 (73.5)	82 (79.6)	20 (50.0)	30 (93.8)	0.0149
Number (%) of patients censored	26 (26.5)	21 (20.4)	20 (50.0)	2 (6.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.9528 (0.5914 to 1.4456)	0.6571 (0.4600 to 0.8214)	1.8398 (0.5914 to 2.2669)	0.6571 (0.2628 to 0.8871)	
Median (95% CI)	2.0370 (1.6099 to 3.5154)	2.6283 (1.3142 to 3.9097)	6.5051 (2.0370 to NC)	1.8891 (0.6899 to 2.5955)	
75% quantile (95% CI)	9.3306 (5.2895 to NC)	6.3409 (4.5339 to NC)	NC (NC to NC)	3.7782 (2.1684 to 6.6694)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5281		0.0004	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.81 to 1.52)		2.68 (1.51 to 4.75)	
P-value	-	0.5288		0.0007	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_semm_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.37 (0.21 to 0.66)		
Events probability (95% CI)[b]					
2 Months	0.5025 (0.3990 to 0.5972)	0.5452 (0.4433 to 0.6362)	0.6943 (0.5247 to 0.8135)	0.4688 (0.2915 to 0.6277)	
4 Months	0.3635 (0.2681 to 0.4593)	0.3861 (0.2915 to 0.4796)	0.5260 (0.3556 to 0.6709)	0.1875 (0.0761 to 0.3369)	
6 Months	0.3290 (0.2365 to 0.4244)	0.2740 (0.1906 to 0.3637)	0.5260 (0.3556 to 0.6709)	0.1250 (0.0395 to 0.2623)	
8 Months	0.2803 (0.1925 to 0.3745)	0.2213 (0.1454 to 0.3074)	0.4532 (0.2831 to 0.6087)	0.0938 (0.0240 to 0.2228)	
10 Months	0.2420 (0.1589 to 0.3349)	0.1980 (0.1255 to 0.2825)	0.4532 (0.2831 to 0.6087)	0.0938 (0.0240 to 0.2228)	
12 Months	0.2420 (0.1589 to 0.3349)	0.1980 (0.1255 to 0.2825)	0.4532 (0.2831 to 0.6087)	0.0625 (0.0111 to 0.1811)	
14 Months	0.2248 (0.1428 to 0.3183)	0.1838 (0.1131 to 0.2681)	0.4532 (0.2831 to 0.6087)	0.0625 (0.0111 to 0.1811)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.2248 (0.1428 to 0.3183)	0.1838 (0.1131 to 0.2681)	0.4532 (0.2831 to 0.6087)	0.0625 (0.0111 to 0.1811)	
Number of patients at risk[b]					
2 Months	48	55	26	15	
4 Months	34	38	17	6	
6 Months	28	26	16	4	
8 Months	22	21	12	3	
10 Months	19	17	12	3	
12 Months	16	15	9	2	
14 Months	8	9	6	2	
16 Months	4	4	4	2	
Injury, poisoning and procedural complications (days)					
Number (%) of events	13 (13.3)	42 (40.8)	3 (7.5)	20 (62.5)	0.0993
Number (%) of patients censored	85 (86.7)	61 (59.2)	37 (92.5)	12 (37.5)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (9.4620 to NC)	0.1643 (0.0986 to 3.0554)	NC (NC to NC)	0.0986 (0.0657 to 0.1643)	
Median (95% CI)	NC (NC to NC)	NC (11.4661 to NC)	NC (NC to NC)	0.1971 (0.1314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.7310 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Pd	-	3.77 (2.02 to 7.03)		17.62 (4.10 to 75.65)	
P-value	-	<.0001		0.0001	
Hazard ratio inverted (95% CI) vs IPd	0.27 (0.14 to 0.49)		0.06 (0.01 to 0.24)		
Events probability (95% CI)[b]					
2 Months	0.9476 (0.8787 to 0.9779)	0.6695 (0.5696 to 0.7512)	0.9737 (0.8275 to 0.9963)	0.4688 (0.2915 to 0.6277)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	0.9262 (0.8514 to 0.9641)	0.6593 (0.5590 to 0.7421)	0.9450 (0.7973 to 0.9860)	0.4375 (0.2646 to 0.5981)	
6 Months	0.9151 (0.8372 to 0.9566)	0.6484 (0.5474 to 0.7323)	0.9450 (0.7973 to 0.9860)	0.4063 (0.2383 to 0.5679)	
8 Months	0.8745 (0.7836 to 0.9289)	0.6144 (0.5117 to 0.7018)	0.9450 (0.7973 to 0.9860)	0.4063 (0.2383 to 0.5679)	
10 Months	0.8448 (0.7458 to 0.9076)	0.6144 (0.5117 to 0.7018)	0.9450 (0.7973 to 0.9860)	0.3750 (0.2128 to 0.5371)	
12 Months	0.8448 (0.7458 to 0.9076)	0.6001 (0.4959 to 0.6895)	0.9450 (0.7973 to 0.9860)	0.3750 (0.2128 to 0.5371)	
14 Months	0.8448 (0.7458 to 0.9076)	0.6001 (0.4959 to 0.6895)	0.9450 (0.7973 to 0.9860)	0.3750 (0.2128 to 0.5371)	
16 Months	0.8448 (0.7458 to 0.9076)	0.5224 (0.3841 to 0.6437)	0.9450 (0.7973 to 0.9860)	0.3750 (0.2128 to 0.5371)	
Number of patients at risk[b]					
2 Months	89	68	36	15	
4 Months	85	64	33	14	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	71	58	32	13	
8 Months	61	51	28	13	
10 Months	57	46	28	12	
12 Months	47	39	24	11	
14 Months	28	25	13	4	
16 Months	13	9	7	0	
Investigations (days)					
Number (%) of events	9 (9.2)	14 (13.6)	1 (2.5)	2 (6.3)	0.9590
Number (%) of patients censored	89 (90.8)	89 (86.4)	39 (97.5)	30 (93.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.3532 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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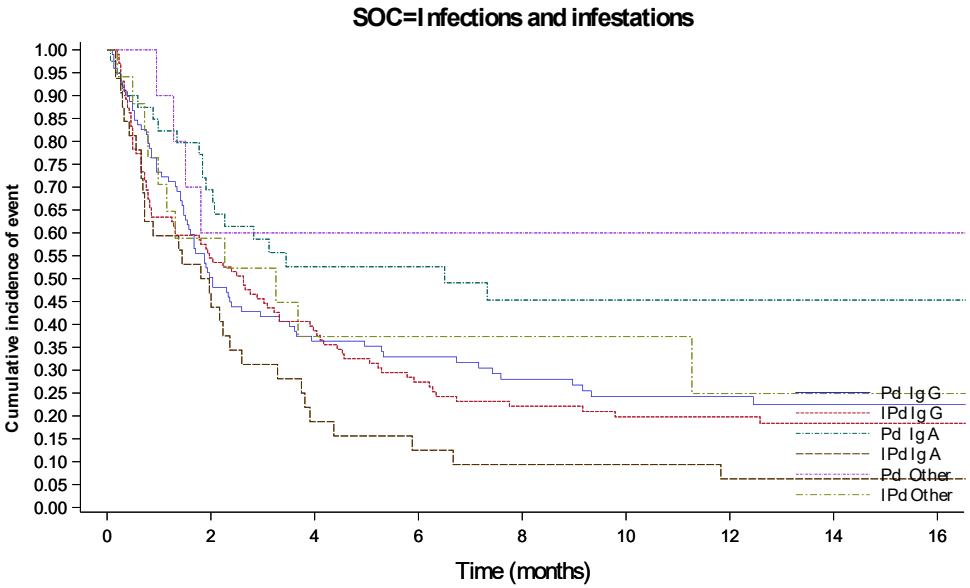
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group according to MM type at SE - Safety population



Number at Risk

Pd Ig G	98	48	34	28	22	19	16	8	4
IPd Ig G	102	55	38	26	21	17	15	9	4
Pd Ig A	40	26	17	16	12	12	9	6	4
IPd Ig A	32	15	6	4	3	3	2	2	2
Pd Other	11	6	6	5	5	4	3	3	1
IPd Other	17	9	5	3	3	3	2	2	2

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.5 Treatment emergent serious adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	79	85	35	27	
4 Months	67	77	29	25	
6 Months	58	63	28	23	
8 Months	51	58	24	22	
10 Months	50	52	24	19	
12 Months	42	46	20	16	
14 Months	25	31	12	10	
16 Months	12	13	7	3	
Injury, poisoning and procedural complications (days)					
Number (%) of events	1 (1.0)	6 (5.8)	1 (2.5)	3 (9.4)	0.9659
Number (%) of patients censored	97 (99.0)	97 (94.2)	39 (97.5)	29 (90.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.5298 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.5 Treatment emergent serious adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0696		0.2214	
Hazard ratio (95% CI) vs Pd	-	5.66 (0.68 to 47.01)		3.73 (0.39 to 35.81)	
P-value	-	0.1084		0.2547	
Events probability (95% CI)[b]					
2 Months	0.9898 (0.9298 to 0.9986)	0.9709 (0.9124 to 0.9905)	0.9744 (0.8316 to 0.9963)	0.9375 (0.7725 to 0.9840)	
4 Months	0.9898 (0.9298 to 0.9986)	0.9510 (0.8862 to 0.9793)	0.9744 (0.8316 to 0.9963)	0.9063 (0.7369 to 0.9688)	
6 Months	0.9898 (0.9298 to 0.9986)	0.9510 (0.8862 to 0.9793)	0.9744 (0.8316 to 0.9963)	0.9063 (0.7369 to 0.9688)	
8 Months	0.9898 (0.9298 to 0.9986)	0.9395 (0.8700 to 0.9724)	0.9744 (0.8316 to 0.9963)	0.9063 (0.7369 to 0.9688)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.5 Treatment emergent serious adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.9898 (0.9298 to 0.9986)	0.9395 (0.8700 to 0.9724)	0.9744 (0.8316 to 0.9963)	0.9063 (0.7369 to 0.9688)	
12 Months	0.9898 (0.9298 to 0.9986)	0.9395 (0.8700 to 0.9724)	0.9744 (0.8316 to 0.9963)	0.9063 (0.7369 to 0.9688)	
14 Months	0.9898 (0.9298 to 0.9986)	0.9395 (0.8700 to 0.9724)	0.9744 (0.8316 to 0.9963)	0.9063 (0.7369 to 0.9688)	
16 Months	0.9898 (0.9298 to 0.9986)	0.9395 (0.8700 to 0.9724)	0.9744 (0.8316 to 0.9963)	0.9063 (0.7369 to 0.9688)	
Number of patients at risk[b]					
2 Months	93	99	37	30	
4 Months	90	93	34	29	
6 Months	75	85	33	28	
8 Months	68	79	29	28	
10 Months	66	73	28	27	
12 Months	56	64	24	25	
14 Months	34	45	13	15	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.5 Treatment emergent serious adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	17	17	7	6	
Metabolism and nutrition disorders (days)					
Number (%) of events	4 (4.1)	5 (4.9)	1 (2.5)	2 (6.3)	0.7608
Number (%) of patients censored	94 (95.9)	98 (95.1)	39 (97.5)	30 (93.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8228		0.4625	
Hazard ratio (95% CI) vs Pd	-	1.16 (0.31 to 4.33)		2.39 (0.22 to 26.38)	
P-value	-	0.8229		0.4765	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.13 Treatment emergent severe adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	58	61	27	21	
8 Months	51	55	23	20	
10 Months	51	49	23	18	
12 Months	42	44	19	15	
14 Months	25	29	11	10	
16 Months	13	12	6	4	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	4 (3.9)	0 (0.0)	3 (9.4)	1.0000
Number (%) of patients censored	98 (100.0)	99 (96.1)	40 (100.0)	29 (90.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.5298 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_semm_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.13 Treatment emergent severe adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Log-Rank test p-value[a] vs Pd	-	0.0506		0.0520	
Hazard ratio (95% CI) vs Pd	-	NC		NC	
P-value	-	0.9950		0.9956	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9709 (0.9124 to 0.9905)	1.0000 (1.0000 to 1.0000)	0.9375 (0.7725 to 0.9840)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9610 (0.8993 to 0.9852)	1.0000 (1.0000 to 1.0000)	0.9063 (0.7369 to 0.9688)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9610 (0.8993 to 0.9852)	1.0000 (1.0000 to 1.0000)	0.9063 (0.7369 to 0.9688)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9610 (0.8993 to 0.9852)	1.0000 (1.0000 to 1.0000)	0.9063 (0.7369 to 0.9688)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9610 (0.8993 to 0.9852)	1.0000 (1.0000 to 1.0000)	0.9063 (0.7369 to 0.9688)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9610 (0.8993 to 0.9852)	1.0000 (1.0000 to 1.0000)	0.9063 (0.7369 to 0.9688)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.13 Treatment emergent severe adverse event according to SOC by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	1.0000 (1.0000 to 1.0000)	0.9610 (0.8993 to 0.9852)	1.0000 (1.0000 to 1.0000)	0.9063 (0.7369 to 0.9688)	
16 Months	1.0000 (1.0000 to 1.0000)	0.9610 (0.8993 to 0.9852)	1.0000 (1.0000 to 1.0000)	0.9063 (0.7369 to 0.9688)	
Number of patients at risk[b]					
2 Months	94	99	38	30	
4 Months	91	94	34	29	
6 Months	76	86	33	28	
8 Months	69	81	29	28	
10 Months	67	75	28	27	
12 Months	57	66	24	25	
14 Months	35	46	13	15	
16 Months	17	18	7	6	
Metabolism and nutrition disorders (days)					
Number (%) of events	7 (7.1)	8 (7.8)	1 (2.5)	4 (12.5)	0.4621

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_semm_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0.3197 (0.2217 to 0.4217)	0.4464 (0.3443 to 0.5433)	0.4340 (0.2868 to 0.5725)	0.5127 (0.3656 to 0.6417)	
16 Months	0.3197 (0.2217 to 0.4217)	0.3777 (0.2575 to 0.4973)	0.4340 (0.2868 to 0.5725)	0.4486 (0.2764 to 0.6067)	
Number of patients at risk[b]					
2 Months	53	76	36	32	
4 Months	43	61	27	28	
6 Months	34	51	25	24	
8 Months	29	45	21	23	
10 Months	24	35	19	22	
12 Months	22	29	14	20	
14 Months	12	22	9	14	
16 Months	6	12	5	6	
Infections and infestations (days)					
Number (%) of events	71 (73.2)	80 (79.2)	24 (47.1)	42 (84.0)	0.0070

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_dghc_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of patients censored	26 (26.8)	21 (20.8)	27 (52.9)	8 (16.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.9528 (0.5914 to 1.4456)	0.6571 (0.4600 to 0.8214)	1.8070 (0.9528 to 2.2669)	0.7228 (0.4271 to 1.1499)	
Median (95% CI)	1.9713 (1.5770 to 3.3183)	2.6283 (1.3142 to 3.3183)	7.3265 (2.0698 to NC)	1.9713 (0.9856 to 3.2526)	
75% quantile (95% CI)	9.3306 (5.3224 to NC)	6.3409 (4.5339 to NC)	NC (NC to NC)	3.9097 (2.5955 to 11.8275)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5508		0.0004	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.80 to 1.52)		2.44 (1.47 to 4.04)	
P-value	-	0.5514		0.0005	
Hazard ratio inverted (95% CI) vs IPd			0.41 (0.25 to 0.68)		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.4973 (0.3934 to 0.5926)	0.5461 (0.4431 to 0.6379)	0.6758 (0.5262 to 0.7873)	0.4985 (0.3537 to 0.6272)	
4 Months	0.3676 (0.2713 to 0.4640)	0.3838 (0.2885 to 0.4782)	0.5442 (0.3932 to 0.6726)	0.2419 (0.1320 to 0.3698)	
6 Months	0.3327 (0.2393 to 0.4287)	0.2797 (0.1948 to 0.3707)	0.5442 (0.3932 to 0.6726)	0.1924 (0.0935 to 0.3178)	
8 Months	0.2834 (0.1947 to 0.3784)	0.2259 (0.1485 to 0.3133)	0.4883 (0.3360 to 0.6243)	0.1649 (0.0732 to 0.2887)	
10 Months	0.2447 (0.1607 to 0.3383)	0.2021 (0.1282 to 0.2880)	0.4883 (0.3360 to 0.6243)	0.1649 (0.0732 to 0.2887)	
12 Months	0.2447 (0.1607 to 0.3383)	0.2021 (0.1282 to 0.2880)	0.4883 (0.3360 to 0.6243)	0.1100 (0.0375 to 0.2268)	
14 Months	0.2272 (0.1444 to 0.3216)	0.1877 (0.1156 to 0.2733)	0.4883 (0.3360 to 0.6243)	0.1100 (0.0375 to 0.2268)	
16 Months	0.2272 (0.1444 to 0.3216)	0.1877 (0.1156 to 0.2733)	0.4883 (0.3360 to 0.6243)	0.1100 (0.0375 to 0.2268)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_dghc_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	47	54	32	24	
4 Months	34	37	23	11	
6 Months	28	26	21	7	
8 Months	22	21	17	6	
10 Months	19	17	16	6	
12 Months	16	15	12	4	
14 Months	8	9	9	4	
16 Months	4	4	5	4	
Injury, poisoning and procedural complications (days)					
Number (%) of events	13 (13.4)	42 (41.6)	4 (7.8)	30 (60.0)	0.0360
Number (%) of patients censored	84 (86.6)	59 (58.4)	47 (92.2)	20 (40.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (9.4620 to NC)	0.1643 (0.0986 to 1.5113)	NC (NC to NC)	0.0657 (0.0657 to 0.1314)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_dghc_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (11.4661 to NC)	NC (NC to NC)	0.1971 (0.1314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Pd	-	3.82 (2.05 to 7.12)		14.49 (4.41 to 47.66)	
P-value	-	<.0001		<.0001	
Hazard ratio inverted (95% CI) vs IPd	0.26 (0.14 to 0.49)		0.07 (0.02 to 0.23)		
Events probability (95% CI)[b]					
2 Months	0.9471 (0.8775 to 0.9776)	0.6629 (0.5617 to 0.7460)	0.9792 (0.8612 to 0.9970)	0.4800 (0.3371 to 0.6093)	
4 Months	0.9254 (0.8499 to 0.9638)	0.6526 (0.5510 to 0.7367)	0.9564 (0.8364 to 0.9889)	0.4600 (0.3188 to 0.5901)	
6 Months	0.9142 (0.8356 to 0.9561)	0.6413 (0.5391 to 0.7266)	0.9564 (0.8364 to 0.9889)	0.4391 (0.2997 to 0.5700)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.8730 (0.7812 to 0.9280)	0.6065 (0.5026 to 0.6953)	0.9325 (0.8046 to 0.9778)	0.4147 (0.2766 to 0.5473)	
10 Months	0.8429 (0.7428 to 0.9065)	0.6065 (0.5026 to 0.6953)	0.9325 (0.8046 to 0.9778)	0.3903 (0.2540 to 0.5242)	
12 Months	0.8429 (0.7428 to 0.9065)	0.5918 (0.4863 to 0.6826)	0.9325 (0.8046 to 0.9778)	0.3903 (0.2540 to 0.5242)	
14 Months	0.8429 (0.7428 to 0.9065)	0.5918 (0.4863 to 0.6826)	0.9325 (0.8046 to 0.9778)	0.3903 (0.2540 to 0.5242)	
16 Months	0.8429 (0.7428 to 0.9065)	0.5151 (0.3776 to 0.6365)	0.9325 (0.8046 to 0.9778)	0.3903 (0.2540 to 0.5242)	
Number of patients at risk[b]					
2 Months	88	66	46	24	
4 Months	84	62	42	22	
6 Months	70	56	40	18	
8 Months	60	49	35	17	
10 Months	56	44	34	16	
12 Months	46	37	29	14	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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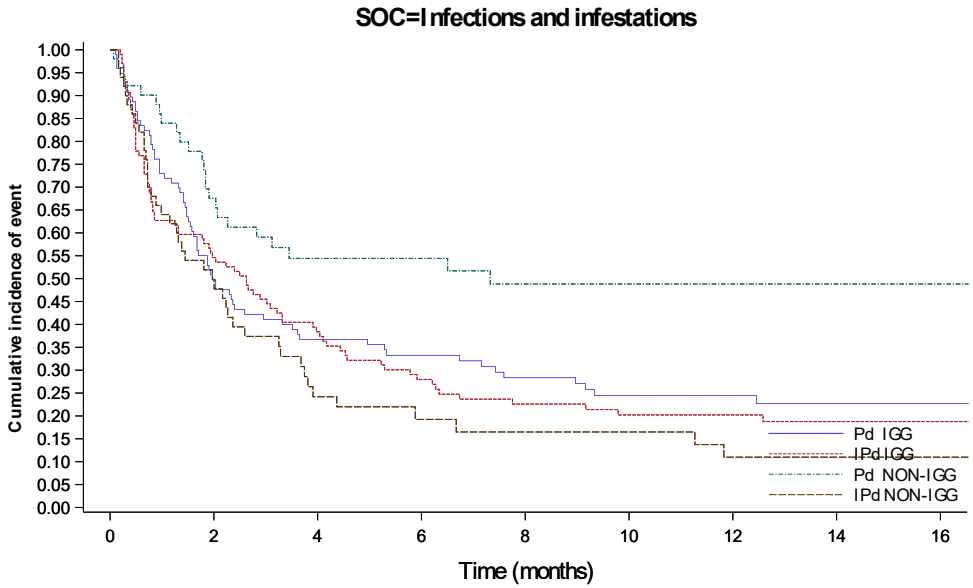
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.1 Treatment emergent adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	27	24	18	6	
16 Months	12	9	9	1	
Investigations (days)					
Number (%) of events	9 (9.3)	14 (13.9)	1 (2.0)	3 (6.0)	0.6356
Number (%) of patients censored	88 (90.7)	87 (86.1)	50 (98.0)	47 (94.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2689		0.3444	
Hazard ratio (95% CI) vs Pd	-	1.62 (0.68 to 3.87)		2.84 (0.30 to 27.38)	
P-value	-	0.2736		0.3660	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_dghc_s_t_x.rtf (16FEB2021 22:52)

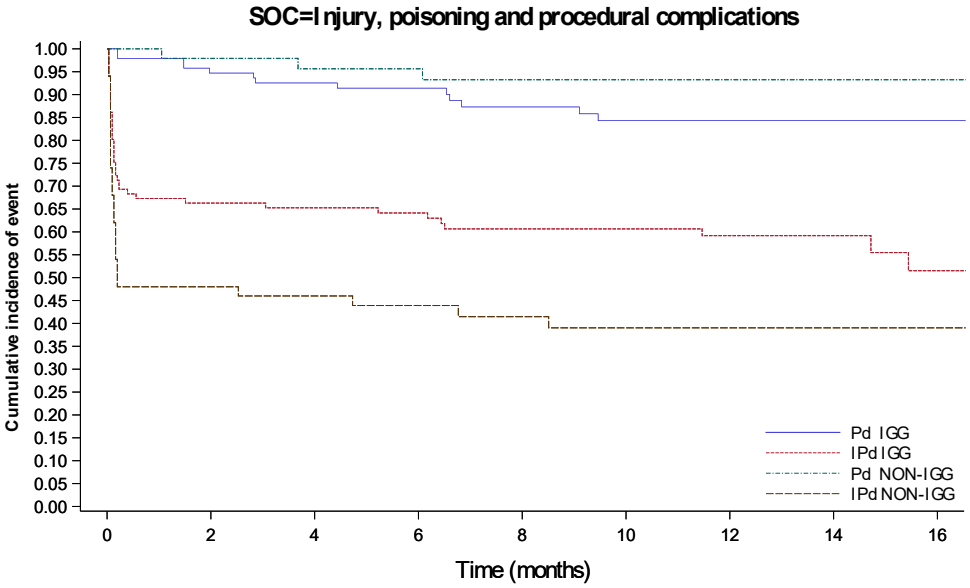
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population



Number at Risk

Pd IGG	97	47	34	28	22	19	16	8	4
IPd IGG	100	54	37	26	21	17	15	9	4
Pd NON-IGG	51	32	23	21	17	16	12	9	5
IPd NON-IGG	50	24	11	7	6	6	4	4	4

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population



Number at Risk

Pd IGG	97	88	84	70	60	56	46	27	12
IPd IGG	101	66	62	56	49	44	37	24	9
Pd NON-IGG	50	46	42	40	35	34	29	18	9
IPd NON-IGG	50	24	22	18	17	16	14	6	1

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.5 Treatment emergent serious adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	78	83	43	40	
4 Months	66	75	37	36	
6 Months	57	61	34	32	
8 Months	51	56	30	31	
10 Months	50	50	29	28	
12 Months	42	45	24	22	
14 Months	25	31	16	14	
16 Months	12	13	8	6	
Injury, poisoning and procedural complications (days)					
Number (%) of events	1 (1.0)	6 (5.9)	1 (2.0)	5 (10.0)	0.9534
Number (%) of patients censored	96 (99.0)	95 (94.1)	50 (98.0)	45 (90.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.5 Treatment emergent serious adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0677		0.0964	
Hazard ratio (95% CI) vs Pd	-	5.72 (0.69 to 47.48)		5.12 (0.60 to 43.83)	
P-value	-	0.1064		0.1359	
Events probability (95% CI)[b]					
2 Months	0.9897 (0.9291 to 0.9985)	0.9703 (0.9107 to 0.9903)	0.9796 (0.8638 to 0.9971)	0.9200 (0.8007 to 0.9692)	
4 Months	0.9897 (0.9291 to 0.9985)	0.9500 (0.8840 to 0.9789)	0.9796 (0.8638 to 0.9971)	0.8996 (0.7753 to 0.9569)	
6 Months	0.9897 (0.9291 to 0.9985)	0.9500 (0.8840 to 0.9789)	0.9796 (0.8638 to 0.9971)	0.8996 (0.7753 to 0.9569)	
8 Months	0.9897 (0.9291 to 0.9985)	0.9382 (0.8674 to 0.9718)	0.9796 (0.8638 to 0.9971)	0.8996 (0.7753 to 0.9569)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.5 Treatment emergent serious adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.9897 (0.9291 to 0.9985)	0.9382 (0.8674 to 0.9718)	0.9796 (0.8638 to 0.9971)	0.8996 (0.7753 to 0.9569)	
12 Months	0.9897 (0.9291 to 0.9985)	0.9382 (0.8674 to 0.9718)	0.9796 (0.8638 to 0.9971)	0.8996 (0.7753 to 0.9569)	
14 Months	0.9897 (0.9291 to 0.9985)	0.9382 (0.8674 to 0.9718)	0.9796 (0.8638 to 0.9971)	0.8996 (0.7753 to 0.9569)	
16 Months	0.9897 (0.9291 to 0.9985)	0.9382 (0.8674 to 0.9718)	0.9796 (0.8638 to 0.9971)	0.8996 (0.7753 to 0.9569)	
Number of patients at risk[b]					
2 Months	92	97	47	45	
4 Months	89	91	43	42	
6 Months	74	83	41	37	
8 Months	67	77	37	37	
10 Months	65	71	35	36	
12 Months	55	62	30	33	
14 Months	33	44	19	21	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.5 Treatment emergent serious adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	16	17	9	10	
Metabolism and nutrition disorders (days)					
Number (%) of events	4 (4.1)	5 (5.0)	2 (3.9)	3 (6.0)	0.8198
Number (%) of patients censored	93 (95.9)	96 (95.0)	49 (96.1)	47 (94.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8116		0.6492	
Hazard ratio (95% CI) vs Pd	-	1.17 (0.31 to 4.37)		1.51 (0.25 to 9.04)	
P-value	-	0.8118		0.6515	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.14 Treatment emergent severe adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	57	59	33	31	
8 Months	51	53	29	30	
10 Months	51	47	28	28	
12 Months	42	43	23	22	
14 Months	25	29	15	15	
16 Months	13	12	7	7	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	4 (4.0)	0 (0.0)	4 (8.0)	0.9999
Number (%) of patients censored	97 (100.0)	97 (96.0)	51 (100.0)	46 (92.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.14 Treatment emergent severe adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Log-Rank test p-value[a] vs Pd	-	0.0495		0.0500	
Hazard ratio (95% CI) vs Pd	-	NC		NC	
P-value	-	0.9950		0.9950	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9703 (0.9107 to 0.9903)	1.0000 (1.0000 to 1.0000)	0.9600 (0.8494 to 0.9898)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9602 (0.8974 to 0.9849)	1.0000 (1.0000 to 1.0000)	0.9396 (0.8242 to 0.9801)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9602 (0.8974 to 0.9849)	1.0000 (1.0000 to 1.0000)	0.9396 (0.8242 to 0.9801)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9602 (0.8974 to 0.9849)	1.0000 (1.0000 to 1.0000)	0.9396 (0.8242 to 0.9801)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9602 (0.8974 to 0.9849)	1.0000 (1.0000 to 1.0000)	0.9396 (0.8242 to 0.9801)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9602 (0.8974 to 0.9849)	1.0000 (1.0000 to 1.0000)	0.9396 (0.8242 to 0.9801)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.14 Treatment emergent severe adverse event according to SOC by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	1.0000 (1.0000 to 1.0000)	0.9602 (0.8974 to 0.9849)	1.0000 (1.0000 to 1.0000)	0.9127 (0.7817 to 0.9667)	
16 Months	1.0000 (1.0000 to 1.0000)	0.9602 (0.8974 to 0.9849)	1.0000 (1.0000 to 1.0000)	0.9127 (0.7817 to 0.9667)	
Number of patients at risk[b]					
2 Months	93	97	48	47	
4 Months	90	92	43	44	
6 Months	75	84	41	39	
8 Months	68	79	37	39	
10 Months	66	73	35	38	
12 Months	56	64	30	35	
14 Months	34	45	19	22	
16 Months	16	18	9	10	
Metabolism and nutrition disorders (days)					
Number (%) of events	7 (7.2)	7 (6.9)	1 (2.0)	6 (12.0)	0.1176

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.1 Treatment emergent adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0.4375 (0.1187 to 0.7256)	0.7143 (0.4063 to 0.8819)	0.3644 (0.2795 to 0.4496)	0.4406 (0.3543 to 0.5235)	
16 Months	0.4375 (0.1187 to 0.7256)	0.7143 (0.4063 to 0.8819)	0.3644 (0.2795 to 0.4496)	0.3644 (0.2601 to 0.4692)	
Number of patients at risk[b]					
2 Months	5	11	85	98	
4 Months	3	10	68	80	
6 Months	2	9	58	67	
8 Months	1	8	50	60	
10 Months	1	8	43	49	
12 Months	1	6	36	43	
14 Months	1	5	21	31	
16 Months	0	4	12	14	
Infections and infestations (days)					
Number (%) of events	4 (40.0)	9 (64.3)	92 (66.2)	114 (82.6)	0.9147

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.1 Treatment emergent adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of patients censored	6 (60.0)	5 (35.7)	47 (33.8)	24 (17.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.6099 (0.3285 to NC)	0.5585 (0.2300 to 1.2485)	1.1828 (0.8214 to 1.5113)	0.7228 (0.4928 to 0.8214)	
Median (95% CI)	NC (0.3285 to NC)	2.1684 (0.4600 to NC)	2.3655 (1.8727 to 3.9425)	2.2341 (1.7741 to 3.0226)	
75% quantile (95% CI)	NC (2.8255 to NC)	NC (1.2485 to NC)	NC (9.1663 to NC)	5.8809 (4.0411 to 9.1663)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3772		0.0093	
Hazard ratio (95% CI) vs Pd	-	1.70 (0.52 to 5.56)		1.44 (1.09 to 1.90)	
P-value	-	0.3826		0.0097	
Hazard ratio inverted (95% CI) vs IPd			0.69 (0.53 to 0.92)		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.1 Treatment emergent adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.6750 (0.2906 to 0.8825)	0.5000 (0.2286 to 0.7221)	0.5534 (0.4661 to 0.6323)	0.5366 (0.4493 to 0.6162)	
4 Months	0.5400 (0.1812 to 0.8007)	0.4286 (0.1773 to 0.6604)	0.4153 (0.3313 to 0.4972)	0.3331 (0.2548 to 0.4132)	
6 Months	0.5400 (0.1812 to 0.8007)	0.3571 (0.1303 to 0.5944)	0.3912 (0.3082 to 0.4731)	0.2381 (0.1691 to 0.3138)	
8 Months	0.5400 (0.1812 to 0.8007)	0.3571 (0.1303 to 0.5944)	0.3397 (0.2595 to 0.4215)	0.1871 (0.1247 to 0.2592)	
10 Months	0.5400 (0.1812 to 0.8007)	0.3571 (0.1303 to 0.5944)	0.3122 (0.2336 to 0.3938)	0.1683 (0.1087 to 0.2392)	
12 Months	0.5400 (0.1812 to 0.8007)	0.3571 (0.1303 to 0.5944)	0.3122 (0.2336 to 0.3938)	0.1485 (0.0919 to 0.2179)	
14 Months	0.5400 (0.1812 to 0.8007)	0.3571 (0.1303 to 0.5944)	0.2997 (0.2212 to 0.3820)	0.1371 (0.0821 to 0.2060)	
16 Months	0.5400 (0.1812 to 0.8007)	0.3571 (0.1303 to 0.5944)	0.2997 (0.2212 to 0.3820)	0.1371 (0.0821 to 0.2060)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.1 Treatment emergent adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	6	7	74	72	
4 Months	4	6	53	43	
6 Months	2	5	47	28	
8 Months	1	5	38	22	
10 Months	1	5	34	18	
12 Months	1	5	27	14	
14 Months	1	4	16	9	
16 Months	0	4	9	4	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	8 (57.1)	17 (12.2)	64 (46.4)	0.9855
Number (%) of patients censored	10 (100.0)	6 (42.9)	122 (87.8)	74 (53.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0657 to 1.5113)	NC (NC to NC)	0.1314 (0.0986 to 0.1643)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.1 Treatment emergent adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	2.0205 (0.0657 to NC)	NC (NC to NC)	15.4415 (6.1766 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.5113 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0070		<.0001	
Hazard ratio (95% CI) vs Pd	-	NC		5.27 (3.04 to 9.13)	
P-value	-	0.9955		<.0001	
Hazard ratio inverted (95% CI) vs IPd			0.19 (0.11 to 0.33)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.2286 to 0.7221)	0.9554 (0.9034 to 0.9797)	0.6158 (0.5292 to 0.6911)	
4 Months	1.0000 (1.0000 to 1.0000)	0.4286 (0.1773 to 0.6604)	0.9325 (0.8742 to 0.9643)	0.6082 (0.5214 to 0.6840)	
6 Months	1.0000 (1.0000 to 1.0000)	0.4286 (0.1773 to 0.6604)	0.9246 (0.8643 to 0.9587)	0.5923 (0.5051 to 0.6692)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.1 Treatment emergent adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	1.0000 (1.0000 to 1.0000)	0.4286 (0.1773 to 0.6604)	0.8886 (0.8185 to 0.9327)	0.5584 (0.4703 to 0.6376)	
10 Months	1.0000 (1.0000 to 1.0000)	0.4286 (0.1773 to 0.6604)	0.8690 (0.7943 to 0.9180)	0.5493 (0.4608 to 0.6291)	
12 Months	1.0000 (1.0000 to 1.0000)	0.4286 (0.1773 to 0.6604)	0.8690 (0.7943 to 0.9180)	0.5391 (0.4501 to 0.6199)	
14 Months	1.0000 (1.0000 to 1.0000)	0.4286 (0.1773 to 0.6604)	0.8690 (0.7943 to 0.9180)	0.5391 (0.4501 to 0.6199)	
16 Months	1.0000 (1.0000 to 1.0000)	0.4286 (0.1773 to 0.6604)	0.8690 (0.7943 to 0.9180)	0.4711 (0.3524 to 0.5809)	
Number of patients at risk[b]					
2 Months	9	7	126	84	
4 Months	7	6	120	79	
6 Months	5	5	106	70	
8 Months	2	4	94	63	
10 Months	2	4	89	57	
12 Months	2	3	74	49	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.1 Treatment emergent adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	2	2	44	28	
16 Months	0	1	22	9	
Investigations (days)					
Number (%) of events	0 (0.0)	1 (7.1)	10 (7.2)	16 (11.6)	0.9922
Number (%) of patients censored	10 (100.0)	13 (92.9)	129 (92.8)	122 (88.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (3.7125 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4631		0.1743	
Hazard ratio (95% CI) vs Pd	-	NC		1.75 (0.77 to 3.96)	
P-value	-	0.9985		0.1799	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.3 Treatment emergent serious adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4497		0.0193	
Hazard ratio (95% CI) vs Pd	-	NC		5.09 (1.11 to 23.22)	
P-value	-	0.9985		0.0357	
Hazard ratio inverted (95% CI) vs IPd			0.20 (0.04 to 0.90)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9854 (0.9429 to 0.9963)	0.9492 (0.8964 to 0.9755)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9854 (0.9429 to 0.9963)	0.9343 (0.8776 to 0.9653)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9854 (0.9429 to 0.9963)	0.9343 (0.8776 to 0.9653)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9854 (0.9429 to 0.9963)	0.9258 (0.8662 to 0.9594)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.3 Treatment emergent serious adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9854 (0.9429 to 0.9963)	0.9258 (0.8662 to 0.9594)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9854 (0.9429 to 0.9963)	0.9258 (0.8662 to 0.9594)	
14 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9854 (0.9429 to 0.9963)	0.9258 (0.8662 to 0.9594)	
16 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9854 (0.9429 to 0.9963)	0.9258 (0.8662 to 0.9594)	
Number of patients at risk[b]					
2 Months	9	14	131	129	
4 Months	7	13	126	121	
6 Months	5	11	111	110	
8 Months	2	10	103	105	
10 Months	2	10	99	98	
12 Months	2	8	84	88	
14 Months	2	7	51	58	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.3 Treatment emergent serious adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0	5	26	22	
Metabolism and nutrition disorders (days)					
Number (%) of events	0 (0.0)	2 (14.3)	6 (4.3)	6 (4.3)	0.9905
Number (%) of patients censored	10 (100.0)	12 (85.7)	133 (95.7)	132 (95.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.1314 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2233		0.9794	
Hazard ratio (95% CI) vs Pd	-	NC		0.99 (0.32 to 3.06)	
P-value	-	0.9978		0.9794	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.9 Treatment emergent severe adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	1	8	78	68	
12 Months	1	8	64	58	
14 Months	1	6	39	38	
16 Months	0	4	20	15	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	1 (7.1)	0 (0.0)	7 (5.1)	1.0000
Number (%) of patients censored	10 (100.0)	13 (92.9)	139 (100.0)	131 (94.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (2.5298 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4497		0.0082	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.9 Treatment emergent severe adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	NC		NC	
P-value	-	0.9985		0.9933	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9637 (0.9150 to 0.9847)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	1.0000 (1.0000 to 1.0000)	0.9563 (0.9053 to 0.9801)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	1.0000 (1.0000 to 1.0000)	0.9563 (0.9053 to 0.9801)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	1.0000 (1.0000 to 1.0000)	0.9563 (0.9053 to 0.9801)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	1.0000 (1.0000 to 1.0000)	0.9563 (0.9053 to 0.9801)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	1.0000 (1.0000 to 1.0000)	0.9563 (0.9053 to 0.9801)	
14 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	1.0000 (1.0000 to 1.0000)	0.9457 (0.8884 to 0.9740)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.9 Treatment emergent severe adverse event according to SOC by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	1.0000 (1.0000 to 1.0000)	0.9457 (0.8884 to 0.9740)	
Number of patients at risk[b]					
2 Months	9	14	133	131	
4 Months	7	13	127	124	
6 Months	5	11	112	113	
8 Months	2	10	104	109	
10 Months	2	10	100	102	
12 Months	2	8	85	92	
14 Months	2	7	52	60	
16 Months	0	5	26	23	
Metabolism and nutrition disorders (days)					
Number (%) of events	1 (10.0)	3 (21.4)	7 (5.0)	10 (7.2)	0.7706
Number (%) of patients censored	9 (90.0)	11 (78.6)	132 (95.0)	128 (92.8)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.1 Treatment emergent adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Infections and infestations (days)					
Number (%) of events	62 (66.0)	67 (77.9)	30 (63.8)	49 (90.7)	0.6128
Number (%) of patients censored	32 (34.0)	19 (22.1)	17 (36.2)	5 (9.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.3470 (0.8871 to 1.7084)	0.6571 (0.4600 to 0.8542)	0.7885 (0.2628 to 1.5770)	0.6571 (0.4600 to 0.8871)	
Median (95% CI)	2.3984 (1.8727 to 6.5051)	2.2669 (1.4456 to 3.7454)	2.0370 (1.4127 to 5.3224)	2.1191 (0.8871 to 3.2197)	
75% quantile (95% CI)	NC (7.5893 to NC)	9.1663 (4.1725 to NC)	NC (5.2895 to NC)	4.4353 (3.2197 to 6.2752)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0939		0.0500	
Hazard ratio (95% CI) vs Pd	-	1.34 (0.95 to 1.90)		1.57 (1.00 to 2.49)	
P-value	-	0.0951		0.0519	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.1 Treatment emergent adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.5561 (0.4490 to 0.6505)	0.5398 (0.4281 to 0.6388)	0.5459 (0.3925 to 0.6759)	0.5185 (0.3786 to 0.6414)	
4 Months	0.4227 (0.3205 to 0.5212)	0.3817 (0.2783 to 0.4843)	0.4035 (0.2601 to 0.5425)	0.2593 (0.1518 to 0.3804)	
6 Months	0.4106 (0.3090 to 0.5093)	0.2799 (0.1875 to 0.3796)	0.3531 (0.2158 to 0.4932)	0.1616 (0.0776 to 0.2727)	
8 Months	0.3382 (0.2420 to 0.4367)	0.2533 (0.1646 to 0.3516)	0.3531 (0.2158 to 0.4932)	0.1010 (0.0378 to 0.2009)	
10 Months	0.3131 (0.2193 to 0.4112)	0.2251 (0.1406 to 0.3219)	0.3138 (0.1772 to 0.4602)	0.1010 (0.0378 to 0.2009)	
12 Months	0.3131 (0.2193 to 0.4112)	0.2101 (0.1279 to 0.3061)	0.3138 (0.1772 to 0.4602)	0.0758 (0.0225 to 0.1729)	
14 Months	0.3131 (0.2193 to 0.4112)	0.1940 (0.1143 to 0.2893)	0.3138 (0.1772 to 0.4602)	0.0758 (0.0225 to 0.1729)	
16 Months	0.3131 (0.2193 to 0.4112)	0.1940 (0.1143 to 0.2893)	0.3138 (0.1772 to 0.4602)	0.0758 (0.0225 to 0.1729)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.1 Treatment emergent adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	51	45	24	28	
4 Months	37	30	17	14	
6 Months	34	21	13	8	
8 Months	27	19	10	5	
10 Months	25	16	8	4	
12 Months	20	13	7	3	
14 Months	13	10	4	1	
16 Months	7	6	2	1	
Injury, poisoning and procedural complications (days)					
Number (%) of events	11 (11.7)	41 (47.7)	6 (12.8)	26 (48.1)	0.9841
Number (%) of patients censored	83 (88.3)	45 (52.3)	41 (87.2)	28 (51.9)	
Kaplan-Meier estimates of event in months					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.1 Treatment emergent adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0657 to 0.1643)	NC (6.6037 to NC)	0.1314 (0.0657 to 4.7310)	
Median (95% CI)	NC (NC to NC)	15.4415 (0.1971 to NC)	NC (NC to NC)	14.7187 (4.7310 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.7187 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Pd	-	5.43 (2.78 to 10.58)		5.57 (2.13 to 14.52)	
P-value	-	<.0001		0.0004	
Hazard ratio inverted (95% CI) vs IPd	0.18 (0.09 to 0.36)		0.18 (0.07 to 0.47)		
Events probability (95% CI)[b]					
2 Months	0.9569 (0.8891 to 0.9836)	0.5698 (0.4585 to 0.6664)	0.9540 (0.8283 to 0.9883)	0.6667 (0.5243 to 0.7752)	
4 Months	0.9231 (0.8453 to 0.9626)	0.5581 (0.4471 to 0.6555)	0.9540 (0.8283 to 0.9883)	0.6481 (0.5055 to 0.7591)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.1 Treatment emergent adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9112 (0.8302 to 0.9546)	0.5581 (0.4471 to 0.6555)	0.9540 (0.8283 to 0.9883)	0.6048 (0.4599 to 0.7222)	
8 Months	0.8858 (0.7976 to 0.9370)	0.5455 (0.4343 to 0.6437)	0.8943 (0.7396 to 0.9594)	0.5376 (0.3915 to 0.6632)	
10 Months	0.8719 (0.7799 to 0.9272)	0.5455 (0.4343 to 0.6437)	0.8585 (0.6880 to 0.9397)	0.5120 (0.3653 to 0.6409)	
12 Months	0.8719 (0.7799 to 0.9272)	0.5311 (0.4196 to 0.6306)	0.8585 (0.6880 to 0.9397)	0.5120 (0.3653 to 0.6409)	
14 Months	0.8719 (0.7799 to 0.9272)	0.5311 (0.4196 to 0.6306)	0.8585 (0.6880 to 0.9397)	0.5120 (0.3653 to 0.6409)	
16 Months	0.8719 (0.7799 to 0.9272)	0.4780 (0.3362 to 0.6066)	0.8585 (0.6880 to 0.9397)	0.4096 (0.2035 to 0.6063)	
Number of patients at risk[b]					
2 Months	87	49	41	36	
4 Months	81	48	40	33	
6 Months	74	45	33	27	
8 Months	66	43	26	21	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.1 Treatment emergent adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	63	40	24	18	
12 Months	55	34	19	15	
14 Months	33	19	11	9	
16 Months	15	7	5	2	
Investigations (days)					
Number (%) of events	7 (7.4)	11 (12.8)	3 (6.4)	5 (9.3)	0.8860
Number (%) of patients censored	87 (92.6)	75 (87.2)	44 (93.6)	49 (90.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2713		0.4139	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.3 Treatment emergent serious adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	79	73	36	42	
4 Months	69	68	29	36	
6 Months	64	60	24	29	
8 Months	59	56	18	27	
10 Months	59	51	17	23	
12 Months	51	44	14	19	
14 Months	31	28	9	13	
16 Months	15	14	4	4	
Injury, poisoning and procedural complications (days)					
Number (%) of events	2 (2.1)	4 (4.7)	0 (0.0)	6 (11.1)	0.9925
Number (%) of patients censored	92 (97.9)	82 (95.3)	47 (100.0)	48 (88.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.3 Treatment emergent serious adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3579		0.0230	
Hazard ratio (95% CI) vs Pd	-	2.17 (0.40 to 11.87)		NC	
P-value	-	0.3700		0.9939	
Events probability (95% CI)[b]					
2 Months	0.9785 (0.9167 to 0.9946)	0.9767 (0.9102 to 0.9941)	1.0000 (1.0000 to 1.0000)	0.9259 (0.8146 to 0.9715)	
4 Months	0.9785 (0.9167 to 0.9946)	0.9532 (0.8801 to 0.9822)	1.0000 (1.0000 to 1.0000)	0.9074 (0.7917 to 0.9604)	
6 Months	0.9785 (0.9167 to 0.9946)	0.9532 (0.8801 to 0.9822)	1.0000 (1.0000 to 1.0000)	0.9074 (0.7917 to 0.9604)	
8 Months	0.9785 (0.9167 to 0.9946)	0.9532 (0.8801 to 0.9822)	1.0000 (1.0000 to 1.0000)	0.8853 (0.7616 to 0.9469)	
10 Months	0.9785 (0.9167 to 0.9946)	0.9532 (0.8801 to 0.9822)	1.0000 (1.0000 to 1.0000)	0.8853 (0.7616 to 0.9469)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.3 Treatment emergent serious adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
12 Months	0.9785 (0.9167 to 0.9946)	0.9532 (0.8801 to 0.9822)	1.0000 (1.0000 to 1.0000)	0.8853 (0.7616 to 0.9469)	
14 Months	0.9785 (0.9167 to 0.9946)	0.9532 (0.8801 to 0.9822)	1.0000 (1.0000 to 1.0000)	0.8853 (0.7616 to 0.9469)	
16 Months	0.9785 (0.9167 to 0.9946)	0.9532 (0.8801 to 0.9822)	1.0000 (1.0000 to 1.0000)	0.8853 (0.7616 to 0.9469)	
Number of patients at risk[b]					
2 Months	89	83	44	50	
4 Months	86	80	41	46	
6 Months	78	75	34	41	
8 Months	72	73	29	37	
10 Months	69	70	28	33	
12 Months	61	61	23	30	
14 Months	36	42	15	19	
16 Months	17	19	7	7	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.10 Treatment emergent severe adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	58	47	17	24	
12 Months	50	41	13	20	
14 Months	30	27	8	13	
16 Months	14	14	4	4	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	3 (3.5)	0 (0.0)	4 (7.4)	0.9999
Number (%) of patients censored	94 (100.0)	83 (96.5)	47 (100.0)	50 (92.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0700		0.0756	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.10 Treatment emergent severe adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	NC		NC	
P-value	-	0.9956		0.9951	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9767 (0.9102 to 0.9941)	1.0000 (1.0000 to 1.0000)	0.9630 (0.8599 to 0.9906)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9650 (0.8953 to 0.9886)	1.0000 (1.0000 to 1.0000)	0.9444 (0.8376 to 0.9817)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9650 (0.8953 to 0.9886)	1.0000 (1.0000 to 1.0000)	0.9444 (0.8376 to 0.9817)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9650 (0.8953 to 0.9886)	1.0000 (1.0000 to 1.0000)	0.9444 (0.8376 to 0.9817)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9650 (0.8953 to 0.9886)	1.0000 (1.0000 to 1.0000)	0.9444 (0.8376 to 0.9817)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9650 (0.8953 to 0.9886)	1.0000 (1.0000 to 1.0000)	0.9444 (0.8376 to 0.9817)	
14 Months	1.0000 (1.0000 to 1.0000)	0.9650 (0.8953 to 0.9886)	1.0000 (1.0000 to 1.0000)	0.9158 (0.7863 to 0.9684)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.10 Treatment emergent severe adverse event according to SOC by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.9650 (0.8953 to 0.9886)	1.0000 (1.0000 to 1.0000)	0.9158 (0.7863 to 0.9684)	
Number of patients at risk[b]					
2 Months	91	83	44	52	
4 Months	87	81	41	48	
6 Months	79	76	34	43	
8 Months	73	74	29	40	
10 Months	70	71	28	36	
12 Months	62	62	23	33	
14 Months	37	42	15	21	
16 Months	17	19	7	8	
Metabolism and nutrition disorders (days)					
Number (%) of events	3 (3.2)	7 (8.1)	4 (8.5)	5 (9.3)	0.3399
Number (%) of patients censored	91 (96.8)	79 (91.9)	43 (91.5)	49 (90.7)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.1 Treatment emergent adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Infections and infestations (days)					
Number (%) of events	1 (50.0)	2 (100.0)	95 (64.6)	121 (80.7)	0.2901
Number (%) of patients censored	1 (50.0)	0 (0.0)	52 (35.4)	29 (19.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.4271 (0.4271 to NC)	0.5585 (0.5585 to 0.8871)	1.3142 (0.8542 to 1.5441)	0.6899 (0.4928 to 0.7885)	
Median (95% CI)	NC (0.4271 to NC)	0.7228 (0.5585 to 0.8871)	2.3984 (1.9055 to 4.9610)	2.2669 (1.7741 to 3.2197)	
75% quantile (95% CI)	NC (0.4271 to NC)	0.8871 (0.5585 to 0.8871)	NC (9.1663 to NC)	6.2094 (4.3696 to 11.8275)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6949		0.0134	
Hazard ratio (95% CI) vs Pd	-	1.62 (0.14 to 18.31)		1.40 (1.07 to 1.84)	
P-value	-	0.6975		0.0139	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.1 Treatment emergent adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.71 (0.54 to 0.93)		
Events probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.5617 (0.4765 to 0.6383)	0.5405 (0.4568 to 0.6168)	
4 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.4223 (0.3398 to 0.5023)	0.3469 (0.2708 to 0.4241)	
6 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3982 (0.3166 to 0.4785)	0.2532 (0.1853 to 0.3266)	
8 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3468 (0.2673 to 0.4274)	0.2072 (0.1445 to 0.2777)	
10 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3194 (0.2413 to 0.4001)	0.1906 (0.1300 to 0.2601)	
12 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3194 (0.2413 to 0.4001)	0.1733 (0.1150 to 0.2416)	
14 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3071 (0.2290 to 0.3886)	0.1637 (0.1065 to 0.2316)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.1 Treatment emergent adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3071 (0.2290 to 0.3886)	0.1637 (0.1065 to 0.2316)	
Number of patients at risk[b]					
2 Months	1	0	79	79	
4 Months	1	0	56	49	
6 Months	1	0	48	33	
8 Months	0	0	39	27	
10 Months	0	0	35	23	
12 Months	0	0	28	19	
14 Months	0	0	17	13	
16 Months	0	0	9	8	
Injury, poisoning and procedural complications (days)					
Number (%) of events	1 (50.0)	1 (50.0)	16 (10.9)	71 (47.3)	0.1550
Number (%) of patients censored	1 (50.0)	1 (50.0)	131 (89.1)	79 (52.7)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.1 Treatment emergent adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.1971 (0.1971 to NC)	4.7310 (4.7310 to NC)	NC (NC to NC)	0.1314 (0.0657 to 0.1643)	
Median (95% CI)	NC (0.1971 to NC)	NC (4.7310 to NC)	NC (NC to NC)	14.7187 (5.2238 to NC)	
75% quantile (95% CI)	NC (0.1971 to NC)	NC (4.7310 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8084		<.0001	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.04 to 11.79)		6.09 (3.49 to 10.64)	
P-value	-	0.8092		<.0001	
Hazard ratio inverted (95% CI) vs IPd			0.16 (0.09 to 0.29)		
Events probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.9646 (0.9170 to 0.9851)	0.5998 (0.5167 to 0.6731)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.1 Treatment emergent adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.9425 (0.8882 to 0.9708)	0.5860 (0.5028 to 0.6601)	
6 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.9348 (0.8784 to 0.9656)	0.5785 (0.4951 to 0.6530)	
8 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.8996 (0.8328 to 0.9407)	0.5469 (0.4626 to 0.6234)	
10 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.8803 (0.8083 to 0.9264)	0.5383 (0.4538 to 0.6155)	
12 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.8803 (0.8083 to 0.9264)	0.5287 (0.4437 to 0.6067)	
14 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.8803 (0.8083 to 0.9264)	0.5287 (0.4437 to 0.6067)	
16 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.8803 (0.8083 to 0.9264)	0.4661 (0.3543 to 0.5702)	
Number of patients at risk[b]					
2 Months	1	2	134	89	
4 Months	1	2	126	83	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.1 Treatment emergent adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	1	1	110	74	
8 Months	0	1	96	66	
10 Months	0	1	91	60	
12 Months	0	1	76	51	
14 Months	0	1	46	29	
16 Months	0	0	22	10	
Investigations (days)					
Number (%) of events	0 (0.0)	1 (50.0)	10 (6.8)	16 (10.7)	0.9886
Number (%) of patients censored	2 (100.0)	1 (50.0)	137 (93.2)	134 (89.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	3.7125 (3.7125 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (3.7125 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (3.7125 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.3 Treatment emergent serious adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1	2	121	122	
4 Months	1	2	103	110	
6 Months	1	2	91	92	
8 Months	0	2	81	86	
10 Months	0	2	79	77	
12 Months	0	2	66	66	
14 Months	0	2	41	43	
16 Months	0	0	20	19	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	0 (0.0)	2 (1.4)	11 (7.3)	0.9996
Number (%) of patients censored	2 (100.0)	2 (100.0)	145 (98.6)	139 (92.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.3 Treatment emergent serious adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0137	
Hazard ratio (95% CI) vs Pd	-	NC		5.40 (1.20 to 24.38)	
P-value	-			0.0282	
Hazard ratio inverted (95% CI) vs IPd			0.19 (0.04 to 0.83)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9862 (0.9458 to 0.9965)	0.9533 (0.9045 to 0.9775)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9862 (0.9458 to 0.9965)	0.9328 (0.8787 to 0.9633)	
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9862 (0.9458 to 0.9965)	0.9328 (0.8787 to 0.9633)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9862 (0.9458 to 0.9965)	0.9248 (0.8682 to 0.9577)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.3 Treatment emergent serious adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9862 (0.9458 to 0.9965)	0.9248 (0.8682 to 0.9577)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9862 (0.9458 to 0.9965)	0.9248 (0.8682 to 0.9577)	
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9862 (0.9458 to 0.9965)	0.9248 (0.8682 to 0.9577)	
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9862 (0.9458 to 0.9965)	0.9248 (0.8682 to 0.9577)	
Number of patients at risk[b]					
2 Months	2	2	138	141	
4 Months	2	2	131	132	
6 Months	1	2	115	119	
8 Months	0	2	105	113	
10 Months	0	2	101	106	
12 Months	0	2	86	94	
14 Months	0	2	53	63	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.3 Treatment emergent serious adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0	0	26	27	
Metabolism and nutrition disorders (days)					
Number (%) of events	0 (0.0)	0 (0.0)	6 (4.1)	8 (5.3)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	141 (95.9)	142 (94.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.6386	
Hazard ratio (95% CI) vs Pd	-	NC		1.29 (0.45 to 3.71)	
P-value	-			0.6395	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.9 Treatment emergent severe adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0	2	79	74	
12 Months	0	2	65	64	
14 Months	0	2	40	42	
16 Months	0	0	20	19	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	0 (0.0)	0 (0.0)	8 (5.3)	0.9994
Number (%) of patients censored	2 (100.0)	2 (100.0)	147 (100.0)	142 (94.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0054	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.9 Treatment emergent severe adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	NC		NC	
P-value	-			0.9929	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9666 (0.9217 to 0.9860)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9530 (0.9039 to 0.9773)	
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9530 (0.9039 to 0.9773)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9530 (0.9039 to 0.9773)	
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9530 (0.9039 to 0.9773)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9530 (0.9039 to 0.9773)	
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9431 (0.8885 to 0.9714)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_prmab_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.9 Treatment emergent severe adverse event according to SOC by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9431 (0.8885 to 0.9714)	
Number of patients at risk[b]					
2 Months	2	2	140	143	
4 Months	2	2	132	135	
6 Months	1	2	116	122	
8 Months	0	2	106	117	
10 Months	0	2	102	110	
12 Months	0	2	87	98	
14 Months	0	2	54	65	
16 Months	0	0	26	28	
Metabolism and nutrition disorders (days)					
Number (%) of events	0 (0.0)	0 (0.0)	8 (5.4)	13 (8.7)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	139 (94.6)	137 (91.3)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0.3653 (0.2709 to 0.4600)	0.4838 (0.3886 to 0.5725)	0.3720 (0.2106 to 0.5338)	0.4062 (0.2396 to 0.5667)	
16 Months	0.3653 (0.2709 to 0.4600)	0.4011 (0.2864 to 0.5129)	0.3720 (0.2106 to 0.5338)	0.4062 (0.2396 to 0.5667)	
Number of patients at risk[b]					
2 Months	67	87	23	22	
4 Months	52	72	19	18	
6 Months	44	60	16	16	
8 Months	38	54	13	14	
10 Months	32	45	12	12	
12 Months	26	39	11	10	
14 Months	17	30	5	6	
16 Months	8	15	4	3	
Infections and infestations (days)					
Number (%) of events	74 (66.7)	92 (78.6)	22 (57.9)	31 (88.6)	0.0476

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of patients censored	37 (33.3)	25 (21.4)	16 (42.1)	4 (11.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.3142 (0.8214 to 1.5441)	0.7228 (0.4928 to 0.8871)	0.9856 (0.2628 to 2.3655)	0.4600 (0.2628 to 0.7228)	
Median (95% CI)	2.0370 (1.8070 to 3.6140)	2.6612 (1.8070 to 3.6797)	7.1622 (2.2998 to NC)	1.3142 (0.6571 to 2.2341)	
75% quantile (95% CI)	NC (6.5051 to NC)	6.6694 (4.4353 to NC)	NC (9.3306 to NC)	4.1725 (2.1684 to 9.1663)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1918		0.0031	
Hazard ratio (95% CI) vs Pd	-	1.23 (0.90 to 1.67)		2.26 (1.30 to 3.94)	
P-value	-	0.1926		0.0039	
Hazard ratio inverted (95% CI) vs IPd			0.44 (0.25 to 0.77)		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.5205 (0.4225 to 0.6096)	0.5563 (0.4607 to 0.6416)	0.6791 (0.5044 to 0.8035)	0.4571 (0.2890 to 0.6105)	
4 Months	0.3828 (0.2904 to 0.4744)	0.3682 (0.2801 to 0.4563)	0.5419 (0.3699 to 0.6856)	0.2571 (0.1280 to 0.4077)	
6 Months	0.3503 (0.2598 to 0.4419)	0.2738 (0.1943 to 0.3591)	0.5419 (0.3699 to 0.6856)	0.1714 (0.0696 to 0.3113)	
8 Months	0.3144 (0.2262 to 0.4063)	0.2231 (0.1498 to 0.3057)	0.4496 (0.2832 to 0.6026)	0.1429 (0.0522 to 0.2774)	
10 Months	0.3018 (0.2144 to 0.3938)	0.2119 (0.1400 to 0.2940)	0.3804 (0.2206 to 0.5390)	0.1143 (0.0362 to 0.2423)	
12 Months	0.3018 (0.2144 to 0.3938)	0.1884 (0.1196 to 0.2693)	0.3804 (0.2206 to 0.5390)	0.1143 (0.0362 to 0.2423)	
14 Months	0.2851 (0.1977 to 0.3784)	0.1758 (0.1087 to 0.2562)	0.3804 (0.2206 to 0.5390)	0.1143 (0.0362 to 0.2423)	
16 Months	0.2851 (0.1977 to 0.3784)	0.1758 (0.1087 to 0.2562)	0.3804 (0.2206 to 0.5390)	0.1143 (0.0362 to 0.2423)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	55	63	25	16	
4 Months	38	40	19	9	
6 Months	31	27	18	6	
8 Months	26	22	13	5	
10 Months	24	19	11	4	
12 Months	19	15	9	4	
14 Months	13	10	4	3	
16 Months	6	6	3	2	
Injury, poisoning and procedural complications (days)					
Number (%) of events	12 (10.8)	54 (46.2)	5 (13.2)	18 (51.4)	0.6543
Number (%) of patients censored	99 (89.2)	63 (53.8)	33 (86.8)	17 (48.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0657 to 0.1971)	NC (6.5380 to NC)	0.0986 (0.0657 to 0.1643)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	15.4415 (6.1766 to NC)	NC (NC to NC)	8.5092 (0.0986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Pd	-	5.42 (2.90 to 10.14)		6.72 (2.26 to 19.96)	
P-value	-	<.0001		0.0006	
Hazard ratio inverted (95% CI) vs IPd	0.18 (0.10 to 0.35)		0.15 (0.05 to 0.44)		
Events probability (95% CI)[b]					
2 Months	0.9532 (0.8913 to 0.9803)	0.6323 (0.5380 to 0.7124)	0.9730 (0.8232 to 0.9961)	0.5143 (0.3399 to 0.6638)	
4 Months	0.9337 (0.8658 to 0.9678)	0.6147 (0.5201 to 0.6961)	0.9452 (0.7980 to 0.9860)	0.5143 (0.3399 to 0.6638)	
6 Months	0.9337 (0.8658 to 0.9678)	0.5965 (0.5014 to 0.6792)	0.9156 (0.7604 to 0.9720)	0.5143 (0.3399 to 0.6638)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_refr4_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.8982 (0.8181 to 0.9442)	0.5573 (0.4614 to 0.6429)	0.8829 (0.7163 to 0.9546)	0.5143 (0.3399 to 0.6638)	
10 Months	0.8718 (0.7836 to 0.9257)	0.5573 (0.4614 to 0.6429)	0.8829 (0.7163 to 0.9546)	0.4747 (0.2997 to 0.6309)	
12 Months	0.8718 (0.7836 to 0.9257)	0.5455 (0.4489 to 0.6322)	0.8829 (0.7163 to 0.9546)	0.4747 (0.2997 to 0.6309)	
14 Months	0.8718 (0.7836 to 0.9257)	0.5455 (0.4489 to 0.6322)	0.8829 (0.7163 to 0.9546)	0.4747 (0.2997 to 0.6309)	
16 Months	0.8718 (0.7836 to 0.9257)	0.4721 (0.3445 to 0.5894)	0.8829 (0.7163 to 0.9546)	0.4747 (0.2997 to 0.6309)	
Number of patients at risk[b]					
2 Months	100	73	35	18	
4 Months	94	70	33	15	
6 Months	82	61	29	14	
8 Months	71	54	25	13	
10 Months	66	49	25	12	
12 Months	54	44	22	8	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	32	26	14	4	
16 Months	14	10	8	0	
Investigations (days)					
Number (%) of events	6 (5.4)	11 (9.4)	4 (10.5)	6 (17.1)	0.8768
Number (%) of patients censored	105 (94.6)	106 (90.6)	34 (89.5)	29 (82.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.6160 to NC)	NC (1.2156 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2030		0.4162	
Hazard ratio (95% CI) vs Pd	-	1.96 (0.68 to 5.65)		1.68 (0.47 to 5.96)	
P-value	-	0.2117		0.4214	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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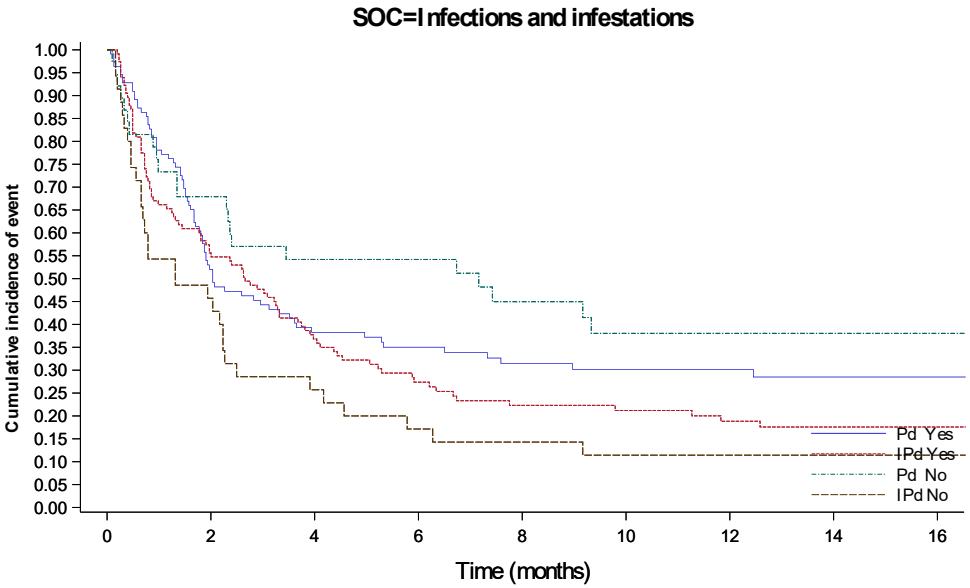
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group according to refractory to PI status - Safety population



Number at Risk

Pd Yes	111	55	38	31	26	24	19	13	6
IPd Yes	116	63	40	27	22	19	15	10	6
Pd No	38	25	19	18	13	11	9	4	3
IPd No	35	16	9	6	5	4	4	3	2

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.4 Treatment emergent serious adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	88	96	34	28	
4 Months	76	89	28	23	
6 Months	65	75	27	19	
8 Months	56	70	25	18	
10 Months	54	64	25	15	
12 Months	44	54	22	14	
14 Months	28	37	13	8	
16 Months	12	17	8	2	
Injury, poisoning and procedural complications (days)					
Number (%) of events	2 (1.8)	7 (6.0)	0 (0.0)	4 (11.4)	0.9930
Number (%) of patients censored	109 (98.2)	110 (94.0)	38 (100.0)	31 (88.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.6940 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.4 Treatment emergent serious adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1126		0.0348	
Hazard ratio (95% CI) vs Pd	-	3.32 (0.69 to 15.97)		NC	
P-value	-	0.1348		0.9949	
Events probability (95% CI)[b]					
2 Months	0.9816 (0.9286 to 0.9954)	0.9573 (0.9004 to 0.9820)	1.0000 (1.0000 to 1.0000)	0.9429 (0.7903 to 0.9854)	
4 Months	0.9816 (0.9286 to 0.9954)	0.9485 (0.8889 to 0.9765)	1.0000 (1.0000 to 1.0000)	0.8848 (0.7215 to 0.9551)	
6 Months	0.9816 (0.9286 to 0.9954)	0.9485 (0.8889 to 0.9765)	1.0000 (1.0000 to 1.0000)	0.8848 (0.7215 to 0.9551)	
8 Months	0.9816 (0.9286 to 0.9954)	0.9384 (0.8749 to 0.9702)	1.0000 (1.0000 to 1.0000)	0.8848 (0.7215 to 0.9551)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.4 Treatment emergent serious adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.9816 (0.9286 to 0.9954)	0.9384 (0.8749 to 0.9702)	1.0000 (1.0000 to 1.0000)	0.8848 (0.7215 to 0.9551)	
12 Months	0.9816 (0.9286 to 0.9954)	0.9384 (0.8749 to 0.9702)	1.0000 (1.0000 to 1.0000)	0.8848 (0.7215 to 0.9551)	
14 Months	0.9816 (0.9286 to 0.9954)	0.9384 (0.8749 to 0.9702)	1.0000 (1.0000 to 1.0000)	0.8848 (0.7215 to 0.9551)	
16 Months	0.9816 (0.9286 to 0.9954)	0.9384 (0.8749 to 0.9702)	1.0000 (1.0000 to 1.0000)	0.8848 (0.7215 to 0.9551)	
Number of patients at risk[b]					
2 Months	103	110	37	33	
4 Months	98	106	35	28	
6 Months	85	95	31	26	
8 Months	77	90	28	25	
10 Months	73	83	28	25	
12 Months	61	75	25	21	
14 Months	38	52	15	13	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.4 Treatment emergent serious adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	17	23	9	4	
Metabolism and nutrition disorders (days)					
Number (%) of events	5 (4.5)	6 (5.1)	1 (2.6)	2 (5.7)	0.6369
Number (%) of patients censored	106 (95.5)	111 (94.9)	37 (97.4)	33 (94.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8512		0.5191	
Hazard ratio (95% CI) vs Pd	-	1.12 (0.34 to 3.67)		2.16 (0.20 to 23.83)	
P-value	-	0.8517		0.5294	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.11 Treatment emergent severe adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	65	73	26	18	
8 Months	56	67	24	17	
10 Months	55	61	24	15	
12 Months	44	52	21	14	
14 Months	29	35	11	9	
16 Months	13	16	7	3	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	5 (4.3)	0 (0.0)	3 (8.6)	0.9999
Number (%) of patients censored	111 (100.0)	112 (95.7)	38 (100.0)	32 (91.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.11 Treatment emergent severe adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Log-Rank test p-value[a] vs Pd	-	0.0329		0.0695	
Hazard ratio (95% CI) vs Pd	-	NC		NC	
P-value	-	0.9944		0.9956	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9744 (0.9226 to 0.9917)	1.0000 (1.0000 to 1.0000)	0.9429 (0.7903 to 0.9854)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9656 (0.9109 to 0.9869)	1.0000 (1.0000 to 1.0000)	0.9143 (0.7573 to 0.9715)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9656 (0.9109 to 0.9869)	1.0000 (1.0000 to 1.0000)	0.9143 (0.7573 to 0.9715)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9656 (0.9109 to 0.9869)	1.0000 (1.0000 to 1.0000)	0.9143 (0.7573 to 0.9715)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9656 (0.9109 to 0.9869)	1.0000 (1.0000 to 1.0000)	0.9143 (0.7573 to 0.9715)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9656 (0.9109 to 0.9869)	1.0000 (1.0000 to 1.0000)	0.9143 (0.7573 to 0.9715)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.11 Treatment emergent severe adverse event according to SOC by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	1.0000 (1.0000 to 1.0000)	0.9530 (0.8894 to 0.9805)	1.0000 (1.0000 to 1.0000)	0.9143 (0.7573 to 0.9715)	
16 Months	1.0000 (1.0000 to 1.0000)	0.9530 (0.8894 to 0.9805)	1.0000 (1.0000 to 1.0000)	0.9143 (0.7573 to 0.9715)	
Number of patients at risk[b]					
2 Months	105	112	37	33	
4 Months	99	108	35	29	
6 Months	86	97	31	27	
8 Months	78	93	28	26	
10 Months	74	86	28	26	
12 Months	62	78	25	22	
14 Months	39	54	15	13	
16 Months	17	24	9	4	
Metabolism and nutrition disorders (days)					
Number (%) of events	6 (5.4)	9 (7.7)	2 (5.3)	4 (11.4)	0.6538

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Infections and infestations (days)					
Number (%) of events	90 (64.3)	117 (80.7)	6 (66.7)	6 (85.7)	0.2284
Number (%) of patients censored	50 (35.7)	28 (19.3)	3 (33.3)	1 (14.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.2813 (0.8542 to 1.5441)	0.7228 (0.4928 to 0.8214)	1.3470 (0.1971 to 3.6140)	0.2628 (0.2628 to 0.5585)	
Median (95% CI)	2.3984 (1.8727 to 4.9610)	2.3984 (1.8070 to 3.2526)	3.6140 (0.1971 to NC)	0.5585 (0.2628 to 1.8070)	
75% quantile (95% CI)	NC (9.1663 to NC)	6.2094 (4.3696 to 11.8275)	NC (2.3326 to NC)	1.8070 (0.4928 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0199		0.1276	
Hazard ratio (95% CI) vs Pd	-	1.39 (1.05 to 1.83)		2.43 (0.75 to 7.83)	
P-value	-	0.0204		0.1381	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.3 Treatment emergent serious adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	114	118	8	6	
4 Months	97	106	7	6	
6 Months	86	89	6	5	
8 Months	75	84	6	4	
10 Months	73	75	6	4	
12 Months	61	64	5	4	
14 Months	38	43	3	2	
16 Months	18	19	2	0	
Injury, poisoning and procedural complications (days)					
Number (%) of events	2 (1.4)	11 (7.6)	0 (0.0)	0 (0.0)	0.9995
Number (%) of patients censored	138 (98.6)	134 (92.4)	9 (100.0)	7 (100.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.3 Treatment emergent serious adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0149			
Hazard ratio (95% CI) vs Pd	-	5.32 (1.18 to 23.98)		NC	
P-value	-	0.0297			
Hazard ratio inverted (95% CI) vs IPd	0.19 (0.04 to 0.85)				
Events probability (95% CI)[b]					
2 Months	0.9854 (0.9431 to 0.9963)	0.9517 (0.9013 to 0.9767)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9854 (0.9431 to 0.9963)	0.9305 (0.8746 to 0.9620)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9854 (0.9431 to 0.9963)	0.9305 (0.8746 to 0.9620)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
8 Months	0.9854 (0.9431 to 0.9963)	0.9222 (0.8637 to 0.9562)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.3 Treatment emergent serious adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.9854 (0.9431 to 0.9963)	0.9222 (0.8637 to 0.9562)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
12 Months	0.9854 (0.9431 to 0.9963)	0.9222 (0.8637 to 0.9562)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
14 Months	0.9854 (0.9431 to 0.9963)	0.9222 (0.8637 to 0.9562)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
16 Months	0.9854 (0.9431 to 0.9963)	0.9222 (0.8637 to 0.9562)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
Number of patients at risk[b]					
2 Months	131	136	9	7	
4 Months	124	127	9	7	
6 Months	107	114	9	7	
8 Months	96	110	9	5	
10 Months	92	103	9	5	
12 Months	78	91	8	5	
14 Months	48	62	5	3	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.3 Treatment emergent serious adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	24	27	2	0	
Metabolism and nutrition disorders (days)					
Number (%) of events	5 (3.6)	8 (5.5)	1 (11.1)	0 (0.0)	0.9904
Number (%) of patients censored	135 (96.4)	137 (94.5)	8 (88.9)	7 (100.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.1971 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.1971 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4612		0.3778	
Hazard ratio (95% CI) vs Pd	-	1.52 (0.50 to 4.64)		NC	
P-value	-	0.4644		0.9984	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.72 (0.55 to 0.95)				
Events probability (95% CI)[b]					
2 Months	0.5538 (0.4664 to 0.6326)	0.5524 (0.4671 to 0.6295)	0.6667 (0.2817 to 0.8783)	0.1429 (0.0071 to 0.4649)	
4 Months	0.4223 (0.3378 to 0.5043)	0.3520 (0.2742 to 0.4307)	0.4444 (0.1359 to 0.7193)	0.1429 (0.0071 to 0.4649)	
6 Months	0.4054 (0.3214 to 0.4877)	0.2549 (0.1856 to 0.3298)	0.3333 (0.0783 to 0.6226)	0.1429 (0.0071 to 0.4649)	
8 Months	0.3496 (0.2676 to 0.4327)	0.2071 (0.1434 to 0.2790)	0.3333 (0.0783 to 0.6226)	0.1429 (0.0071 to 0.4649)	
10 Months	0.3197 (0.2390 to 0.4030)	0.1899 (0.1283 to 0.2607)	0.3333 (0.0783 to 0.6226)	0.1429 (0.0071 to 0.4649)	
12 Months	0.3197 (0.2390 to 0.4030)	0.1718 (0.1127 to 0.2414)	0.3333 (0.0783 to 0.6226)	0.1429 (0.0071 to 0.4649)	
14 Months	0.3063 (0.2256 to 0.3906)	0.1617 (0.1038 to 0.2309)	0.3333 (0.0783 to 0.6226)	0.1429 (0.0071 to 0.4649)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.3063 (0.2256 to 0.3906)	0.1617 (0.1038 to 0.2309)	0.3333 (0.0783 to 0.6226)	0.1429 (0.0071 to 0.4649)	
Number of patients at risk[b]					
2 Months	74	78	6	1	
4 Months	53	48	4	1	
6 Months	46	32	3	1	
8 Months	36	26	3	1	
10 Months	32	22	3	1	
12 Months	25	18	3	1	
14 Months	16	12	1	1	
16 Months	8	8	1	0	
Injury, poisoning and procedural complications (days)					
Number (%) of events	15 (10.7)	69 (47.6)	2 (22.2)	3 (42.9)	0.3107
Number (%) of patients censored	125 (89.3)	76 (52.4)	7 (77.8)	4 (57.1)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0657 to 0.1643)	NC (4.4353 to NC)	3.0554 (0.0329 to NC)	
Median (95% CI)	NC (NC to NC)	14.7187 (4.7310 to NC)	NC (4.4353 to NC)	8.5092 (0.0329 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.5092 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		0.2986	
Hazard ratio (95% CI) vs Pd	-	6.22 (3.50 to 11.06)		2.51 (0.42 to 15.17)	
P-value	-	<.0001		0.3152	
Hazard ratio inverted (95% CI) vs IPd	0.16 (0.09 to 0.29)				
Events probability (95% CI)[b]					
2 Months	0.9555 (0.9036 to 0.9798)	0.5929 (0.5083 to 0.6677)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	0.9322 (0.8737 to 0.9642)	0.5858 (0.5011 to 0.6611)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	
6 Months	0.9322 (0.8737 to 0.9642)	0.5705 (0.4855 to 0.6467)	0.8889 (0.4330 to 0.9836)	0.7143 (0.2582 to 0.9198)	
8 Months	0.9040 (0.8365 to 0.9446)	0.5375 (0.4517 to 0.6158)	0.7778 (0.3648 to 0.9393)	0.7143 (0.2582 to 0.9198)	
10 Months	0.8830 (0.8091 to 0.9295)	0.5375 (0.4517 to 0.6158)	0.7778 (0.3648 to 0.9393)	0.4762 (0.0751 to 0.8085)	
12 Months	0.8830 (0.8091 to 0.9295)	0.5278 (0.4414 to 0.6068)	0.7778 (0.3648 to 0.9393)	0.4762 (0.0751 to 0.8085)	
14 Months	0.8830 (0.8091 to 0.9295)	0.5278 (0.4414 to 0.6068)	0.7778 (0.3648 to 0.9393)	0.4762 (0.0751 to 0.8085)	
16 Months	0.8830 (0.8091 to 0.9295)	0.4652 (0.3529 to 0.5699)	0.7778 (0.3648 to 0.9393)	0.4762 (0.0751 to 0.8085)	
Number of patients at risk[b]					
2 Months	126	85	9	6	
4 Months	118	80	9	5	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	103	70	8	5	
8 Months	89	64	7	3	
10 Months	84	59	7	2	
12 Months	70	50	6	2	
14 Months	43	29	3	1	
16 Months	21	10	1	0	
Investigations (days)					
Number (%) of events	9 (6.4)	16 (11.0)	1 (11.1)	1 (14.3)	0.8392
Number (%) of patients censored	131 (93.6)	129 (89.0)	8 (88.9)	6 (85.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.6160 to NC)	NC (3.5483 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.6160 to NC)	NC (3.5483 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.9 Treatment emergent severe adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	73	72	6	4	
12 Months	60	62	5	4	
14 Months	37	42	3	2	
16 Months	18	19	2	0	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	8 (5.5)	0 (0.0)	0 (0.0)	0.9988
Number (%) of patients censored	140 (100.0)	137 (94.5)	9 (100.0)	7 (100.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0059			

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.9 Treatment emergent severe adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	NC		NC	
P-value	-	0.9929			
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9655 (0.9190 to 0.9855)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9514 (0.9007 to 0.9765)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9514 (0.9007 to 0.9765)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9514 (0.9007 to 0.9765)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9514 (0.9007 to 0.9765)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9514 (0.9007 to 0.9765)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
14 Months	1.0000 (1.0000 to 1.0000)	0.9411 (0.8848 to 0.9704)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.9 Treatment emergent severe adverse event according to SOC by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.9411 (0.8848 to 0.9704)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
Number of patients at risk[b]					
2 Months	133	138	9	7	
4 Months	125	130	9	7	
6 Months	108	117	9	7	
8 Months	97	114	9	5	
10 Months	93	107	9	5	
12 Months	79	95	8	5	
14 Months	49	64	5	3	
16 Months	24	28	2	0	
Metabolism and nutrition disorders (days)					
Number (%) of events	6 (4.3)	13 (9.0)	2 (22.2)	0 (0.0)	0.9885
Number (%) of patients censored	134 (95.7)	132 (91.0)	7 (77.8)	7 (100.0)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0.3685 (0.2610 to 0.4763)	0.4523 (0.3444 to 0.5541)	0.3603 (0.2338 to 0.4882)	0.4833 (0.3516 to 0.6030)	
16 Months	0.3685 (0.2610 to 0.4763)	0.4523 (0.3444 to 0.5541)	0.3603 (0.2338 to 0.4882)	0.3489 (0.1965 to 0.5059)	
Number of patients at risk[b]					
2 Months	54	64	36	45	
4 Months	43	53	28	37	
6 Months	37	44	23	32	
8 Months	30	39	21	29	
10 Months	27	33	17	24	
12 Months	24	31	13	18	
14 Months	14	19	8	17	
16 Months	7	10	5	8	
Infections and infestations (days)					
Number (%) of events	56 (64.4)	73 (80.2)	40 (64.5)	50 (82.0)	0.9589

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of patients censored	31 (35.6)	18 (19.8)	22 (35.5)	11 (18.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.1828 (0.8214 to 1.6756)	0.7228 (0.4928 to 1.1499)	1.3470 (0.2957 to 1.5441)	0.5585 (0.4271 to 0.7556)	
Median (95% CI)	2.9569 (1.9055 to 7.1622)	2.2669 (1.3799 to 3.2854)	2.3326 (1.6756 to 5.3224)	2.0041 (0.8214 to 3.7454)	
75% quantile (95% CI)	NC (7.4251 to NC)	6.2752 (4.1725 to NC)	NC (5.3224 to NC)	5.9138 (3.7454 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0368		0.1273	
Hazard ratio (95% CI) vs Pd	-	1.45 (1.02 to 2.06)		1.38 (0.91 to 2.09)	
P-value	-	0.0380		0.1292	
Hazard ratio inverted (95% CI) vs IPd	0.69 (0.49 to 0.98)				
Events probability (95% CI)[b]					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.5770 (0.4650 to 0.6737)	0.5514 (0.4425 to 0.6476)	0.5377 (0.4045 to 0.6535)	0.5067 (0.3755 to 0.6239)	
4 Months	0.4537 (0.3447 to 0.5563)	0.3598 (0.2616 to 0.4587)	0.3816 (0.2593 to 0.5028)	0.3167 (0.2033 to 0.4361)	
6 Months	0.4269 (0.3191 to 0.5304)	0.2529 (0.1672 to 0.3476)	0.3625 (0.2420 to 0.4840)	0.2463 (0.1451 to 0.3617)	
8 Months	0.3526 (0.2485 to 0.4582)	0.1996 (0.1220 to 0.2912)	0.3424 (0.2238 to 0.4642)	0.2111 (0.1175 to 0.3231)	
10 Months	0.3205 (0.2188 to 0.4266)	0.1854 (0.1101 to 0.2760)	0.3210 (0.2045 to 0.4433)	0.1919 (0.1026 to 0.3023)	
12 Months	0.3205 (0.2188 to 0.4266)	0.1699 (0.0973 to 0.2597)	0.3210 (0.2045 to 0.4433)	0.1727 (0.0881 to 0.2811)	
14 Months	0.2992 (0.1977 to 0.4072)	0.1699 (0.0973 to 0.2597)	0.3210 (0.2045 to 0.4433)	0.1511 (0.0718 to 0.2578)	
16 Months	0.2992 (0.1977 to 0.4072)	0.1699 (0.0973 to 0.2597)	0.3210 (0.2045 to 0.4433)	0.1511 (0.0718 to 0.2578)	

Number of patients at risk[b]

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	48	49	32	30	
4 Months	35	31	22	18	
6 Months	30	19	19	14	
8 Months	22	15	17	12	
10 Months	20	13	15	10	
12 Months	16	11	12	8	
14 Months	10	7	7	6	
16 Months	4	5	5	3	
Injury, poisoning and procedural complications (days)					
Number (%) of events	7 (8.0)	51 (56.0)	10 (16.1)	21 (34.4)	0.0105
Number (%) of patients censored	80 (92.0)	40 (44.0)	52 (83.9)	40 (65.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1314)	NC (6.6037 to NC)	5.2238 (0.1314 to 15.4415)	
Median (95% CI)	NC (NC to NC)	0.5585 (0.1643 to NC)	NC (NC to NC)	NC (14.7187 to NC)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		0.0162	
Hazard ratio (95% CI) vs Pd	-	10.14 (4.59 to 22.41)		2.52 (1.15 to 5.51)	
P-value	-	<.0001		0.0204	
Hazard ratio inverted (95% CI) vs IPd	0.10 (0.04 to 0.22)		0.40 (0.18 to 0.87)		
Events probability (95% CI)[b]					
2 Months	0.9767 (0.9102 to 0.9941)	0.4940 (0.3878 to 0.5916)	0.9318 (0.8284 to 0.9739)	0.7705 (0.6435 to 0.8571)	
4 Months	0.9520 (0.8771 to 0.9817)	0.4825 (0.3767 to 0.5805)	0.9143 (0.8061 to 0.9634)	0.7541 (0.6257 to 0.8438)	
6 Months	0.9520 (0.8771 to 0.9817)	0.4698 (0.3642 to 0.5684)	0.8956 (0.7820 to 0.9518)	0.7370 (0.6070 to 0.8298)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.9374 (0.8554 to 0.9736)	0.4275 (0.3222 to 0.5286)	0.8310 (0.6986 to 0.9089)	0.7190 (0.5873 to 0.8151)	
10 Months	0.9056 (0.8106 to 0.9542)	0.4275 (0.3222 to 0.5286)	0.8310 (0.6986 to 0.9089)	0.6996 (0.5657 to 0.7992)	
12 Months	0.9056 (0.8106 to 0.9542)	0.4275 (0.3222 to 0.5286)	0.8310 (0.6986 to 0.9089)	0.6770 (0.5397 to 0.7813)	
14 Months	0.9056 (0.8106 to 0.9542)	0.4275 (0.3222 to 0.5286)	0.8310 (0.6986 to 0.9089)	0.6770 (0.5397 to 0.7813)	
16 Months	0.9056 (0.8106 to 0.9542)	0.4275 (0.3222 to 0.5286)	0.8310 (0.6986 to 0.9089)	0.5762 (0.3957 to 0.7205)	
Number of patients at risk[b]					
2 Months	81	44	54	47	
4 Months	76	39	51	46	
6 Months	68	34	43	41	
8 Months	59	30	37	37	
10 Months	57	28	34	33	
12 Months	48	24	28	28	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.1 Treatment emergent adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	30	10	16	20	
16 Months	13	2	9	8	
Investigations (days)					
Number (%) of events	7 (8.0)	10 (11.0)	3 (4.8)	7 (11.5)	0.6616
Number (%) of patients censored	80 (92.0)	81 (89.0)	59 (95.2)	54 (88.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3893		0.2213	
Hazard ratio (95% CI) vs Pd	-	1.55 (0.56 to 4.28)		2.27 (0.59 to 8.79)	
P-value	-	0.3931		0.2344	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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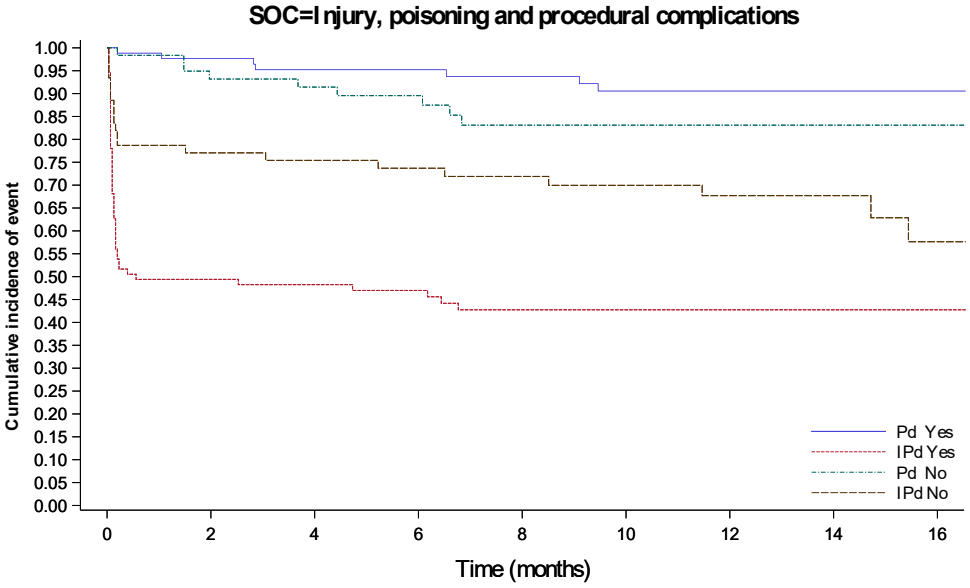
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population



Number at Risk

Pd Yes	87	81	76	68	59	57	48	30	13
IPd Yes	91	44	39	34	30	28	24	10	2
Pd No	61	54	51	43	37	34	28	16	9
IPd No	61	47	46	41	37	33	28	20	8

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.5 Treatment emergent serious adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	74	72	48	52	
4 Months	62	66	42	46	
6 Months	55	52	37	42	
8 Months	47	48	34	40	
10 Months	46	44	33	35	
12 Months	40	41	26	27	
14 Months	24	26	17	19	
16 Months	10	10	10	9	
Injury, poisoning and procedural complications (days)					
Number (%) of events	1 (1.1)	10 (11.0)	1 (1.6)	1 (1.6)	0.1904
Number (%) of patients censored	86 (98.9)	81 (89.0)	61 (98.4)	60 (98.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.5 Treatment emergent serious adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0072		0.9862	
Hazard ratio (95% CI) vs Pd	-	9.83 (1.26 to 76.80)		1.02 (0.06 to 16.38)	
P-value	-	0.0293		0.9862	
Hazard ratio inverted (95% CI) vs IPd	0.10 (0.01 to 0.79)				
Events probability (95% CI)[b]					
2 Months	0.9882 (0.9194 to 0.9983)	0.9339 (0.8588 to 0.9698)	0.9839 (0.8910 to 0.9977)	0.9836 (0.8893 to 0.9977)	
4 Months	0.9882 (0.9194 to 0.9983)	0.9000 (0.8167 to 0.9467)	0.9839 (0.8910 to 0.9977)	0.9836 (0.8893 to 0.9977)	
6 Months	0.9882 (0.9194 to 0.9983)	0.9000 (0.8167 to 0.9467)	0.9839 (0.8910 to 0.9977)	0.9836 (0.8893 to 0.9977)	
8 Months	0.9882 (0.9194 to 0.9983)	0.8864 (0.7987 to 0.9374)	0.9839 (0.8910 to 0.9977)	0.9836 (0.8893 to 0.9977)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.5 Treatment emergent serious adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.9882 (0.9194 to 0.9983)	0.8864 (0.7987 to 0.9374)	0.9839 (0.8910 to 0.9977)	0.9836 (0.8893 to 0.9977)	
12 Months	0.9882 (0.9194 to 0.9983)	0.8864 (0.7987 to 0.9374)	0.9839 (0.8910 to 0.9977)	0.9836 (0.8893 to 0.9977)	
14 Months	0.9882 (0.9194 to 0.9983)	0.8864 (0.7987 to 0.9374)	0.9839 (0.8910 to 0.9977)	0.9836 (0.8893 to 0.9977)	
16 Months	0.9882 (0.9194 to 0.9983)	0.8864 (0.7987 to 0.9374)	0.9839 (0.8910 to 0.9977)	0.9836 (0.8893 to 0.9977)	
Number of patients at risk[b]					
2 Months	82	84	58	59	
4 Months	79	76	54	58	
6 Months	70	68	46	53	
8 Months	62	65	43	50	
10 Months	62	62	39	46	
12 Months	53	57	33	39	
14 Months	33	37	20	28	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.5 Treatment emergent serious adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	15	14	11	13	
Metabolism and nutrition disorders (days)					
Number (%) of events	1 (1.1)	6 (6.6)	5 (8.1)	2 (3.3)	0.0466
Number (%) of patients censored	86 (98.9)	85 (93.4)	57 (91.9)	59 (96.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0652		0.2254	
Hazard ratio (95% CI) vs Pd	-	5.79 (0.70 to 48.08)		0.38 (0.07 to 1.94)	
P-value	-	0.1039		0.2437	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.14 Treatment emergent severe adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	46	42	33	34	
12 Months	39	39	26	27	
14 Months	23	25	17	19	
16 Months	10	10	10	9	
Injury, poisoning and procedural complications (days)					
Number (%) of events	0 (0.0)	7 (7.7)	0 (0.0)	1 (1.6)	0.9997
Number (%) of patients censored	87 (100.0)	84 (92.3)	62 (100.0)	60 (98.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0091		0.3576	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.14 Treatment emergent severe adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	NC		NC	
P-value	-	0.9933		0.9975	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9449 (0.8727 to 0.9767)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9224 (0.8441 to 0.9623)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9224 (0.8441 to 0.9623)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9224 (0.8441 to 0.9623)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9224 (0.8441 to 0.9623)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9224 (0.8441 to 0.9623)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
14 Months	1.0000 (1.0000 to 1.0000)	0.9224 (0.8441 to 0.9623)	1.0000 (1.0000 to 1.0000)	0.9744 (0.8316 to 0.9963)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.14 Treatment emergent severe adverse event according to SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.9224 (0.8441 to 0.9623)	1.0000 (1.0000 to 1.0000)	0.9744 (0.8316 to 0.9963)	
Number of patients at risk[b]					
2 Months	83	85	59	60	
4 Months	79	78	55	59	
6 Months	70	70	47	54	
8 Months	62	68	44	51	
10 Months	62	65	40	47	
12 Months	53	60	34	40	
14 Months	33	39	21	28	
16 Months	15	15	11	13	
Metabolism and nutrition disorders (days)					
Number (%) of events	3 (3.4)	7 (7.7)	5 (8.1)	6 (9.8)	0.4688
Number (%) of patients censored	84 (96.6)	84 (92.3)	57 (91.9)	55 (90.2)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_llen_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.7604 (0.6326 to 0.8490)	0.9067 (0.7901 to 0.9601)	0.8033 (0.6649 to 0.8892)	0.7412 (0.6117 to 0.8332)	0.7397 (0.5289 to 0.8670)	0.8218 (0.6186 to 0.9229)	
Number of patients at risk[b]							
2 Months	57	49	42	57	20	29	
4 Months	52	45	38	55	17	24	
6 Months	47	40	35	48	13	22	
8 Months	40	37	33	43	11	21	
10 Months	37	35	32	38	10	19	
12 Months	34	32	27	35	7	16	
14 Months	21	20	15	25	4	12	
16 Months	10	10	7	12	2	4	
Febrile neutropenia (days)							
Number (%) of events	2 (2.9)	6 (11.1)	1 (1.9)	8 (12.1)	0 (0.0)	4 (12.5)	0.9321
Number (%) of patients censored	66 (97.1)	48 (88.9)	52 (98.1)	58 (87.9)	28 (100.0)	28 (87.5)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_age_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.8727 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0675		0.0422		0.0625	
Hazard ratio (95% CI) vs Pd	-	3.98 (0.80 to 19.72)		6.49 (0.81 to 51.88)		NC	
P-value	-	0.0908		0.0779		0.9950	
Events probability (95% CI)[b]							
2 Months	0.9851 (0.8987 to 0.9979)	0.8889 (0.7693 to 0.9485)	0.9800 (0.8664 to 0.9972)	0.9233 (0.8255 to 0.9673)	1.0000 (1.0000 to 1.0000)	0.9063 (0.7369 to 0.9688)	
4 Months	0.9851 (0.8987 to 0.9979)	0.8889 (0.7693 to 0.9485)	0.9800 (0.8664 to 0.9972)	0.9233 (0.8255 to 0.9673)	1.0000 (1.0000 to 1.0000)	0.8739 (0.6979 to 0.9507)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_age_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9851 (0.8987 to 0.9979)	0.8889 (0.7693 to 0.9485)	0.9800 (0.8664 to 0.9972)	0.8920 (0.7867 to 0.9470)	1.0000 (1.0000 to 1.0000)	0.8739 (0.6979 to 0.9507)	
8 Months	0.9851 (0.8987 to 0.9979)	0.8889 (0.7693 to 0.9485)	0.9800 (0.8664 to 0.9972)	0.8920 (0.7867 to 0.9470)	1.0000 (1.0000 to 1.0000)	0.8739 (0.6979 to 0.9507)	
10 Months	0.9641 (0.8613 to 0.9911)	0.8889 (0.7693 to 0.9485)	0.9800 (0.8664 to 0.9972)	0.8920 (0.7867 to 0.9470)	1.0000 (1.0000 to 1.0000)	0.8739 (0.6979 to 0.9507)	
12 Months	0.9641 (0.8613 to 0.9911)	0.8889 (0.7693 to 0.9485)	0.9800 (0.8664 to 0.9972)	0.8726 (0.7605 to 0.9344)	1.0000 (1.0000 to 1.0000)	0.8739 (0.6979 to 0.9507)	
14 Months	0.9641 (0.8613 to 0.9911)	0.8889 (0.7693 to 0.9485)	0.9800 (0.8664 to 0.9972)	0.8726 (0.7605 to 0.9344)	1.0000 (1.0000 to 1.0000)	0.8739 (0.6979 to 0.9507)	
16 Months	0.9641 (0.8613 to 0.9911)	0.8889 (0.7693 to 0.9485)	0.9800 (0.8664 to 0.9972)	0.8726 (0.7605 to 0.9344)	1.0000 (1.0000 to 1.0000)	0.8739 (0.6979 to 0.9507)	
Number of patients at risk[b]							
2 Months	65	47	49	59	26	29	
4 Months	61	44	47	59	24	26	
6 Months	54	39	44	51	18	24	
8 Months	49	35	40	51	16	24	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_age_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	46	34	39	49	15	24	
12 Months	41	30	34	43	11	21	
14 Months	25	20	21	29	8	15	
16 Months	14	9	8	13	4	4	
Headache (days)							
Number (%) of events	5 (7.4)	6 (11.1)	2 (3.8)	6 (9.1)	1 (3.6)	3 (9.4)	0.6446
Number (%) of patients censored	63 (92.6)	48 (88.9)	51 (96.2)	60 (90.9)	27 (96.4)	29 (90.6)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (10.2177 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.2320 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5402		0.1221		0.4938	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.6 Treatment emergent serious adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)							
Number (%) of events	2 (2.9)	4 (7.4)	1 (1.9)	5 (7.6)	0 (0.0)	1 (3.1)	0.9474
Number (%) of patients censored	66 (97.1)	50 (92.6)	52 (98.1)	61 (92.4)	28 (100.0)	31 (96.9)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2552		0.1690		0.3711	
Hazard ratio (95% CI) vs Pd	-	2.58 (0.47 to 14.11)		4.02 (0.47 to 34.42)		NC	
P-value	-	0.2730		0.2040		0.9975	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.6 Treatment emergent serious adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]							
2 Months	0.9851 (0.8987 to 0.9979)	0.9259 (0.8146 to 0.9715)	0.9800 (0.8664 to 0.9972)	0.9387 (0.8448 to 0.9765)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9851 (0.8987 to 0.9979)	0.9259 (0.8146 to 0.9715)	0.9800 (0.8664 to 0.9972)	0.9387 (0.8448 to 0.9765)	1.0000 (1.0000 to 1.0000)	0.9667 (0.7861 to 0.9952)	
6 Months	0.9851 (0.8987 to 0.9979)	0.9259 (0.8146 to 0.9715)	0.9800 (0.8664 to 0.9972)	0.9387 (0.8448 to 0.9765)	1.0000 (1.0000 to 1.0000)	0.9667 (0.7861 to 0.9952)	
8 Months	0.9851 (0.8987 to 0.9979)	0.9259 (0.8146 to 0.9715)	0.9800 (0.8664 to 0.9972)	0.9387 (0.8448 to 0.9765)	1.0000 (1.0000 to 1.0000)	0.9667 (0.7861 to 0.9952)	
10 Months	0.9641 (0.8613 to 0.9911)	0.9259 (0.8146 to 0.9715)	0.9800 (0.8664 to 0.9972)	0.9387 (0.8448 to 0.9765)	1.0000 (1.0000 to 1.0000)	0.9667 (0.7861 to 0.9952)	
12 Months	0.9641 (0.8613 to 0.9911)	0.9259 (0.8146 to 0.9715)	0.9800 (0.8664 to 0.9972)	0.9187 (0.8144 to 0.9656)	1.0000 (1.0000 to 1.0000)	0.9667 (0.7861 to 0.9952)	
14 Months	0.9641 (0.8613 to 0.9911)	0.9259 (0.8146 to 0.9715)	0.9800 (0.8664 to 0.9972)	0.9187 (0.8144 to 0.9656)	1.0000 (1.0000 to 1.0000)	0.9667 (0.7861 to 0.9952)	
16 Months	0.9641 (0.8613 to 0.9911)	0.9259 (0.8146 to 0.9715)	0.9800 (0.8664 to 0.9972)	0.9187 (0.8144 to 0.9656)	1.0000 (1.0000 to 1.0000)	0.9667 (0.7861 to 0.9952)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.6 Treatment emergent serious adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	65	49	49	60	26	32	
4 Months	61	46	47	60	24	26	
6 Months	54	41	44	54	18	24	
8 Months	49	37	40	53	16	24	
10 Months	46	36	39	50	15	24	
12 Months	41	32	34	44	11	21	
14 Months	25	20	21	30	8	15	
16 Months	14	9	8	14	4	4	
Pneumonia (days)							
Number (%) of events	14 (20.6)	5 (9.3)	7 (13.2)	14 (21.2)	2 (7.1)	4 (12.5)	0.1395
Number (%) of patients censored	54 (79.4)	49 (90.7)	46 (86.8)	52 (78.8)	26 (92.9)	28 (87.5)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (2.7598 to NC)	NC (NC to NC)	NC (5.4209 to NC)	NC (4.7310 to NC)	NC (1.6756 to NC)	NC (2.8583 to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.14 Treatment emergent severe adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)							
Number (%) of events	2 (2.9)	6 (11.1)	1 (1.9)	8 (12.1)	0 (0.0)	4 (12.5)	0.9321
Number (%) of patients censored	66 (97.1)	48 (88.9)	52 (98.1)	58 (87.9)	28 (100.0)	28 (87.5)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.8727 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0675		0.0422		0.0625	
Hazard ratio (95% CI) vs Pd	-	3.98 (0.80 to 19.72)		6.49 (0.81 to 51.88)		NC	
P-value	-	0.0908		0.0779		0.9950	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.14 Treatment emergent severe adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]							
2 Months	0.9851 (0.8987 to 0.9979)	0.8889 (0.7693 to 0.9485)	0.9800 (0.8664 to 0.9972)	0.9233 (0.8255 to 0.9673)	1.0000 (1.0000 to 1.0000)	0.9063 (0.7369 to 0.9688)	
4 Months	0.9851 (0.8987 to 0.9979)	0.8889 (0.7693 to 0.9485)	0.9800 (0.8664 to 0.9972)	0.9233 (0.8255 to 0.9673)	1.0000 (1.0000 to 1.0000)	0.8739 (0.6979 to 0.9507)	
6 Months	0.9851 (0.8987 to 0.9979)	0.8889 (0.7693 to 0.9485)	0.9800 (0.8664 to 0.9972)	0.8920 (0.7867 to 0.9470)	1.0000 (1.0000 to 1.0000)	0.8739 (0.6979 to 0.9507)	
8 Months	0.9851 (0.8987 to 0.9979)	0.8889 (0.7693 to 0.9485)	0.9800 (0.8664 to 0.9972)	0.8920 (0.7867 to 0.9470)	1.0000 (1.0000 to 1.0000)	0.8739 (0.6979 to 0.9507)	
10 Months	0.9641 (0.8613 to 0.9911)	0.8889 (0.7693 to 0.9485)	0.9800 (0.8664 to 0.9972)	0.8920 (0.7867 to 0.9470)	1.0000 (1.0000 to 1.0000)	0.8739 (0.6979 to 0.9507)	
12 Months	0.9641 (0.8613 to 0.9911)	0.8889 (0.7693 to 0.9485)	0.9800 (0.8664 to 0.9972)	0.8726 (0.7605 to 0.9344)	1.0000 (1.0000 to 1.0000)	0.8739 (0.6979 to 0.9507)	
14 Months	0.9641 (0.8613 to 0.9911)	0.8889 (0.7693 to 0.9485)	0.9800 (0.8664 to 0.9972)	0.8726 (0.7605 to 0.9344)	1.0000 (1.0000 to 1.0000)	0.8739 (0.6979 to 0.9507)	
16 Months	0.9641 (0.8613 to 0.9911)	0.8889 (0.7693 to 0.9485)	0.9800 (0.8664 to 0.9972)	0.8726 (0.7605 to 0.9344)	1.0000 (1.0000 to 1.0000)	0.8739 (0.6979 to 0.9507)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_age_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.14 Treatment emergent severe adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	65	47	49	59	26	29	
4 Months	61	44	47	59	24	26	
6 Months	54	39	44	51	18	24	
8 Months	49	35	40	51	16	24	
10 Months	46	34	39	49	15	24	
12 Months	41	30	34	43	11	21	
14 Months	25	20	21	29	8	15	
16 Months	14	9	8	13	4	4	
Neutropenia (days)							
Number (%) of events	18 (26.5)	24 (44.4)	17 (32.1)	29 (43.9)	13 (46.4)	16 (50.0)	0.4497
Number (%) of patients censored	50 (73.5)	30 (55.6)	36 (67.9)	37 (56.1)	15 (53.6)	16 (50.0)	
Kaplan-Meier estimates of event in months							

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.2 Treatment emergent adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	83	89	36	46	
4 Months	74	79	33	45	
6 Months	65	70	30	40	
8 Months	59	64	25	37	
10 Months	57	58	22	34	
12 Months	48	53	20	30	
14 Months	28	36	12	21	
16 Months	12	17	7	9	
Febrile neutropenia (days)					
Number (%) of events	3 (3.0)	15 (14.9)	0 (0.0)	3 (5.9)	0.9909
Number (%) of patients censored	97 (97.0)	86 (85.1)	49 (100.0)	48 (94.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.2 Treatment emergent adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0039		0.0909	
Hazard ratio (95% CI) vs Pd	-	5.13 (1.48 to 17.71)		NC	
P-value	-	0.0097		0.9956	
Hazard ratio inverted (95% CI) vs IPd	0.20 (0.06 to 0.67)				
Events probability (95% CI)[b]					
2 Months	0.9789 (0.9184 to 0.9947)	0.8801 (0.7985 to 0.9300)	1.0000 (1.0000 to 1.0000)	0.9608 (0.8522 to 0.9900)	
4 Months	0.9789 (0.9184 to 0.9947)	0.8697 (0.7862 to 0.9222)	1.0000 (1.0000 to 1.0000)	0.9608 (0.8522 to 0.9900)	
6 Months	0.9789 (0.9184 to 0.9947)	0.8590 (0.7734 to 0.9140)	1.0000 (1.0000 to 1.0000)	0.9408 (0.8275 to 0.9805)	
8 Months	0.9789 (0.9184 to 0.9947)	0.8590 (0.7734 to 0.9140)	1.0000 (1.0000 to 1.0000)	0.9408 (0.8275 to 0.9805)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.2 Treatment emergent adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.9652 (0.8948 to 0.9888)	0.8590 (0.7734 to 0.9140)	1.0000 (1.0000 to 1.0000)	0.9408 (0.8275 to 0.9805)	
12 Months	0.9652 (0.8948 to 0.9888)	0.8458 (0.7566 to 0.9043)	1.0000 (1.0000 to 1.0000)	0.9408 (0.8275 to 0.9805)	
14 Months	0.9652 (0.8948 to 0.9888)	0.8458 (0.7566 to 0.9043)	1.0000 (1.0000 to 1.0000)	0.9408 (0.8275 to 0.9805)	
16 Months	0.9652 (0.8948 to 0.9888)	0.8458 (0.7566 to 0.9043)	1.0000 (1.0000 to 1.0000)	0.9408 (0.8275 to 0.9805)	
Number of patients at risk[b]					
2 Months	92	87	48	48	
4 Months	87	81	45	48	
6 Months	78	72	38	42	
8 Months	72	71	33	39	
10 Months	70	69	30	38	
12 Months	59	62	27	32	
14 Months	37	42	17	22	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.2 Treatment emergent adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	16	18	10	8	
Headache (days)					
Number (%) of events	5 (5.0)	11 (10.9)	3 (6.1)	4 (7.8)	0.4231
Number (%) of patients censored	95 (95.0)	90 (89.1)	46 (93.9)	47 (92.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0930		0.8184	
Hazard ratio (95% CI) vs Pd	-	2.57 (0.82 to 8.08)		1.19 (0.27 to 5.33)	
P-value	-	0.1055		0.8186	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.5 Treatment emergent serious adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	3 (3.0)	9 (8.9)	0 (0.0)	1 (2.0)	0.9928
Number (%) of patients censored	97 (97.0)	92 (91.1)	49 (100.0)	50 (98.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0844		0.3320	
Hazard ratio (95% CI) vs Pd	-	2.99 (0.81 to 11.04)		NC	
P-value	-	0.1005		0.9975	
Events probability (95% CI)[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_plne_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.5 Treatment emergent serious adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9789 (0.9184 to 0.9947)	0.9301 (0.8589 to 0.9660)	1.0000 (1.0000 to 1.0000)	0.9804 (0.8689 to 0.9972)	
4 Months	0.9789 (0.9184 to 0.9947)	0.9196 (0.8457 to 0.9590)	1.0000 (1.0000 to 1.0000)	0.9804 (0.8689 to 0.9972)	
6 Months	0.9789 (0.9184 to 0.9947)	0.9196 (0.8457 to 0.9590)	1.0000 (1.0000 to 1.0000)	0.9804 (0.8689 to 0.9972)	
8 Months	0.9789 (0.9184 to 0.9947)	0.9196 (0.8457 to 0.9590)	1.0000 (1.0000 to 1.0000)	0.9804 (0.8689 to 0.9972)	
10 Months	0.9652 (0.8948 to 0.9888)	0.9196 (0.8457 to 0.9590)	1.0000 (1.0000 to 1.0000)	0.9804 (0.8689 to 0.9972)	
12 Months	0.9652 (0.8948 to 0.9888)	0.9059 (0.8261 to 0.9502)	1.0000 (1.0000 to 1.0000)	0.9804 (0.8689 to 0.9972)	
14 Months	0.9652 (0.8948 to 0.9888)	0.9059 (0.8261 to 0.9502)	1.0000 (1.0000 to 1.0000)	0.9804 (0.8689 to 0.9972)	
16 Months	0.9652 (0.8948 to 0.9888)	0.9059 (0.8261 to 0.9502)	1.0000 (1.0000 to 1.0000)	0.9804 (0.8689 to 0.9972)	
Number of patients at risk[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.5 Treatment emergent serious adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	92	92	48	49	
4 Months	87	83	45	49	
6 Months	78	75	38	44	
8 Months	72	73	33	41	
10 Months	70	71	30	39	
12 Months	59	64	27	33	
14 Months	37	43	17	22	
16 Months	16	19	10	8	
Pneumonia (days)					
Number (%) of events	14 (14.0)	14 (13.9)	9 (18.4)	9 (17.6)	0.8610
Number (%) of patients censored	86 (86.0)	87 (86.1)	40 (81.6)	42 (82.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.0370 to NC)	NC (5.9795 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.12 Treatment emergent severe adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	3 (3.0)	15 (14.9)	0 (0.0)	3 (5.9)	0.9909
Number (%) of patients censored	97 (97.0)	86 (85.1)	49 (100.0)	48 (94.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0039		0.0909	
Hazard ratio (95% CI) vs Pd	-	5.13 (1.48 to 17.71)		NC	
P-value	-	0.0097		0.9956	
Hazard ratio inverted (95% CI) vs IPd	0.20 (0.06 to 0.67)				

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_plne_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.12 Treatment emergent severe adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9789 (0.9184 to 0.9947)	0.8801 (0.7985 to 0.9300)	1.0000 (1.0000 to 1.0000)	0.9608 (0.8522 to 0.9900)	
4 Months	0.9789 (0.9184 to 0.9947)	0.8697 (0.7862 to 0.9222)	1.0000 (1.0000 to 1.0000)	0.9608 (0.8522 to 0.9900)	
6 Months	0.9789 (0.9184 to 0.9947)	0.8590 (0.7734 to 0.9140)	1.0000 (1.0000 to 1.0000)	0.9408 (0.8275 to 0.9805)	
8 Months	0.9789 (0.9184 to 0.9947)	0.8590 (0.7734 to 0.9140)	1.0000 (1.0000 to 1.0000)	0.9408 (0.8275 to 0.9805)	
10 Months	0.9652 (0.8948 to 0.9888)	0.8590 (0.7734 to 0.9140)	1.0000 (1.0000 to 1.0000)	0.9408 (0.8275 to 0.9805)	
12 Months	0.9652 (0.8948 to 0.9888)	0.8458 (0.7566 to 0.9043)	1.0000 (1.0000 to 1.0000)	0.9408 (0.8275 to 0.9805)	
14 Months	0.9652 (0.8948 to 0.9888)	0.8458 (0.7566 to 0.9043)	1.0000 (1.0000 to 1.0000)	0.9408 (0.8275 to 0.9805)	
16 Months	0.9652 (0.8948 to 0.9888)	0.8458 (0.7566 to 0.9043)	1.0000 (1.0000 to 1.0000)	0.9408 (0.8275 to 0.9805)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.12 Treatment emergent severe adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	92	87	48	48	
4 Months	87	81	45	48	
6 Months	78	72	38	42	
8 Months	72	71	33	39	
10 Months	70	69	30	38	
12 Months	59	62	27	32	
14 Months	37	42	17	22	
16 Months	16	18	10	8	
Neutropenia (days)					
Number (%) of events	34 (34.0)	44 (43.6)	14 (28.6)	25 (49.0)	0.3485
Number (%) of patients censored	66 (66.0)	57 (56.4)	35 (71.4)	26 (51.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.5441 (0.7885 to 4.9938)	0.8542 (0.7556 to 1.8398)	2.4312 (0.7885 to NC)	0.8214 (0.5914 to 1.0185)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.3 Treatment emergent adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	57	81	62	54	
4 Months	52	75	55	49	
6 Months	48	66	47	44	
8 Months	46	59	38	42	
10 Months	42	53	37	39	
12 Months	35	47	33	36	
14 Months	22	30	18	27	
16 Months	11	14	8	12	
Febrile neutropenia (days)					
Number (%) of events	1 (1.5)	12 (13.6)	2 (2.5)	6 (9.4)	0.4732
Number (%) of patients censored	67 (98.5)	76 (86.4)	79 (97.5)	58 (90.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.3 Treatment emergent adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0073		0.0890	
Hazard ratio (95% CI) vs Pd	-	9.71 (1.26 to 74.64)		3.66 (0.74 to 18.13)	
P-value	-	0.0290		0.1124	
Hazard ratio inverted (95% CI) vs IPd	0.10 (0.01 to 0.79)				
Events probability (95% CI)[b]					
2 Months	0.9846 (0.8958 to 0.9978)	0.8851 (0.7970 to 0.9365)	0.9872 (0.9125 to 0.9982)	0.9375 (0.8420 to 0.9761)	
4 Months	0.9846 (0.8958 to 0.9978)	0.8851 (0.7970 to 0.9365)	0.9872 (0.9125 to 0.9982)	0.9216 (0.8219 to 0.9666)	
6 Months	0.9846 (0.8958 to 0.9978)	0.8612 (0.7685 to 0.9187)	0.9872 (0.9125 to 0.9982)	0.9216 (0.8219 to 0.9666)	
8 Months	0.9846 (0.8958 to 0.9978)	0.8612 (0.7685 to 0.9187)	0.9872 (0.9125 to 0.9982)	0.9216 (0.8219 to 0.9666)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.3 Treatment emergent adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.9846 (0.8958 to 0.9978)	0.8612 (0.7685 to 0.9187)	0.9678 (0.8739 to 0.9921)	0.9216 (0.8219 to 0.9666)	
12 Months	0.9846 (0.8958 to 0.9978)	0.8612 (0.7685 to 0.9187)	0.9678 (0.8739 to 0.9921)	0.9002 (0.7895 to 0.9543)	
14 Months	0.9846 (0.8958 to 0.9978)	0.8612 (0.7685 to 0.9187)	0.9678 (0.8739 to 0.9921)	0.9002 (0.7895 to 0.9543)	
16 Months	0.9846 (0.8958 to 0.9978)	0.8612 (0.7685 to 0.9187)	0.9678 (0.8739 to 0.9921)	0.9002 (0.7895 to 0.9543)	
Number of patients at risk[b]					
2 Months	64	76	76	59	
4 Months	61	74	71	55	
6 Months	55	64	61	50	
8 Months	53	62	52	48	
10 Months	50	59	50	48	
12 Months	41	52	45	42	
14 Months	27	34	27	30	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.3 Treatment emergent adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	15	15	11	11	
Headache (days)					
Number (%) of events	1 (1.5)	11 (12.5)	7 (8.6)	4 (6.3)	0.0469
Number (%) of patients censored	67 (98.5)	77 (87.5)	74 (91.4)	60 (93.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (12.5503 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0137		0.6639	
Hazard ratio (95% CI) vs Pd	-	8.51 (1.10 to 65.92)		0.76 (0.21 to 2.68)	
P-value	-	0.0404		0.6650	
Hazard ratio inverted (95% CI) vs IPd	0.12 (0.02 to 0.91)				

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.6 Treatment emergent serious adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	1 (1.5)	4 (4.5)	2 (2.5)	6 (9.4)	0.8970
Number (%) of patients censored	67 (98.5)	84 (95.5)	79 (97.5)	58 (90.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2837		0.0890	
Hazard ratio (95% CI) vs Pd	-	3.12 (0.35 to 27.88)		3.66 (0.74 to 18.13)	
P-value	-	0.3094		0.1124	
Events probability (95% CI)[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.6 Treatment emergent serious adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9846 (0.8958 to 0.9978)	0.9540 (0.8821 to 0.9825)	0.9872 (0.9125 to 0.9982)	0.9375 (0.8420 to 0.9761)	
4 Months	0.9846 (0.8958 to 0.9978)	0.9540 (0.8821 to 0.9825)	0.9872 (0.9125 to 0.9982)	0.9216 (0.8219 to 0.9666)	
6 Months	0.9846 (0.8958 to 0.9978)	0.9540 (0.8821 to 0.9825)	0.9872 (0.9125 to 0.9982)	0.9216 (0.8219 to 0.9666)	
8 Months	0.9846 (0.8958 to 0.9978)	0.9540 (0.8821 to 0.9825)	0.9872 (0.9125 to 0.9982)	0.9216 (0.8219 to 0.9666)	
10 Months	0.9846 (0.8958 to 0.9978)	0.9540 (0.8821 to 0.9825)	0.9678 (0.8739 to 0.9921)	0.9216 (0.8219 to 0.9666)	
12 Months	0.9846 (0.8958 to 0.9978)	0.9540 (0.8821 to 0.9825)	0.9678 (0.8739 to 0.9921)	0.9002 (0.7895 to 0.9543)	
14 Months	0.9846 (0.8958 to 0.9978)	0.9540 (0.8821 to 0.9825)	0.9678 (0.8739 to 0.9921)	0.9002 (0.7895 to 0.9543)	
16 Months	0.9846 (0.8958 to 0.9978)	0.9540 (0.8821 to 0.9825)	0.9678 (0.8739 to 0.9921)	0.9002 (0.7895 to 0.9543)	

Number of patients at risk[b]

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.6 Treatment emergent serious adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	64	82	76	59	
4 Months	61	77	71	55	
6 Months	55	69	61	50	
8 Months	53	66	52	48	
10 Months	50	62	50	48	
12 Months	41	55	45	42	
14 Months	27	35	27	30	
16 Months	15	16	11	11	
Pneumonia (days)					
Number (%) of events	11 (16.2)	15 (17.0)	12 (14.8)	8 (12.5)	0.6729
Number (%) of patients censored	57 (83.8)	73 (83.0)	69 (85.2)	56 (87.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (4.1396 to NC)	NC (6.2752 to NC)	NC (5.4209 to NC)	NC (11.6304 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.15 Treatment emergent severe adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	1 (1.5)	12 (13.6)	2 (2.5)	6 (9.4)	0.4732
Number (%) of patients censored	67 (98.5)	76 (86.4)	79 (97.5)	58 (90.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0073		0.0890	
Hazard ratio (95% CI) vs Pd	-	9.71 (1.26 to 74.64)		3.66 (0.74 to 18.13)	
P-value	-	0.0290		0.1124	
Hazard ratio inverted (95% CI) vs IPd	0.10 (0.01 to 0.79)				

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.15 Treatment emergent severe adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9846 (0.8958 to 0.9978)	0.8851 (0.7970 to 0.9365)	0.9872 (0.9125 to 0.9982)	0.9375 (0.8420 to 0.9761)	
4 Months	0.9846 (0.8958 to 0.9978)	0.8851 (0.7970 to 0.9365)	0.9872 (0.9125 to 0.9982)	0.9216 (0.8219 to 0.9666)	
6 Months	0.9846 (0.8958 to 0.9978)	0.8612 (0.7685 to 0.9187)	0.9872 (0.9125 to 0.9982)	0.9216 (0.8219 to 0.9666)	
8 Months	0.9846 (0.8958 to 0.9978)	0.8612 (0.7685 to 0.9187)	0.9872 (0.9125 to 0.9982)	0.9216 (0.8219 to 0.9666)	
10 Months	0.9846 (0.8958 to 0.9978)	0.8612 (0.7685 to 0.9187)	0.9678 (0.8739 to 0.9921)	0.9216 (0.8219 to 0.9666)	
12 Months	0.9846 (0.8958 to 0.9978)	0.8612 (0.7685 to 0.9187)	0.9678 (0.8739 to 0.9921)	0.9002 (0.7895 to 0.9543)	
14 Months	0.9846 (0.8958 to 0.9978)	0.8612 (0.7685 to 0.9187)	0.9678 (0.8739 to 0.9921)	0.9002 (0.7895 to 0.9543)	
16 Months	0.9846 (0.8958 to 0.9978)	0.8612 (0.7685 to 0.9187)	0.9678 (0.8739 to 0.9921)	0.9002 (0.7895 to 0.9543)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.15 Treatment emergent severe adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	64	76	76	59	
4 Months	61	74	71	55	
6 Months	55	64	61	50	
8 Months	53	62	52	48	
10 Months	50	59	50	48	
12 Months	41	52	45	42	
14 Months	27	34	27	30	
16 Months	15	15	11	11	
Neutropenia (days)					
Number (%) of events	18 (26.5)	36 (40.9)	30 (37.0)	33 (51.6)	0.6608
Number (%) of patients censored	50 (73.5)	52 (59.1)	51 (63.0)	31 (48.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	3.3840 (1.1170 to NC)	0.9856 (0.7556 to 2.0370)	1.1499 (0.7228 to 4.3039)	0.8214 (0.5585 to 0.9199)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_sex_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.2 Treatment emergent adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	96	105	17	20	
4 Months	85	97	17	19	
6 Months	75	86	17	19	
8 Months	64	79	17	17	
10 Months	60	71	16	16	
12 Months	54	64	12	14	
14 Months	35	43	3	10	
16 Months	16	21	1	4	
Febrile neutropenia (days)					
Number (%) of events	3 (2.5)	14 (12.1)	0 (0.0)	3 (12.5)	0.9899
Number (%) of patients censored	119 (97.5)	102 (87.9)	19 (100.0)	21 (87.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.8727 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.2 Treatment emergent adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0050		0.1073	
Hazard ratio (95% CI) vs Pd	-	4.99 (1.43 to 17.35)		NC	
P-value	-	0.0116		0.9972	
Hazard ratio inverted (95% CI) vs IPd	0.20 (0.06 to 0.70)				
Events probability (95% CI)[b]					
2 Months	0.9829 (0.9334 to 0.9957)	0.8966 (0.8250 to 0.9399)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
4 Months	0.9829 (0.9334 to 0.9957)	0.8966 (0.8250 to 0.9399)	1.0000 (1.0000 to 1.0000)	0.9130 (0.6949 to 0.9775)	
6 Months	0.9829 (0.9334 to 0.9957)	0.8877 (0.8144 to 0.9332)	1.0000 (1.0000 to 1.0000)	0.8696 (0.6481 to 0.9560)	
8 Months	0.9829 (0.9334 to 0.9957)	0.8877 (0.8144 to 0.9332)	1.0000 (1.0000 to 1.0000)	0.8696 (0.6481 to 0.9560)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.2 Treatment emergent adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.9706 (0.9100 to 0.9906)	0.8877 (0.8144 to 0.9332)	1.0000 (1.0000 to 1.0000)	0.8696 (0.6481 to 0.9560)	
12 Months	0.9706 (0.9100 to 0.9906)	0.8760 (0.7990 to 0.9248)	1.0000 (1.0000 to 1.0000)	0.8696 (0.6481 to 0.9560)	
14 Months	0.9706 (0.9100 to 0.9906)	0.8760 (0.7990 to 0.9248)	1.0000 (1.0000 to 1.0000)	0.8696 (0.6481 to 0.9560)	
16 Months	0.9706 (0.9100 to 0.9906)	0.8760 (0.7990 to 0.9248)	1.0000 (1.0000 to 1.0000)	0.8696 (0.6481 to 0.9560)	
Number of patients at risk[b]					
2 Months	114	104	19	22	
4 Months	107	101	19	21	
6 Months	93	90	19	20	
8 Months	83	87	18	19	
10 Months	79	84	17	19	
12 Months	71	73	13	17	
14 Months	49	48	3	13	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.2 Treatment emergent adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	23	21	1	5	
Headache (days)					
Number (%) of events	7 (5.7)	12 (10.3)	1 (5.3)	3 (12.5)	0.7985
Number (%) of patients censored	115 (94.3)	104 (89.7)	18 (94.7)	21 (87.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.3881 to NC)	NC (1.9055 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1930		0.4001	
Hazard ratio (95% CI) vs Pd	-	1.90 (0.71 to 5.05)		2.55 (0.27 to 24.61)	
P-value	-	0.2007		0.4171	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.5 Treatment emergent serious adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	3 (2.5)	9 (7.8)	0 (0.0)	1 (4.2)	0.9918
Number (%) of patients censored	119 (97.5)	107 (92.2)	19 (100.0)	23 (95.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.9569 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0712		0.3634	
Hazard ratio (95% CI) vs Pd	-	3.13 (0.85 to 11.56)		NC	
P-value	-	0.0873		0.9984	
Events probability (95% CI)[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.5 Treatment emergent serious adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9829 (0.9334 to 0.9957)	0.9310 (0.8668 to 0.9649)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9829 (0.9334 to 0.9957)	0.9310 (0.8668 to 0.9649)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
6 Months	0.9829 (0.9334 to 0.9957)	0.9310 (0.8668 to 0.9649)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
8 Months	0.9829 (0.9334 to 0.9957)	0.9310 (0.8668 to 0.9649)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
10 Months	0.9706 (0.9100 to 0.9906)	0.9310 (0.8668 to 0.9649)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
12 Months	0.9706 (0.9100 to 0.9906)	0.9191 (0.8495 to 0.9573)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
14 Months	0.9706 (0.9100 to 0.9906)	0.9191 (0.8495 to 0.9573)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
16 Months	0.9706 (0.9100 to 0.9906)	0.9191 (0.8495 to 0.9573)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
Number of patients at risk[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.5 Treatment emergent serious adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	114	108	19	23	
4 Months	107	103	19	21	
6 Months	93	93	19	21	
8 Months	83	90	18	19	
10 Months	79	86	17	19	
12 Months	71	75	13	17	
14 Months	49	48	3	13	
16 Months	23	21	1	5	
Pneumonia (days)					
Number (%) of events	20 (16.4)	19 (16.4)	3 (15.8)	4 (16.7)	0.8910
Number (%) of patients censored	102 (83.6)	97 (83.6)	16 (84.2)	20 (83.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (5.6838 to NC)	NC (11.6304 to NC)	NC (1.5770 to NC)	NC (1.0185 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.12 Treatment emergent severe adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	3 (2.5)	14 (12.1)	0 (0.0)	3 (12.5)	0.9899
Number (%) of patients censored	119 (97.5)	102 (87.9)	19 (100.0)	21 (87.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.8727 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0050		0.1073	
Hazard ratio (95% CI) vs Pd	-	4.99 (1.43 to 17.35)		NC	
P-value	-	0.0116		0.9972	
Hazard ratio inverted (95% CI) vs IPd	0.20 (0.06 to 0.70)				

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.12 Treatment emergent severe adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9829 (0.9334 to 0.9957)	0.8966 (0.8250 to 0.9399)	1.0000 (1.0000 to 1.0000)	0.9565 (0.7293 to 0.9938)	
4 Months	0.9829 (0.9334 to 0.9957)	0.8966 (0.8250 to 0.9399)	1.0000 (1.0000 to 1.0000)	0.9130 (0.6949 to 0.9775)	
6 Months	0.9829 (0.9334 to 0.9957)	0.8877 (0.8144 to 0.9332)	1.0000 (1.0000 to 1.0000)	0.8696 (0.6481 to 0.9560)	
8 Months	0.9829 (0.9334 to 0.9957)	0.8877 (0.8144 to 0.9332)	1.0000 (1.0000 to 1.0000)	0.8696 (0.6481 to 0.9560)	
10 Months	0.9706 (0.9100 to 0.9906)	0.8877 (0.8144 to 0.9332)	1.0000 (1.0000 to 1.0000)	0.8696 (0.6481 to 0.9560)	
12 Months	0.9706 (0.9100 to 0.9906)	0.8760 (0.7990 to 0.9248)	1.0000 (1.0000 to 1.0000)	0.8696 (0.6481 to 0.9560)	
14 Months	0.9706 (0.9100 to 0.9906)	0.8760 (0.7990 to 0.9248)	1.0000 (1.0000 to 1.0000)	0.8696 (0.6481 to 0.9560)	
16 Months	0.9706 (0.9100 to 0.9906)	0.8760 (0.7990 to 0.9248)	1.0000 (1.0000 to 1.0000)	0.8696 (0.6481 to 0.9560)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.12 Treatment emergent severe adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	114	104	19	22	
4 Months	107	101	19	21	
6 Months	93	90	19	20	
8 Months	83	87	18	19	
10 Months	79	84	17	19	
12 Months	71	73	13	17	
14 Months	49	48	3	13	
16 Months	23	21	1	5	
Neutropenia (days)					
Number (%) of events	41 (33.6)	49 (42.2)	6 (31.6)	17 (70.8)	0.0537
Number (%) of patients censored	81 (66.4)	67 (57.8)	13 (68.4)	7 (29.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.4456 (0.7885 to 4.3039)	0.8542 (0.7556 to 1.4456)	4.6653 (1.1499 to NC)	0.6571 (0.2300 to 0.8542)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.3 Treatment emergent adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1	4	103	113	
4 Months	1	4	93	104	
6 Months	0	4	84	93	
8 Months	0	4	73	85	
10 Months	0	4	68	76	
12 Months	0	4	58	67	
14 Months	0	4	34	45	
16 Months	0	1	16	22	
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	1 (25.0)	3 (2.3)	14 (10.9)	0.9927
Number (%) of patients censored	3 (100.0)	3 (75.0)	127 (97.7)	114 (89.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.4271 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (0.4271 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.4271 to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_ethn_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.3 Treatment emergent adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.0061	
Hazard ratio (95% CI) vs Pd	-	NC		4.84 (1.39 to 16.85)	
P-value	-	0.9985		0.0132	
Hazard ratio inverted (95% CI) vs IPd			0.21 (0.06 to 0.72)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9841 (0.9380 to 0.9960)	0.9140 (0.8501 to 0.9514)	
4 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9841 (0.9380 to 0.9960)	0.9060 (0.8405 to 0.9455)	
6 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9841 (0.9380 to 0.9960)	0.8899 (0.8211 to 0.9333)	
8 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9841 (0.9380 to 0.9960)	0.8899 (0.8211 to 0.9333)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.3 Treatment emergent adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9731 (0.9176 to 0.9914)	0.8899 (0.8211 to 0.9333)	
12 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9731 (0.9176 to 0.9914)	0.8899 (0.8211 to 0.9333)	
14 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9731 (0.9176 to 0.9914)	0.8899 (0.8211 to 0.9333)	
16 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9731 (0.9176 to 0.9914)	0.8899 (0.8211 to 0.9333)	
Number of patients at risk[b]					
2 Months	2	3	123	116	
4 Months	2	3	117	112	
6 Months	1	3	104	100	
8 Months	1	3	93	96	
10 Months	1	3	88	93	
12 Months	0	3	76	81	
14 Months	0	3	48	55	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.3 Treatment emergent adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0	1	23	24	
Headache (days)					
Number (%) of events	1 (33.3)	1 (25.0)	7 (5.4)	13 (10.2)	0.1805
Number (%) of patients censored	2 (66.7)	3 (75.0)	123 (94.6)	115 (89.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.9528 (0.9528 to NC)	NC (5.8480 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (0.9528 to NC)	NC (5.8480 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (0.9528 to NC)	NC (5.8480 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4504		0.1319	
Hazard ratio (95% CI) vs Pd	-	0.35 (0.02 to 5.89)		2.07 (0.79 to 5.45)	
P-value	-	0.4689		0.1406	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.5 Treatment emergent serious adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	1 (25.0)	3 (2.3)	7 (5.5)	0.9942
Number (%) of patients censored	3 (100.0)	3 (75.0)	127 (97.7)	121 (94.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.4271 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (0.4271 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.4271 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.1979	
Hazard ratio (95% CI) vs Pd	-	NC		2.37 (0.61 to 9.15)	
P-value	-	0.9985		0.2120	
Events probability (95% CI)[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.5 Treatment emergent serious adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9841 (0.9380 to 0.9960)	0.9531 (0.8986 to 0.9787)	
4 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9841 (0.9380 to 0.9960)	0.9451 (0.8883 to 0.9735)	
6 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9841 (0.9380 to 0.9960)	0.9451 (0.8883 to 0.9735)	
8 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9841 (0.9380 to 0.9960)	0.9451 (0.8883 to 0.9735)	
10 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9731 (0.9176 to 0.9914)	0.9451 (0.8883 to 0.9735)	
12 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9731 (0.9176 to 0.9914)	0.9451 (0.8883 to 0.9735)	
14 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9731 (0.9176 to 0.9914)	0.9451 (0.8883 to 0.9735)	
16 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9731 (0.9176 to 0.9914)	0.9451 (0.8883 to 0.9735)	

Number of patients at risk[b]

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.5 Treatment emergent serious adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	2	3	123	121	
4 Months	2	3	117	114	
6 Months	1	3	104	104	
8 Months	1	3	93	99	
10 Months	1	3	88	95	
12 Months	0	3	76	83	
14 Months	0	3	48	55	
16 Months	0	1	23	24	
Pneumonia (days)					
Number (%) of events	0 (0.0)	1 (25.0)	21 (16.2)	22 (17.2)	0.9856
Number (%) of patients censored	3 (100.0)	3 (75.0)	109 (83.8)	106 (82.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (2.0698 to NC)	NC (NC to NC)	NC (8.5092 to NC)	
Median (95% CI)	NC (NC to NC)	NC (2.0698 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (2.0698 to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_ethn_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.11 Treatment emergent severe adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	1 (25.0)	3 (2.3)	14 (10.9)	0.9927
Number (%) of patients censored	3 (100.0)	3 (75.0)	127 (97.7)	114 (89.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.4271 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (0.4271 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.4271 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.0061	
Hazard ratio (95% CI) vs Pd	-	NC		4.84 (1.39 to 16.85)	
P-value	-	0.9985		0.0132	
Hazard ratio inverted (95% CI) vs IPd			0.21 (0.06 to 0.72)		

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.11 Treatment emergent severe adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9841 (0.9380 to 0.9960)	0.9140 (0.8501 to 0.9514)	
4 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9841 (0.9380 to 0.9960)	0.9060 (0.8405 to 0.9455)	
6 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9841 (0.9380 to 0.9960)	0.8899 (0.8211 to 0.9333)	
8 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9841 (0.9380 to 0.9960)	0.8899 (0.8211 to 0.9333)	
10 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9731 (0.9176 to 0.9914)	0.8899 (0.8211 to 0.9333)	
12 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9731 (0.9176 to 0.9914)	0.8899 (0.8211 to 0.9333)	
14 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9731 (0.9176 to 0.9914)	0.8899 (0.8211 to 0.9333)	
16 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9731 (0.9176 to 0.9914)	0.8899 (0.8211 to 0.9333)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.11 Treatment emergent severe adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	2	3	123	116	
4 Months	2	3	117	112	
6 Months	1	3	104	100	
8 Months	1	3	93	96	
10 Months	1	3	88	93	
12 Months	0	3	76	81	
14 Months	0	3	48	55	
16 Months	0	1	23	24	
Neutropenia (days)					
Number (%) of events	0 (0.0)	2 (50.0)	44 (33.8)	58 (45.3)	0.9850
Number (%) of patients censored	3 (100.0)	2 (50.0)	86 (66.2)	70 (54.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	1.9220 (0.7885 to NC)	1.9384 (0.8871 to 4.6653)	0.8378 (0.7228 to 0.9856)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Febrile neutropenia (days)											
Number (%) of events	1 (1.4)	6 (10.9)	0 (0.0)	1 (3.6)	0 (0.0)	2 (28.6)	0 (0.0)	1 (4.8)	2 (5.7)	8 (19.5)	0.9843
Number (%) of patients censored	73 (98.6)	49 (89.1)	20 (100.0)	27 (96.4)	5 (100.0)	5 (71.4)	15 (100.0)	20 (95.2)	33 (94.3)	33 (80.5)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	2.9569 (0.4271 to NC)	NC (NC to NC)	NC (1.8727 to NC)	NC (9.6920 to NC)	NC (0.5585 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.4271 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_greg_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.0188		0.4142		0.2137		0.3865		0.0972	
Hazard ratio (95% CI) vs Pd	-	8.32 (1.00 to 69.09)		NC		NC		NC		3.44 (0.73 to 16.21)	
P-value	-	0.0498		0.9976		0.9978		0.9984		0.1190	
Hazard ratio inverted (95% CI) vs IPd	0.12 (0.01 to 1.00)										
Events probability (95% CI)[b]											
2 Months	0.9855 (0.9016 to 0.9979)	0.8889 (0.7693 to 0.9485)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	0.9714 (0.8140 to 0.9959)	0.8537 (0.7029 to 0.9314)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_greg_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
4 Months	0.9855 (0.9016 to 0.9979)	0.8889 (0.7693 to 0.9485)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	0.9714 (0.8140 to 0.9959)	0.8537 (0.7029 to 0.9314)	
6 Months	0.9855 (0.9016 to 0.9979)	0.8889 (0.7693 to 0.9485)	1.0000 (1.0000 to 1.0000)	0.9630 (0.7649 to 0.9947)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	0.9714 (0.8140 to 0.9959)	0.8293 (0.6749 to 0.9147)	
8 Months	0.9855 (0.9016 to 0.9979)	0.8889 (0.7693 to 0.9485)	1.0000 (1.0000 to 1.0000)	0.9630 (0.7649 to 0.9947)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	0.9714 (0.8140 to 0.9959)	0.8293 (0.6749 to 0.9147)	
10 Months	0.9855 (0.9016 to 0.9979)	0.8889 (0.7693 to 0.9485)	1.0000 (1.0000 to 1.0000)	0.9630 (0.7649 to 0.9947)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	0.9203 (0.7024 to 0.9807)	0.8293 (0.6749 to 0.9147)	
12 Months	0.9855 (0.9016 to 0.9979)	0.8889 (0.7693 to 0.9485)	1.0000 (1.0000 to 1.0000)	0.9630 (0.7649 to 0.9947)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	0.9203 (0.7024 to 0.9807)	0.7961 (0.6309 to 0.8932)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
14 Months	0.9855 (0.9016 to 0.9979)	0.8889 (0.7693 to 0.9485)	1.0000 (1.0000 to 1.0000)	0.9630 (0.7649 to 0.9947)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	0.9203 (0.7024 to 0.9807)	0.7961 (0.6309 to 0.8932)	
16 Months	0.9855 (0.9016 to 0.9979)	0.8889 (0.7693 to 0.9485)	1.0000 (1.0000 to 1.0000)	0.9630 (0.7649 to 0.9947)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	0.9203 (0.7024 to 0.9807)	0.7961 (0.6309 to 0.8932)	
Number of patients at risk[b]											
2 Months	68	47	19	28	5	6	15	19	33	35	
4 Months	62	43	19	27	5	5	15	19	31	35	
6 Months	58	37	15	23	5	4	15	19	23	31	
8 Months	49	36	15	22	5	4	15	18	21	30	
10 Months	49	36	14	21	5	4	14	18	18	28	
12 Months	43	32	13	18	3	4	11	16	16	24	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_greg_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
14 Months	31	20	9	12	1	1	2	12	11	19	
16 Months	14	6	3	4	0	1	1	5	8	10	
Headache (days)											
Number (%) of events	4 (5.4)	4 (7.3)	2 (10.0)	1 (3.6)	0 (0.0)	3 (42.9)	1 (6.7)	3 (14.3)	1 (2.9)	4 (9.8)	0.6949
Number (%) of patients censored	70 (94.6)	51 (92.7)	18 (90.0)	27 (96.4)	5 (100.0)	4 (57.1)	14 (93.3)	18 (85.7)	34 (97.1)	37 (90.2)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.5441 to NC)	NC (5.0595 to NC)	NC (NC to NC)	5.8480 (1.1499 to NC)	NC (5.3881 to NC)	NC (1.9055 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.1499 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.4 Treatment emergent serious adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Febrile neutropenia (days)											
Number (%) of events	1 (1.4)	3 (5.5)	0 (0.0)	0 (0.0)	0 (0.0)	2 (28.6)	0 (0.0)	0 (0.0)	2 (5.7)	5 (12.2)	0.9958
Number (%) of patients censored	73 (98.6)	52 (94.5)	20 (100.0)	28 (100.0)	5 (100.0)	5 (71.4)	15 (100.0)	21 (100.0)	33 (94.3)	36 (87.8)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	2.9569 (0.4271 to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.6920 to NC)	NC (11.5975 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.4271 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_greg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.4 Treatment emergent serious adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.1917				0.2137				0.3838	
Hazard ratio (95% CI) vs Pd	-	4.02 (0.42 to 38.69)		NC		NC		NC		2.04 (0.40 to 10.58)	
P-value	-	0.2279				0.9978				0.3937	
Events probability (95% CI)[b]											
2 Months	0.9855 (0.9016 to 0.9979)	0.9444 (0.8376 to 0.9817)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9714 (0.8140 to 0.9959)	0.9024 (0.7606 to 0.9622)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_greg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.4 Treatment emergent serious adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
4 Months	0.9855 (0.9016 to 0.9979)	0.9444 (0.8376 to 0.9817)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9714 (0.8140 to 0.9959)	0.9024 (0.7606 to 0.9622)	
6 Months	0.9855 (0.9016 to 0.9979)	0.9444 (0.8376 to 0.9817)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9714 (0.8140 to 0.9959)	0.9024 (0.7606 to 0.9622)	
8 Months	0.9855 (0.9016 to 0.9979)	0.9444 (0.8376 to 0.9817)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9714 (0.8140 to 0.9959)	0.9024 (0.7606 to 0.9622)	
10 Months	0.9855 (0.9016 to 0.9979)	0.9444 (0.8376 to 0.9817)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9203 (0.7024 to 0.9807)	0.9024 (0.7606 to 0.9622)	
12 Months	0.9855 (0.9016 to 0.9979)	0.9444 (0.8376 to 0.9817)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9203 (0.7024 to 0.9807)	0.8677 (0.7072 to 0.9435)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.4 Treatment emergent serious adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
14 Months	0.9855 (0.9016 to 0.9979)	0.9444 (0.8376 to 0.9817)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9203 (0.7024 to 0.9807)	0.8677 (0.7072 to 0.9435)	
16 Months	0.9855 (0.9016 to 0.9979)	0.9444 (0.8376 to 0.9817)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9203 (0.7024 to 0.9807)	0.8677 (0.7072 to 0.9435)	
Number of patients at risk[b]											
2 Months	68	50	19	28	5	6	15	20	33	37	
4 Months	62	45	19	27	5	5	15	19	31	36	
6 Months	58	39	15	24	5	4	15	19	23	33	
8 Months	49	38	15	22	5	4	15	18	21	32	
10 Months	49	38	14	21	5	4	14	18	18	29	
12 Months	43	34	13	18	3	4	11	16	16	25	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_greg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.4 Treatment emergent serious adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
14 Months	31	21	9	12	1	1	2	12	11	19	
16 Months	14	7	3	4	0	1	1	5	8	10	
Pneumonia (days)											
Number (%) of events	6 (8.1)	3 (5.5)	5 (25.0)	4 (14.3)	2 (40.0)	1 (14.3)	3 (20.0)	4 (19.0)	7 (20.0)	11 (26.8)	0.7439
Number (%) of patients censored	68 (91.9)	52 (94.5)	15 (75.0)	24 (85.7)	3 (60.0)	6 (85.7)	12 (80.0)	17 (81.0)	28 (80.0)	30 (73.2)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.1314 to NC)	NC (0.2628 to NC)	5.6838 (0.1971 to NC)	NC (1.0185 to NC)	NC (1.5770 to NC)	NC (1.0185 to NC)	NC (2.2669 to NC)	6.2752 (2.8583 to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_greg_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.10 Treatment emergent severe adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Febrile neutropenia (days)											
Number (%) of events	1 (1.4)	6 (10.9)	0 (0.0)	1 (3.6)	0 (0.0)	2 (28.6)	0 (0.0)	1 (4.8)	2 (5.7)	8 (19.5)	0.9843
Number (%) of patients censored	73 (98.6)	49 (89.1)	20 (100.0)	27 (96.4)	5 (100.0)	5 (71.4)	15 (100.0)	20 (95.2)	33 (94.3)	33 (80.5)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	2.9569 (0.4271 to NC)	NC (NC to NC)	NC (1.8727 to NC)	NC (9.6920 to NC)	NC (0.5585 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.4271 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.10 Treatment emergent severe adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.0188		0.4142		0.2137		0.3865		0.0972	
Hazard ratio (95% CI) vs Pd	-	8.32 (1.00 to 69.09)		NC		NC		NC		3.44 (0.73 to 16.21)	
P-value	-	0.0498		0.9976		0.9978		0.9984		0.1190	
Hazard ratio inverted (95% CI) vs IPd	0.12 (0.01 to 1.00)										
Events probability (95% CI)[b]											
2 Months	0.9855 (0.9016 to 0.9979)	0.8889 (0.7693 to 0.9485)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	0.9714 (0.8140 to 0.9959)	0.8537 (0.7029 to 0.9314)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.10 Treatment emergent severe adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
4 Months	0.9855 (0.9016 to 0.9979)	0.8889 (0.7693 to 0.9485)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	0.9714 (0.8140 to 0.9959)	0.8537 (0.7029 to 0.9314)	
6 Months	0.9855 (0.9016 to 0.9979)	0.8889 (0.7693 to 0.9485)	1.0000 (1.0000 to 1.0000)	0.9630 (0.7649 to 0.9947)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	0.9714 (0.8140 to 0.9959)	0.8293 (0.6749 to 0.9147)	
8 Months	0.9855 (0.9016 to 0.9979)	0.8889 (0.7693 to 0.9485)	1.0000 (1.0000 to 1.0000)	0.9630 (0.7649 to 0.9947)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	0.9714 (0.8140 to 0.9959)	0.8293 (0.6749 to 0.9147)	
10 Months	0.9855 (0.9016 to 0.9979)	0.8889 (0.7693 to 0.9485)	1.0000 (1.0000 to 1.0000)	0.9630 (0.7649 to 0.9947)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	0.9203 (0.7024 to 0.9807)	0.8293 (0.6749 to 0.9147)	
12 Months	0.9855 (0.9016 to 0.9979)	0.8889 (0.7693 to 0.9485)	1.0000 (1.0000 to 1.0000)	0.9630 (0.7649 to 0.9947)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	0.9203 (0.7024 to 0.9807)	0.7961 (0.6309 to 0.8932)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.10 Treatment emergent severe adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
14 Months	0.9855 (0.9016 to 0.9979)	0.8889 (0.7693 to 0.9485)	1.0000 (1.0000 to 1.0000)	0.9630 (0.7649 to 0.9947)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	0.9203 (0.7024 to 0.9807)	0.7961 (0.6309 to 0.8932)	
16 Months	0.9855 (0.9016 to 0.9979)	0.8889 (0.7693 to 0.9485)	1.0000 (1.0000 to 1.0000)	0.9630 (0.7649 to 0.9947)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	0.9203 (0.7024 to 0.9807)	0.7961 (0.6309 to 0.8932)	
Number of patients at risk[b]											
2 Months	68	47	19	28	5	6	15	19	33	35	
4 Months	62	43	19	27	5	5	15	19	31	35	
6 Months	58	37	15	23	5	4	15	19	23	31	
8 Months	49	36	15	22	5	4	15	18	21	30	
10 Months	49	36	14	21	5	4	14	18	18	28	
12 Months	43	32	13	18	3	4	11	16	16	24	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.3 Treatment emergent adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	74	66	45	69	
4 Months	66	60	41	64	
6 Months	61	52	34	58	
8 Months	51	47	33	54	
10 Months	48	43	31	49	
12 Months	43	39	25	44	
14 Months	27	26	13	31	
16 Months	12	11	7	15	
Febrile neutropenia (days)					
Number (%) of events	1 (1.1)	10 (13.0)	2 (3.6)	8 (10.7)	0.2674
Number (%) of patients censored	93 (98.9)	67 (87.0)	53 (96.4)	67 (89.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.3 Treatment emergent adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0017		0.1575	
Hazard ratio (95% CI) vs Pd	-	12.74 (1.63 to 99.49)		2.91 (0.62 to 13.68)	
P-value	-	0.0153		0.1774	
Hazard ratio inverted (95% CI) vs IPd	0.08 (0.01 to 0.61)				
Events probability (95% CI)[b]					
2 Months	0.9888 (0.9229 to 0.9984)	0.8817 (0.7850 to 0.9366)	0.9815 (0.8757 to 0.9974)	0.9331 (0.8468 to 0.9716)	
4 Months	0.9888 (0.9229 to 0.9984)	0.8682 (0.7688 to 0.9268)	0.9815 (0.8757 to 0.9974)	0.9331 (0.8468 to 0.9716)	
6 Months	0.9888 (0.9229 to 0.9984)	0.8682 (0.7688 to 0.9268)	0.9815 (0.8757 to 0.9974)	0.9057 (0.8123 to 0.9539)	
8 Months	0.9888 (0.9229 to 0.9984)	0.8682 (0.7688 to 0.9268)	0.9815 (0.8757 to 0.9974)	0.9057 (0.8123 to 0.9539)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.3 Treatment emergent adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.9888 (0.9229 to 0.9984)	0.8682 (0.7688 to 0.9268)	0.9569 (0.8363 to 0.9892)	0.9057 (0.8123 to 0.9539)	
12 Months	0.9888 (0.9229 to 0.9984)	0.8682 (0.7688 to 0.9268)	0.9569 (0.8363 to 0.9892)	0.8886 (0.7888 to 0.9429)	
14 Months	0.9888 (0.9229 to 0.9984)	0.8682 (0.7688 to 0.9268)	0.9569 (0.8363 to 0.9892)	0.8886 (0.7888 to 0.9429)	
16 Months	0.9888 (0.9229 to 0.9984)	0.8682 (0.7688 to 0.9268)	0.9569 (0.8363 to 0.9892)	0.8886 (0.7888 to 0.9429)	
Number of patients at risk[b]					
2 Months	88	66	52	69	
4 Months	81	61	51	68	
6 Months	74	53	42	61	
8 Months	63	51	42	59	
10 Months	61	51	39	56	
12 Months	53	45	33	49	
14 Months	36	29	18	35	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.3 Treatment emergent adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	16	10	10	16	
Headache (days)					
Number (%) of events	5 (5.3)	9 (11.7)	3 (5.5)	6 (8.0)	0.4902
Number (%) of patients censored	89 (94.7)	68 (88.3)	52 (94.5)	69 (92.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (10.2177 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1000		0.6477	
Hazard ratio (95% CI) vs Pd	-	2.59 (0.80 to 8.41)		1.38 (0.34 to 5.52)	
P-value	-	0.1132		0.6491	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.5 Treatment emergent serious adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	1 (1.1)	6 (7.8)	2 (3.6)	4 (5.3)	0.2454
Number (%) of patients censored	93 (98.9)	71 (92.2)	53 (96.4)	71 (94.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0298		0.6757	
Hazard ratio (95% CI) vs Pd	-	7.37 (0.89 to 61.18)		1.43 (0.26 to 7.83)	
P-value	-	0.0644		0.6774	
Events probability (95% CI)[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.5 Treatment emergent serious adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9888 (0.9229 to 0.9984)	0.9342 (0.8491 to 0.9721)	0.9815 (0.8757 to 0.9974)	0.9600 (0.8811 to 0.9869)	
4 Months	0.9888 (0.9229 to 0.9984)	0.9207 (0.8319 to 0.9636)	0.9815 (0.8757 to 0.9974)	0.9600 (0.8811 to 0.9869)	
6 Months	0.9888 (0.9229 to 0.9984)	0.9207 (0.8319 to 0.9636)	0.9815 (0.8757 to 0.9974)	0.9600 (0.8811 to 0.9869)	
8 Months	0.9888 (0.9229 to 0.9984)	0.9207 (0.8319 to 0.9636)	0.9815 (0.8757 to 0.9974)	0.9600 (0.8811 to 0.9869)	
10 Months	0.9888 (0.9229 to 0.9984)	0.9207 (0.8319 to 0.9636)	0.9569 (0.8363 to 0.9892)	0.9600 (0.8811 to 0.9869)	
12 Months	0.9888 (0.9229 to 0.9984)	0.9207 (0.8319 to 0.9636)	0.9569 (0.8363 to 0.9892)	0.9419 (0.8509 to 0.9780)	
14 Months	0.9888 (0.9229 to 0.9984)	0.9207 (0.8319 to 0.9636)	0.9569 (0.8363 to 0.9892)	0.9419 (0.8509 to 0.9780)	
16 Months	0.9888 (0.9229 to 0.9984)	0.9207 (0.8319 to 0.9636)	0.9569 (0.8363 to 0.9892)	0.9419 (0.8509 to 0.9780)	

Number of patients at risk[b]

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.5 Treatment emergent serious adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	88	70	52	71	
4 Months	81	64	51	68	
6 Months	74	56	42	63	
8 Months	63	54	42	60	
10 Months	61	54	39	56	
12 Months	53	48	33	49	
14 Months	36	30	18	35	
16 Months	16	11	10	16	
Pneumonia (days)					
Number (%) of events	12 (12.8)	7 (9.1)	11 (20.0)	16 (21.3)	0.4834
Number (%) of patients censored	82 (87.2)	70 (90.9)	44 (80.0)	59 (78.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.2669 to NC)	NC (5.1253 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.11 Treatment emergent severe adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	1 (1.1)	10 (13.0)	2 (3.6)	8 (10.7)	0.2674
Number (%) of patients censored	93 (98.9)	67 (87.0)	53 (96.4)	67 (89.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0017		0.1575	
Hazard ratio (95% CI) vs Pd	-	12.74 (1.63 to 99.49)		2.91 (0.62 to 13.68)	
P-value	-	0.0153		0.1774	
Hazard ratio inverted (95% CI) vs IPd	0.08 (0.01 to 0.61)				

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.11 Treatment emergent severe adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9888 (0.9229 to 0.9984)	0.8817 (0.7850 to 0.9366)	0.9815 (0.8757 to 0.9974)	0.9331 (0.8468 to 0.9716)	
4 Months	0.9888 (0.9229 to 0.9984)	0.8682 (0.7688 to 0.9268)	0.9815 (0.8757 to 0.9974)	0.9331 (0.8468 to 0.9716)	
6 Months	0.9888 (0.9229 to 0.9984)	0.8682 (0.7688 to 0.9268)	0.9815 (0.8757 to 0.9974)	0.9057 (0.8123 to 0.9539)	
8 Months	0.9888 (0.9229 to 0.9984)	0.8682 (0.7688 to 0.9268)	0.9815 (0.8757 to 0.9974)	0.9057 (0.8123 to 0.9539)	
10 Months	0.9888 (0.9229 to 0.9984)	0.8682 (0.7688 to 0.9268)	0.9569 (0.8363 to 0.9892)	0.9057 (0.8123 to 0.9539)	
12 Months	0.9888 (0.9229 to 0.9984)	0.8682 (0.7688 to 0.9268)	0.9569 (0.8363 to 0.9892)	0.8886 (0.7888 to 0.9429)	
14 Months	0.9888 (0.9229 to 0.9984)	0.8682 (0.7688 to 0.9268)	0.9569 (0.8363 to 0.9892)	0.8886 (0.7888 to 0.9429)	
16 Months	0.9888 (0.9229 to 0.9984)	0.8682 (0.7688 to 0.9268)	0.9569 (0.8363 to 0.9892)	0.8886 (0.7888 to 0.9429)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.11 Treatment emergent severe adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	88	66	52	69	
4 Months	81	61	51	68	
6 Months	74	53	42	61	
8 Months	63	51	42	59	
10 Months	61	51	39	56	
12 Months	53	45	33	49	
14 Months	36	29	18	35	
16 Months	16	10	10	16	
Neutropenia (days)					
Number (%) of events	23 (24.5)	31 (40.3)	25 (45.5)	38 (50.7)	0.3197
Number (%) of patients censored	71 (75.5)	46 (59.7)	30 (54.5)	37 (49.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	4.9938 (0.9528 to NC)	0.9528 (0.7556 to 2.1027)	1.4456 (0.7885 to 2.8255)	0.7885 (0.6242 to 0.9528)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.2 Treatment emergent adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	106	121	13	14	
4 Months	95	113	12	11	
6 Months	86	102	9	8	
8 Months	76	93	8	8	
10 Months	72	84	7	8	
12 Months	63	75	5	8	
14 Months	37	52	3	5	
16 Months	17	23	2	3	
Febrile neutropenia (days)					
Number (%) of events	3 (2.2)	15 (11.0)	0 (0.0)	3 (18.8)	0.9917
Number (%) of patients censored	132 (97.8)	121 (89.0)	14 (100.0)	13 (81.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	11.5975 (0.4271 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.5975 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.2 Treatment emergent adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0045		0.0829	
Hazard ratio (95% CI) vs Pd	-	5.02 (1.45 to 17.35)		NC	
P-value	-	0.0107		0.9972	
Hazard ratio inverted (95% CI) vs IPd	0.20 (0.06 to 0.69)				
Events probability (95% CI)[b]					
2 Months	0.9845 (0.9394 to 0.9961)	0.9118 (0.8499 to 0.9489)	1.0000 (1.0000 to 1.0000)	0.8615 (0.5497 to 0.9636)	
4 Months	0.9845 (0.9394 to 0.9961)	0.9043 (0.8409 to 0.9433)	1.0000 (1.0000 to 1.0000)	0.8615 (0.5497 to 0.9636)	
6 Months	0.9845 (0.9394 to 0.9961)	0.8891 (0.8228 to 0.9316)	1.0000 (1.0000 to 1.0000)	0.8615 (0.5497 to 0.9636)	
8 Months	0.9845 (0.9394 to 0.9961)	0.8891 (0.8228 to 0.9316)	1.0000 (1.0000 to 1.0000)	0.8615 (0.5497 to 0.9636)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.2 Treatment emergent adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.9739 (0.9202 to 0.9916)	0.8891 (0.8228 to 0.9316)	1.0000 (1.0000 to 1.0000)	0.8615 (0.5497 to 0.9636)	
12 Months	0.9739 (0.9202 to 0.9916)	0.8891 (0.8228 to 0.9316)	1.0000 (1.0000 to 1.0000)	0.7385 (0.3621 to 0.9135)	
14 Months	0.9739 (0.9202 to 0.9916)	0.8891 (0.8228 to 0.9316)	1.0000 (1.0000 to 1.0000)	0.7385 (0.3621 to 0.9135)	
16 Months	0.9739 (0.9202 to 0.9916)	0.8891 (0.8228 to 0.9316)	1.0000 (1.0000 to 1.0000)	0.7385 (0.3621 to 0.9135)	
Number of patients at risk[b]					
2 Months	126	123	14	12	
4 Months	119	119	13	10	
6 Months	106	107	10	7	
8 Months	96	103	9	7	
10 Months	92	100	8	7	
12 Months	80	88	6	6	
14 Months	50	61	4	3	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.2 Treatment emergent adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	23	24	3	2	
Headache (days)					
Number (%) of events	7 (5.2)	13 (9.6)	1 (7.1)	2 (12.5)	0.9678
Number (%) of patients censored	128 (94.8)	123 (90.4)	13 (92.9)	14 (87.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.9528 to NC)	NC (1.1499 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.8480 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1643		0.5841	
Hazard ratio (95% CI) vs Pd	-	1.96 (0.75 to 5.16)		1.93 (0.17 to 21.38)	
P-value	-	0.1724		0.5908	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.5 Treatment emergent serious adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	3 (2.2)	8 (5.9)	0 (0.0)	2 (12.5)	0.9933
Number (%) of patients censored	132 (97.8)	128 (94.1)	14 (100.0)	14 (87.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.4271 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.5975 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1402		0.1645	
Hazard ratio (95% CI) vs Pd	-	2.61 (0.69 to 9.86)		NC	
P-value	-	0.1557		0.9977	
Events probability (95% CI)[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.5 Treatment emergent serious adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9845 (0.9394 to 0.9961)	0.9485 (0.8951 to 0.9751)	1.0000 (1.0000 to 1.0000)	0.9333 (0.6126 to 0.9903)	
4 Months	0.9845 (0.9394 to 0.9961)	0.9410 (0.8855 to 0.9701)	1.0000 (1.0000 to 1.0000)	0.9333 (0.6126 to 0.9903)	
6 Months	0.9845 (0.9394 to 0.9961)	0.9410 (0.8855 to 0.9701)	1.0000 (1.0000 to 1.0000)	0.9333 (0.6126 to 0.9903)	
8 Months	0.9845 (0.9394 to 0.9961)	0.9410 (0.8855 to 0.9701)	1.0000 (1.0000 to 1.0000)	0.9333 (0.6126 to 0.9903)	
10 Months	0.9739 (0.9202 to 0.9916)	0.9410 (0.8855 to 0.9701)	1.0000 (1.0000 to 1.0000)	0.9333 (0.6126 to 0.9903)	
12 Months	0.9739 (0.9202 to 0.9916)	0.9410 (0.8855 to 0.9701)	1.0000 (1.0000 to 1.0000)	0.8000 (0.3735 to 0.9507)	
14 Months	0.9739 (0.9202 to 0.9916)	0.9410 (0.8855 to 0.9701)	1.0000 (1.0000 to 1.0000)	0.8000 (0.3735 to 0.9507)	
16 Months	0.9739 (0.9202 to 0.9916)	0.9410 (0.8855 to 0.9701)	1.0000 (1.0000 to 1.0000)	0.8000 (0.3735 to 0.9507)	

Number of patients at risk[b]

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.5 Treatment emergent serious adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	126	128	14	13	
4 Months	119	122	13	10	
6 Months	106	112	10	7	
8 Months	96	107	9	7	
10 Months	92	103	8	7	
12 Months	80	91	6	6	
14 Months	50	62	4	3	
16 Months	23	25	3	2	
Pneumonia (days)					
Number (%) of events	21 (15.6)	20 (14.7)	2 (14.3)	3 (18.8)	0.5764
Number (%) of patients censored	114 (84.4)	116 (85.3)	12 (85.7)	13 (81.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.6756 to NC)	NC (1.0185 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.0226 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_ecog_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.11 Treatment emergent severe adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	3 (2.2)	15 (11.0)	0 (0.0)	3 (18.8)	0.9917
Number (%) of patients censored	132 (97.8)	121 (89.0)	14 (100.0)	13 (81.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	11.5975 (0.4271 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.5975 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0045		0.0829	
Hazard ratio (95% CI) vs Pd	-	5.02 (1.45 to 17.35)		NC	
P-value	-	0.0107		0.9972	
Hazard ratio inverted (95% CI) vs IPd	0.20 (0.06 to 0.69)				

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_ecog_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.11 Treatment emergent severe adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9845 (0.9394 to 0.9961)	0.9118 (0.8499 to 0.9489)	1.0000 (1.0000 to 1.0000)	0.8615 (0.5497 to 0.9636)	
4 Months	0.9845 (0.9394 to 0.9961)	0.9043 (0.8409 to 0.9433)	1.0000 (1.0000 to 1.0000)	0.8615 (0.5497 to 0.9636)	
6 Months	0.9845 (0.9394 to 0.9961)	0.8891 (0.8228 to 0.9316)	1.0000 (1.0000 to 1.0000)	0.8615 (0.5497 to 0.9636)	
8 Months	0.9845 (0.9394 to 0.9961)	0.8891 (0.8228 to 0.9316)	1.0000 (1.0000 to 1.0000)	0.8615 (0.5497 to 0.9636)	
10 Months	0.9739 (0.9202 to 0.9916)	0.8891 (0.8228 to 0.9316)	1.0000 (1.0000 to 1.0000)	0.8615 (0.5497 to 0.9636)	
12 Months	0.9739 (0.9202 to 0.9916)	0.8891 (0.8228 to 0.9316)	1.0000 (1.0000 to 1.0000)	0.7385 (0.3621 to 0.9135)	
14 Months	0.9739 (0.9202 to 0.9916)	0.8891 (0.8228 to 0.9316)	1.0000 (1.0000 to 1.0000)	0.7385 (0.3621 to 0.9135)	
16 Months	0.9739 (0.9202 to 0.9916)	0.8891 (0.8228 to 0.9316)	1.0000 (1.0000 to 1.0000)	0.7385 (0.3621 to 0.9135)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_ecog_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.11 Treatment emergent severe adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	126	123	14	12	
4 Months	119	119	13	10	
6 Months	106	107	10	7	
8 Months	96	103	9	7	
10 Months	92	100	8	7	
12 Months	80	88	6	6	
14 Months	50	61	4	3	
16 Months	23	24	3	2	
Neutropenia (days)					
Number (%) of events	43 (31.9)	62 (45.6)	5 (35.7)	7 (43.8)	0.6471
Number (%) of patients censored	92 (68.1)	74 (54.4)	9 (64.3)	9 (56.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.8255 (0.9856 to 4.9938)	0.8542 (0.7556 to 0.9856)	0.6899 (0.2300 to NC)	1.4784 (0.5257 to 9.1663)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.11 Treatment emergent severe adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	3 (2.2)	15 (11.0)	0 (0.0)	3 (18.8)	0.9917
Number (%) of patients censored	132 (97.8)	121 (89.0)	14 (100.0)	13 (81.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	11.5975 (0.4271 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.5975 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0045		0.0829	
Hazard ratio (95% CI) vs Pd	-	5.02 (1.45 to 17.35)		NC	
P-value	-	0.0107		0.9972	
Hazard ratio inverted (95% CI) vs IPd	0.20 (0.06 to 0.69)				

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.11 Treatment emergent severe adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9845 (0.9394 to 0.9961)	0.9118 (0.8499 to 0.9489)	1.0000 (1.0000 to 1.0000)	0.8615 (0.5497 to 0.9636)	
4 Months	0.9845 (0.9394 to 0.9961)	0.9043 (0.8409 to 0.9433)	1.0000 (1.0000 to 1.0000)	0.8615 (0.5497 to 0.9636)	
6 Months	0.9845 (0.9394 to 0.9961)	0.8891 (0.8228 to 0.9316)	1.0000 (1.0000 to 1.0000)	0.8615 (0.5497 to 0.9636)	
8 Months	0.9845 (0.9394 to 0.9961)	0.8891 (0.8228 to 0.9316)	1.0000 (1.0000 to 1.0000)	0.8615 (0.5497 to 0.9636)	
10 Months	0.9739 (0.9202 to 0.9916)	0.8891 (0.8228 to 0.9316)	1.0000 (1.0000 to 1.0000)	0.8615 (0.5497 to 0.9636)	
12 Months	0.9739 (0.9202 to 0.9916)	0.8891 (0.8228 to 0.9316)	1.0000 (1.0000 to 1.0000)	0.7385 (0.3621 to 0.9135)	
14 Months	0.9739 (0.9202 to 0.9916)	0.8891 (0.8228 to 0.9316)	1.0000 (1.0000 to 1.0000)	0.7385 (0.3621 to 0.9135)	
16 Months	0.9739 (0.9202 to 0.9916)	0.8891 (0.8228 to 0.9316)	1.0000 (1.0000 to 1.0000)	0.7385 (0.3621 to 0.9135)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.11 Treatment emergent severe adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	126	123	14	12	
4 Months	119	119	13	10	
6 Months	106	107	10	7	
8 Months	96	103	9	7	
10 Months	92	100	8	7	
12 Months	80	88	6	6	
14 Months	50	61	4	3	
16 Months	23	24	3	2	
Neutropenia (days)					
Number (%) of events	43 (31.9)	62 (45.6)	5 (35.7)	7 (43.8)	0.6471
Number (%) of patients censored	92 (68.1)	74 (54.4)	9 (64.3)	9 (56.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.8255 (0.9856 to 4.9938)	0.8542 (0.7556 to 0.9856)	0.6899 (0.2300 to NC)	1.4784 (0.5257 to 9.1663)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_ecog_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	46	56	41	46	29	30	
4 Months	44	53	39	42	22	26	
6 Months	44	46	34	38	15	23	
8 Months	40	44	29	36	13	19	
10 Months	38	41	27	31	12	18	
12 Months	35	37	21	27	10	17	
14 Months	21	25	12	19	7	11	
16 Months	11	13	5	7	3	6	
Febrile neutropenia (days)							
Number (%) of events	2 (3.9)	8 (12.7)	1 (1.8)	6 (11.3)	0 (0.0)	4 (12.1)	0.9010
Number (%) of patients censored	49 (96.1)	55 (87.3)	54 (98.2)	47 (88.7)	40 (100.0)	29 (87.9)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.8727 to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0903		0.0453		0.0338	
Hazard ratio (95% CI) vs Pd	-	3.51 (0.75 to 16.53)		6.52 (0.79 to 54.16)		NC	
P-value	-	0.1123		0.0826		0.9949	
Events probability (95% CI)[b]							
2 Months	0.9804 (0.8689 to 0.9972)	0.8889 (0.7810 to 0.9454)	0.9811 (0.8735 to 0.9973)	0.9245 (0.8113 to 0.9710)	1.0000 (1.0000 to 1.0000)	0.9063 (0.7369 to 0.9688)	
4 Months	0.9804 (0.8689 to 0.9972)	0.8889 (0.7810 to 0.9454)	0.9811 (0.8735 to 0.9973)	0.9044 (0.7854 to 0.9591)	1.0000 (1.0000 to 1.0000)	0.9063 (0.7369 to 0.9688)	
6 Months	0.9804 (0.8689 to 0.9972)	0.8889 (0.7810 to 0.9454)	0.9811 (0.8735 to 0.9973)	0.8834 (0.7583 to 0.9459)	1.0000 (1.0000 to 1.0000)	0.8727 (0.6951 to 0.9503)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.9804 (0.8689 to 0.9972)	0.8889 (0.7810 to 0.9454)	0.9811 (0.8735 to 0.9973)	0.8834 (0.7583 to 0.9459)	1.0000 (1.0000 to 1.0000)	0.8727 (0.6951 to 0.9503)	
10 Months	0.9586 (0.8441 to 0.9895)	0.8889 (0.7810 to 0.9454)	0.9811 (0.8735 to 0.9973)	0.8834 (0.7583 to 0.9459)	1.0000 (1.0000 to 1.0000)	0.8727 (0.6951 to 0.9503)	
12 Months	0.9586 (0.8441 to 0.9895)	0.8691 (0.7545 to 0.9325)	0.9811 (0.8735 to 0.9973)	0.8834 (0.7583 to 0.9459)	1.0000 (1.0000 to 1.0000)	0.8727 (0.6951 to 0.9503)	
14 Months	0.9586 (0.8441 to 0.9895)	0.8691 (0.7545 to 0.9325)	0.9811 (0.8735 to 0.9973)	0.8834 (0.7583 to 0.9459)	1.0000 (1.0000 to 1.0000)	0.8727 (0.6951 to 0.9503)	
16 Months	0.9586 (0.8441 to 0.9895)	0.8691 (0.7545 to 0.9325)	0.9811 (0.8735 to 0.9973)	0.8834 (0.7583 to 0.9459)	1.0000 (1.0000 to 1.0000)	0.8727 (0.6951 to 0.9503)	
Number of patients at risk[b]							
2 Months	50	56	52	47	35	29	
4 Months	49	56	52	43	29	27	
6 Months	49	50	45	39	20	22	
8 Months	46	49	40	38	17	20	
10 Months	44	47	38	38	16	19	
12 Months	41	41	29	33	14	17	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	26	27	18	23	10	11	
16 Months	15	12	7	8	4	6	
Headache (days)							
Number (%) of events	3 (5.9)	9 (14.3)	3 (5.5)	3 (5.7)	2 (5.0)	2 (6.1)	0.7022
Number (%) of patients censored	48 (94.1)	54 (85.7)	52 (94.5)	50 (94.3)	38 (95.0)	31 (93.9)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (10.2177 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.2320 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1441		0.6487		0.9865	
Hazard ratio (95% CI) vs Pd	-	2.56 (0.69 to 9.45)		1.51 (0.25 to 9.05)		0.98 (0.14 to 7.02)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_seiss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.4 Treatment emergent serious adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)							
Number (%) of events	2 (3.9)	4 (6.3)	1 (1.8)	5 (9.4)	0 (0.0)	1 (3.0)	0.7158
Number (%) of patients censored	49 (96.1)	59 (93.7)	54 (98.2)	48 (90.6)	40 (100.0)	32 (97.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.5337		0.0858		0.2822	
Hazard ratio (95% CI) vs Pd	-	1.70 (0.31 to 9.30)		5.36 (0.63 to 45.84)		NC	
P-value	-	0.5385		0.1256		0.9975	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_seiss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.4 Treatment emergent serious adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]							
2 Months	0.9804 (0.8689 to 0.9972)	0.9524 (0.8596 to 0.9844)	0.9811 (0.8735 to 0.9973)	0.9245 (0.8113 to 0.9710)	1.0000 (1.0000 to 1.0000)	0.9688 (0.7982 to 0.9955)	
4 Months	0.9804 (0.8689 to 0.9972)	0.9524 (0.8596 to 0.9844)	0.9811 (0.8735 to 0.9973)	0.9044 (0.7854 to 0.9591)	1.0000 (1.0000 to 1.0000)	0.9688 (0.7982 to 0.9955)	
6 Months	0.9804 (0.8689 to 0.9972)	0.9524 (0.8596 to 0.9844)	0.9811 (0.8735 to 0.9973)	0.9044 (0.7854 to 0.9591)	1.0000 (1.0000 to 1.0000)	0.9688 (0.7982 to 0.9955)	
8 Months	0.9804 (0.8689 to 0.9972)	0.9524 (0.8596 to 0.9844)	0.9811 (0.8735 to 0.9973)	0.9044 (0.7854 to 0.9591)	1.0000 (1.0000 to 1.0000)	0.9688 (0.7982 to 0.9955)	
10 Months	0.9586 (0.8441 to 0.9895)	0.9524 (0.8596 to 0.9844)	0.9811 (0.8735 to 0.9973)	0.9044 (0.7854 to 0.9591)	1.0000 (1.0000 to 1.0000)	0.9688 (0.7982 to 0.9955)	
12 Months	0.9586 (0.8441 to 0.9895)	0.9325 (0.8291 to 0.9743)	0.9811 (0.8735 to 0.9973)	0.9044 (0.7854 to 0.9591)	1.0000 (1.0000 to 1.0000)	0.9688 (0.7982 to 0.9955)	
14 Months	0.9586 (0.8441 to 0.9895)	0.9325 (0.8291 to 0.9743)	0.9811 (0.8735 to 0.9973)	0.9044 (0.7854 to 0.9591)	1.0000 (1.0000 to 1.0000)	0.9688 (0.7982 to 0.9955)	
16 Months	0.9586 (0.8441 to 0.9895)	0.9325 (0.8291 to 0.9743)	0.9811 (0.8735 to 0.9973)	0.9044 (0.7854 to 0.9591)	1.0000 (1.0000 to 1.0000)	0.9688 (0.7982 to 0.9955)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_seiss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.4 Treatment emergent serious adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	50	60	52	47	35	31	
4 Months	49	59	52	43	29	27	
6 Months	49	53	45	40	20	23	
8 Months	46	52	40	39	17	20	
10 Months	44	50	38	38	16	19	
12 Months	41	44	29	33	14	17	
14 Months	26	28	18	23	10	11	
16 Months	15	13	7	8	4	6	
Pneumonia (days)							
Number (%) of events	4 (7.8)	11 (17.5)	11 (20.0)	6 (11.3)	8 (20.0)	6 (18.2)	0.1505
Number (%) of patients censored	47 (92.2)	52 (82.5)	44 (80.0)	47 (88.7)	32 (80.0)	27 (81.8)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (6.3409 to NC)	NC (2.2998 to NC)	NC (NC to NC)	NC (1.6756 to NC)	NC (1.3142 to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_seiss_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.10 Treatment emergent severe adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)							
Number (%) of events	2 (3.9)	8 (12.7)	1 (1.8)	6 (11.3)	0 (0.0)	4 (12.1)	0.9010
Number (%) of patients censored	49 (96.1)	55 (87.3)	54 (98.2)	47 (88.7)	40 (100.0)	29 (87.9)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.8727 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0903		0.0453		0.0338	
Hazard ratio (95% CI) vs Pd	-	3.51 (0.75 to 16.53)		6.52 (0.79 to 54.16)		NC	
P-value	-	0.1123		0.0826		0.9949	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_seiss_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.10 Treatment emergent severe adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]							
2 Months	0.9804 (0.8689 to 0.9972)	0.8889 (0.7810 to 0.9454)	0.9811 (0.8735 to 0.9973)	0.9245 (0.8113 to 0.9710)	1.0000 (1.0000 to 1.0000)	0.9063 (0.7369 to 0.9688)	
4 Months	0.9804 (0.8689 to 0.9972)	0.8889 (0.7810 to 0.9454)	0.9811 (0.8735 to 0.9973)	0.9044 (0.7854 to 0.9591)	1.0000 (1.0000 to 1.0000)	0.9063 (0.7369 to 0.9688)	
6 Months	0.9804 (0.8689 to 0.9972)	0.8889 (0.7810 to 0.9454)	0.9811 (0.8735 to 0.9973)	0.8834 (0.7583 to 0.9459)	1.0000 (1.0000 to 1.0000)	0.8727 (0.6951 to 0.9503)	
8 Months	0.9804 (0.8689 to 0.9972)	0.8889 (0.7810 to 0.9454)	0.9811 (0.8735 to 0.9973)	0.8834 (0.7583 to 0.9459)	1.0000 (1.0000 to 1.0000)	0.8727 (0.6951 to 0.9503)	
10 Months	0.9586 (0.8441 to 0.9895)	0.8889 (0.7810 to 0.9454)	0.9811 (0.8735 to 0.9973)	0.8834 (0.7583 to 0.9459)	1.0000 (1.0000 to 1.0000)	0.8727 (0.6951 to 0.9503)	
12 Months	0.9586 (0.8441 to 0.9895)	0.8691 (0.7545 to 0.9325)	0.9811 (0.8735 to 0.9973)	0.8834 (0.7583 to 0.9459)	1.0000 (1.0000 to 1.0000)	0.8727 (0.6951 to 0.9503)	
14 Months	0.9586 (0.8441 to 0.9895)	0.8691 (0.7545 to 0.9325)	0.9811 (0.8735 to 0.9973)	0.8834 (0.7583 to 0.9459)	1.0000 (1.0000 to 1.0000)	0.8727 (0.6951 to 0.9503)	
16 Months	0.9586 (0.8441 to 0.9895)	0.8691 (0.7545 to 0.9325)	0.9811 (0.8735 to 0.9973)	0.8834 (0.7583 to 0.9459)	1.0000 (1.0000 to 1.0000)	0.8727 (0.6951 to 0.9503)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_seiss_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.10 Treatment emergent severe adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	50	56	52	47	35	29	
4 Months	49	56	52	43	29	27	
6 Months	49	50	45	39	20	22	
8 Months	46	49	40	38	17	20	
10 Months	44	47	38	38	16	19	
12 Months	41	41	29	33	14	17	
14 Months	26	27	18	23	10	11	
16 Months	15	12	7	8	4	6	
Neutropenia (days)							
Number (%) of events	16 (31.4)	31 (49.2)	15 (27.3)	23 (43.4)	17 (42.5)	15 (45.5)	0.4083
Number (%) of patients censored	35 (68.6)	32 (50.8)	40 (72.7)	30 (56.6)	23 (57.5)	18 (54.5)	
Kaplan-Meier estimates of event in months							

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.2 Treatment emergent adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.9032 (0.7293 to 0.9677)	0.7890 (0.6215 to 0.8887)	0.6994 (0.5942 to 0.7822)	0.8314 (0.7345 to 0.8954)	0.9474 (0.6812 to 0.9924)	0.7538 (0.3980 to 0.9170)	
Number of patients at risk[b]							
2 Months	30	35	73	88	16	12	
4 Months	30	32	65	83	12	9	
6 Months	30	29	58	73	7	8	
8 Months	27	28	51	67	6	6	
10 Months	27	28	46	59	6	5	
12 Months	25	26	38	52	5	5	
14 Months	14	16	22	36	4	5	
16 Months	8	9	10	15	1	2	
Febrile neutropenia (days)							
Number (%) of events	1 (3.2)	6 (15.4)	2 (2.1)	10 (10.2)	0 (0.0)	2 (13.3)	0.9988
Number (%) of patients censored	30 (96.8)	33 (84.6)	95 (97.9)	88 (89.8)	21 (100.0)	13 (86.7)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_seriss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.2 Treatment emergent adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (0.5585 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.4928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0892		0.0213		0.0978	
Hazard ratio (95% CI) vs Pd	-	5.18 (0.62 to 43.01)		4.98 (1.09 to 22.73)		NC	
P-value	-	0.1279		0.0382		0.9977	
Hazard ratio inverted (95% CI) vs IPd			0.20 (0.04 to 0.92)				
Events probability (95% CI)[b]							
2 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9894 (0.9269 to 0.9985)	0.9388 (0.8688 to 0.9720)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.2 Treatment emergent adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9894 (0.9269 to 0.9985)	0.9281 (0.8551 to 0.9651)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
6 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9894 (0.9269 to 0.9985)	0.9063 (0.8275 to 0.9501)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
8 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9894 (0.9269 to 0.9985)	0.9063 (0.8275 to 0.9501)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
10 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9744 (0.8994 to 0.9937)	0.9063 (0.8275 to 0.9501)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
12 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9744 (0.8994 to 0.9937)	0.8921 (0.8078 to 0.9408)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
14 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9744 (0.8994 to 0.9937)	0.8921 (0.8078 to 0.9408)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
16 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9744 (0.8994 to 0.9937)	0.8921 (0.8078 to 0.9408)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
Number of patients at risk[b]							
2 Months	30	33	93	90	17	12	
4 Months	30	33	90	85	12	11	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_seriss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.2 Treatment emergent adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	30	31	79	74	7	9	
8 Months	29	31	70	72	6	7	
10 Months	29	31	65	70	6	6	
12 Months	27	28	54	60	5	6	
14 Months	16	17	34	41	4	6	
16 Months	10	9	15	15	1	2	
Headache (days)							
Number (%) of events	2 (6.5)	6 (15.4)	5 (5.2)	8 (8.2)	1 (4.8)	1 (6.7)	0.8664
Number (%) of patients censored	29 (93.5)	33 (84.6)	92 (94.8)	90 (91.8)	20 (95.2)	14 (93.3)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (7.5893 to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.9528 to NC)	NC (2.1027 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.10 Treatment emergent serious adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)							
Number (%) of events	1 (3.2)	3 (7.7)	2 (2.1)	7 (7.1)	0 (0.0)	0 (0.0)	0.9759
Number (%) of patients censored	30 (96.8)	36 (92.3)	95 (97.9)	91 (92.9)	21 (100.0)	15 (100.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4154		0.1029			
Hazard ratio (95% CI) vs Pd	-	2.48 (0.26 to 23.86)		3.42 (0.71 to 16.46)		NC	
P-value	-	0.4312		0.1254			

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.10 Treatment emergent serious adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]							
2 Months	0.9677 (0.7923 to 0.9954)	0.9231 (0.7802 to 0.9745)	0.9894 (0.9269 to 0.9985)	0.9490 (0.8818 to 0.9784)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9677 (0.7923 to 0.9954)	0.9231 (0.7802 to 0.9745)	0.9894 (0.9269 to 0.9985)	0.9383 (0.8678 to 0.9718)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9677 (0.7923 to 0.9954)	0.9231 (0.7802 to 0.9745)	0.9894 (0.9269 to 0.9985)	0.9383 (0.8678 to 0.9718)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
8 Months	0.9677 (0.7923 to 0.9954)	0.9231 (0.7802 to 0.9745)	0.9894 (0.9269 to 0.9985)	0.9383 (0.8678 to 0.9718)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
10 Months	0.9677 (0.7923 to 0.9954)	0.9231 (0.7802 to 0.9745)	0.9744 (0.8994 to 0.9937)	0.9383 (0.8678 to 0.9718)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
12 Months	0.9677 (0.7923 to 0.9954)	0.9231 (0.7802 to 0.9745)	0.9744 (0.8994 to 0.9937)	0.9239 (0.8458 to 0.9633)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
14 Months	0.9677 (0.7923 to 0.9954)	0.9231 (0.7802 to 0.9745)	0.9744 (0.8994 to 0.9937)	0.9239 (0.8458 to 0.9633)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
16 Months	0.9677 (0.7923 to 0.9954)	0.9231 (0.7802 to 0.9745)	0.9744 (0.8994 to 0.9937)	0.9239 (0.8458 to 0.9633)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.10 Treatment emergent serious adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	30	36	93	91	17	14	
4 Months	30	35	90	86	12	11	
6 Months	30	33	79	77	7	9	
8 Months	29	33	70	74	6	7	
10 Months	29	33	65	71	6	6	
12 Months	27	30	54	61	5	6	
14 Months	16	17	34	42	4	6	
16 Months	10	9	15	16	1	2	
Pneumonia (days)							
Number (%) of events	1 (3.2)	4 (10.3)	15 (15.5)	15 (15.3)	7 (33.3)	4 (26.7)	0.4221
Number (%) of patients censored	30 (96.8)	35 (89.7)	82 (84.5)	83 (84.7)	14 (66.7)	11 (73.3)	
Kaplan-Meier estimates of event in months							

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.13 Treatment emergent severe adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)							
Number (%) of events	1 (3.2)	6 (15.4)	2 (2.1)	10 (10.2)	0 (0.0)	2 (13.3)	0.9988
Number (%) of patients censored	30 (96.8)	33 (84.6)	95 (97.9)	88 (89.8)	21 (100.0)	13 (86.7)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (0.5585 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.4928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0892		0.0213		0.0978	
Hazard ratio (95% CI) vs Pd	-	5.18 (0.62 to 43.01)		4.98 (1.09 to 22.73)		NC	
P-value	-	0.1279		0.0382		0.9977	
Hazard ratio inverted (95% CI) vs IPd			0.20 (0.04 to 0.92)				

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.13 Treatment emergent severe adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]							
2 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9894 (0.9269 to 0.9985)	0.9388 (0.8688 to 0.9720)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
4 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9894 (0.9269 to 0.9985)	0.9281 (0.8551 to 0.9651)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
6 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9894 (0.9269 to 0.9985)	0.9063 (0.8275 to 0.9501)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
8 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9894 (0.9269 to 0.9985)	0.9063 (0.8275 to 0.9501)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
10 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9744 (0.8994 to 0.9937)	0.9063 (0.8275 to 0.9501)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
12 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9744 (0.8994 to 0.9937)	0.8921 (0.8078 to 0.9408)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
14 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9744 (0.8994 to 0.9937)	0.8921 (0.8078 to 0.9408)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
16 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9744 (0.8994 to 0.9937)	0.8921 (0.8078 to 0.9408)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.13 Treatment emergent severe adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	30	33	93	90	17	12	
4 Months	30	33	90	85	12	11	
6 Months	30	31	79	74	7	9	
8 Months	29	31	70	72	6	7	
10 Months	29	31	65	70	6	6	
12 Months	27	28	54	60	5	6	
14 Months	16	17	34	41	4	6	
16 Months	10	9	15	15	1	2	
Neutropenia (days)							
Number (%) of events	8 (25.8)	18 (46.2)	31 (32.0)	45 (45.9)	9 (42.9)	6 (40.0)	0.5266
Number (%) of patients censored	23 (74.2)	21 (53.8)	66 (68.0)	53 (54.1)	12 (57.1)	9 (60.0)	
Kaplan-Meier estimates of event in months							

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.13 Treatment emergent severe adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)							
Number (%) of events	1 (3.2)	6 (15.4)	2 (2.1)	10 (10.2)	0 (0.0)	2 (13.3)	0.9988
Number (%) of patients censored	30 (96.8)	33 (84.6)	95 (97.9)	88 (89.8)	21 (100.0)	13 (86.7)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (0.5585 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.4928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0892		0.0213		0.0978	
Hazard ratio (95% CI) vs Pd	-	5.18 (0.62 to 43.01)		4.98 (1.09 to 22.73)		NC	
P-value	-	0.1279		0.0382		0.9977	
Hazard ratio inverted (95% CI) vs IPd			0.20 (0.04 to 0.92)				

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_seriss_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.13 Treatment emergent severe adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]							
2 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9894 (0.9269 to 0.9985)	0.9388 (0.8688 to 0.9720)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
4 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9894 (0.9269 to 0.9985)	0.9281 (0.8551 to 0.9651)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
6 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9894 (0.9269 to 0.9985)	0.9063 (0.8275 to 0.9501)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
8 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9894 (0.9269 to 0.9985)	0.9063 (0.8275 to 0.9501)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
10 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9744 (0.8994 to 0.9937)	0.9063 (0.8275 to 0.9501)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
12 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9744 (0.8994 to 0.9937)	0.8921 (0.8078 to 0.9408)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
14 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9744 (0.8994 to 0.9937)	0.8921 (0.8078 to 0.9408)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	
16 Months	0.9677 (0.7923 to 0.9954)	0.8462 (0.6892 to 0.9278)	0.9744 (0.8994 to 0.9937)	0.8921 (0.8078 to 0.9408)	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.13 Treatment emergent severe adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	30	33	93	90	17	12	
4 Months	30	33	90	85	12	11	
6 Months	30	31	79	74	7	9	
8 Months	29	31	70	72	6	7	
10 Months	29	31	65	70	6	6	
12 Months	27	28	54	60	5	6	
14 Months	16	17	34	41	4	6	
16 Months	10	9	15	15	1	2	
Neutropenia (days)							
Number (%) of events	8 (25.8)	18 (46.2)	31 (32.0)	45 (45.9)	9 (42.9)	6 (40.0)	0.5266
Number (%) of patients censored	23 (74.2)	21 (53.8)	66 (68.0)	53 (54.1)	12 (57.1)	9 (60.0)	
Kaplan-Meier estimates of event in months							

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.2 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	14	9	78	107	
4 Months	11	6	70	99	
6 Months	7	5	62	89	
8 Months	7	4	56	83	
10 Months	6	3	53	75	
12 Months	6	3	45	67	
14 Months	6	2	29	48	
16 Months	2	0	14	23	
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	2 (14.3)	2 (2.2)	13 (11.2)	0.9935
Number (%) of patients censored	21 (100.0)	12 (85.7)	91 (97.8)	103 (88.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.4928 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (1.8727 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.2 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0709		0.0138	
Hazard ratio (95% CI) vs Pd	-	NC		5.31 (1.20 to 23.54)	
P-value	-	0.9978		0.0279	
Hazard ratio inverted (95% CI) vs IPd			0.19 (0.04 to 0.83)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.8392 (0.4940 to 0.9573)	0.9890 (0.9246 to 0.9984)	0.9138 (0.8457 to 0.9527)	
4 Months	1.0000 (1.0000 to 1.0000)	0.8392 (0.4940 to 0.9573)	0.9890 (0.9246 to 0.9984)	0.9050 (0.8350 to 0.9462)	
6 Months	1.0000 (1.0000 to 1.0000)	0.8392 (0.4940 to 0.9573)	0.9890 (0.9246 to 0.9984)	0.8960 (0.8242 to 0.9396)	
8 Months	1.0000 (1.0000 to 1.0000)	0.8392 (0.4940 to 0.9573)	0.9890 (0.9246 to 0.9984)	0.8960 (0.8242 to 0.9396)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.2 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	1.0000 (1.0000 to 1.0000)	0.8392 (0.4940 to 0.9573)	0.9740 (0.8984 to 0.9936)	0.8960 (0.8242 to 0.9396)	
12 Months	1.0000 (1.0000 to 1.0000)	0.8392 (0.4940 to 0.9573)	0.9740 (0.8984 to 0.9936)	0.8850 (0.8098 to 0.9317)	
14 Months	1.0000 (1.0000 to 1.0000)	0.8392 (0.4940 to 0.9573)	0.9740 (0.8984 to 0.9936)	0.8850 (0.8098 to 0.9317)	
16 Months	1.0000 (1.0000 to 1.0000)	0.8392 (0.4940 to 0.9573)	0.9740 (0.8984 to 0.9936)	0.8850 (0.8098 to 0.9317)	
Number of patients at risk[b]					
2 Months	18	10	90	106	
4 Months	15	9	86	101	
6 Months	10	7	76	92	
8 Months	10	6	69	90	
10 Months	10	5	65	88	
12 Months	10	5	55	76	
14 Months	9	4	37	53	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.2 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	4	1	18	22	
Headache (days)					
Number (%) of events	1 (4.8)	2 (14.3)	6 (6.5)	13 (11.2)	0.6937
Number (%) of patients censored	20 (95.2)	12 (85.7)	87 (93.5)	103 (88.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (0.9528 to NC)	10.2177 (5.6181 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (5.6181 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.2177 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2723		0.2022	
Hazard ratio (95% CI) vs Pd	-	3.56 (0.32 to 39.98)		1.93 (0.69 to 5.42)	
P-value	-	0.3029		0.2104	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.4 Treatment emergent serious adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	0 (0.0)	2 (2.2)	9 (7.8)	0.9997
Number (%) of patients censored	21 (100.0)	14 (100.0)	91 (97.8)	107 (92.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0808	
Hazard ratio (95% CI) vs Pd	-	NC		3.59 (0.77 to 16.60)	
P-value	-			0.1024	
Events probability (95% CI)[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.4 Treatment emergent serious adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9890 (0.9246 to 0.9984)	0.9397 (0.8776 to 0.9708)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9890 (0.9246 to 0.9984)	0.9308 (0.8664 to 0.9648)	
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9890 (0.9246 to 0.9984)	0.9308 (0.8664 to 0.9648)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9890 (0.9246 to 0.9984)	0.9308 (0.8664 to 0.9648)	
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9740 (0.8984 to 0.9936)	0.9308 (0.8664 to 0.9648)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9740 (0.8984 to 0.9936)	0.9196 (0.8506 to 0.9575)	
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9740 (0.8984 to 0.9936)	0.9196 (0.8506 to 0.9575)	
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9740 (0.8984 to 0.9936)	0.9196 (0.8506 to 0.9575)	

Number of patients at risk[b]

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.4 Treatment emergent serious adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	18	12	90	109	
4 Months	15	9	86	103	
6 Months	10	7	76	95	
8 Months	10	6	69	93	
10 Months	10	5	65	90	
12 Months	10	5	55	78	
14 Months	9	4	37	54	
16 Months	4	1	18	23	
Pneumonia (days)					
Number (%) of events	6 (28.6)	2 (14.3)	14 (15.1)	18 (15.5)	0.3676
Number (%) of patients censored	15 (71.4)	12 (85.7)	79 (84.9)	98 (84.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.2669 (0.1314 to NC)	NC (1.0185 to NC)	NC (5.6838 to NC)	NC (NC to NC)	
Median (95% CI)	NC (2.2669 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.10 Treatment emergent severe adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	2 (14.3)	2 (2.2)	13 (11.2)	0.9935
Number (%) of patients censored	21 (100.0)	12 (85.7)	91 (97.8)	103 (88.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.4928 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (1.8727 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0709		0.0138	
Hazard ratio (95% CI) vs Pd	-	NC		5.31 (1.20 to 23.54)	
P-value	-	0.9978		0.0279	
Hazard ratio inverted (95% CI) vs IPd			0.19 (0.04 to 0.83)		

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.10 Treatment emergent severe adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.8392 (0.4940 to 0.9573)	0.9890 (0.9246 to 0.9984)	0.9138 (0.8457 to 0.9527)	
4 Months	1.0000 (1.0000 to 1.0000)	0.8392 (0.4940 to 0.9573)	0.9890 (0.9246 to 0.9984)	0.9050 (0.8350 to 0.9462)	
6 Months	1.0000 (1.0000 to 1.0000)	0.8392 (0.4940 to 0.9573)	0.9890 (0.9246 to 0.9984)	0.8960 (0.8242 to 0.9396)	
8 Months	1.0000 (1.0000 to 1.0000)	0.8392 (0.4940 to 0.9573)	0.9890 (0.9246 to 0.9984)	0.8960 (0.8242 to 0.9396)	
10 Months	1.0000 (1.0000 to 1.0000)	0.8392 (0.4940 to 0.9573)	0.9740 (0.8984 to 0.9936)	0.8960 (0.8242 to 0.9396)	
12 Months	1.0000 (1.0000 to 1.0000)	0.8392 (0.4940 to 0.9573)	0.9740 (0.8984 to 0.9936)	0.8850 (0.8098 to 0.9317)	
14 Months	1.0000 (1.0000 to 1.0000)	0.8392 (0.4940 to 0.9573)	0.9740 (0.8984 to 0.9936)	0.8850 (0.8098 to 0.9317)	
16 Months	1.0000 (1.0000 to 1.0000)	0.8392 (0.4940 to 0.9573)	0.9740 (0.8984 to 0.9936)	0.8850 (0.8098 to 0.9317)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_cyto_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.10 Treatment emergent severe adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	18	10	90	106	
4 Months	15	9	86	101	
6 Months	10	7	76	92	
8 Months	10	6	69	90	
10 Months	10	5	65	88	
12 Months	10	5	55	76	
14 Months	9	4	37	53	
16 Months	4	1	18	22	
Neutropenia (days)					
Number (%) of events	6 (28.6)	5 (35.7)	27 (29.0)	56 (48.3)	0.6847
Number (%) of patients censored	15 (71.4)	9 (64.3)	66 (71.0)	60 (51.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	4.9938 (0.5914 to NC)	0.8542 (0.5585 to NC)	2.9569 (1.1499 to NC)	0.8378 (0.7556 to 0.9856)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_cyto_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.3 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	24	15	64	98	
4 Months	20	12	59	90	
6 Months	14	10	53	81	
8 Months	14	9	47	75	
10 Months	13	8	44	67	
12 Months	11	7	38	60	
14 Months	8	5	26	43	
16 Months	3	1	13	21	
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	3 (13.0)	2 (2.6)	12 (11.7)	0.9914
Number (%) of patients censored	34 (100.0)	20 (87.0)	74 (97.4)	91 (88.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.4928 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.3 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0293		0.0299	
Hazard ratio (95% CI) vs Pd	-	NC		4.53 (1.01 to 20.24)	
P-value	-	0.9973		0.0480	
Hazard ratio inverted (95% CI) vs IPd			0.22 (0.05 to 0.99)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.8612 (0.6286 to 0.9531)	0.9865 (0.9079 to 0.9981)	0.9126 (0.8388 to 0.9535)	
4 Months	1.0000 (1.0000 to 1.0000)	0.8612 (0.6286 to 0.9531)	0.9865 (0.9079 to 0.9981)	0.9027 (0.8267 to 0.9464)	
6 Months	1.0000 (1.0000 to 1.0000)	0.8612 (0.6286 to 0.9531)	0.9865 (0.9079 to 0.9981)	0.8926 (0.8144 to 0.9390)	
8 Months	1.0000 (1.0000 to 1.0000)	0.8612 (0.6286 to 0.9531)	0.9865 (0.9079 to 0.9981)	0.8926 (0.8144 to 0.9390)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.3 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	1.0000 (1.0000 to 1.0000)	0.8612 (0.6286 to 0.9531)	0.9682 (0.8769 to 0.9921)	0.8926 (0.8144 to 0.9390)	
12 Months	1.0000 (1.0000 to 1.0000)	0.8612 (0.6286 to 0.9531)	0.9682 (0.8769 to 0.9921)	0.8802 (0.7982 to 0.9303)	
14 Months	1.0000 (1.0000 to 1.0000)	0.8612 (0.6286 to 0.9531)	0.9682 (0.8769 to 0.9921)	0.8802 (0.7982 to 0.9303)	
16 Months	1.0000 (1.0000 to 1.0000)	0.8612 (0.6286 to 0.9531)	0.9682 (0.8769 to 0.9921)	0.8802 (0.7982 to 0.9303)	
Number of patients at risk[b]					
2 Months	31	18	73	94	
4 Months	27	17	72	89	
6 Months	20	15	64	80	
8 Months	20	13	57	79	
10 Months	20	12	53	77	
12 Months	17	10	46	67	
14 Months	13	7	32	47	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.3 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	7	1	15	21	
Headache (days)					
Number (%) of events	2 (5.9)	2 (8.7)	5 (6.6)	13 (12.6)	0.6710
Number (%) of patients censored	32 (94.1)	21 (91.3)	71 (93.4)	90 (87.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (5.6181 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7292		0.1374	
Hazard ratio (95% CI) vs Pd	-	1.41 (0.20 to 10.05)		2.28 (0.74 to 7.00)	
P-value	-	0.7305		0.1487	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.6 Treatment emergent serious adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	0 (0.0)	2 (2.6)	9 (8.7)	0.9998
Number (%) of patients censored	34 (100.0)	23 (100.0)	74 (97.4)	94 (91.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.1025	
Hazard ratio (95% CI) vs Pd	-	NC		3.33 (0.72 to 15.41)	
P-value	-			0.1240	
Events probability (95% CI)[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.6 Treatment emergent serious adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9865 (0.9079 to 0.9981)	0.9320 (0.8627 to 0.9670)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9865 (0.9079 to 0.9981)	0.9220 (0.8501 to 0.9602)	
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9865 (0.9079 to 0.9981)	0.9220 (0.8501 to 0.9602)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9865 (0.9079 to 0.9981)	0.9220 (0.8501 to 0.9602)	
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9682 (0.8769 to 0.9921)	0.9220 (0.8501 to 0.9602)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9682 (0.8769 to 0.9921)	0.9094 (0.8325 to 0.9520)	
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9682 (0.8769 to 0.9921)	0.9094 (0.8325 to 0.9520)	
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9682 (0.8769 to 0.9921)	0.9094 (0.8325 to 0.9520)	

Number of patients at risk[b]

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.6 Treatment emergent serious adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	31	21	73	96	
4 Months	27	18	72	90	
6 Months	20	16	64	82	
8 Months	20	14	57	81	
10 Months	20	13	53	78	
12 Months	17	11	46	68	
14 Months	13	8	32	47	
16 Months	7	2	15	21	
Pneumonia (days)					
Number (%) of events	6 (17.6)	4 (17.4)	14 (18.4)	15 (14.6)	0.7985
Number (%) of patients censored	28 (82.4)	19 (82.6)	62 (81.6)	88 (85.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (1.3799 to NC)	NC (1.0185 to NC)	NC (4.1396 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.14 Treatment emergent severe adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	3 (13.0)	2 (2.6)	12 (11.7)	0.9914
Number (%) of patients censored	34 (100.0)	20 (87.0)	74 (97.4)	91 (88.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.4928 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0293		0.0299	
Hazard ratio (95% CI) vs Pd	-	NC		4.53 (1.01 to 20.24)	
P-value	-	0.9973		0.0480	
Hazard ratio inverted (95% CI) vs IPd			0.22 (0.05 to 0.99)		

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.14 Treatment emergent severe adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.8612 (0.6286 to 0.9531)	0.9865 (0.9079 to 0.9981)	0.9126 (0.8388 to 0.9535)	
4 Months	1.0000 (1.0000 to 1.0000)	0.8612 (0.6286 to 0.9531)	0.9865 (0.9079 to 0.9981)	0.9027 (0.8267 to 0.9464)	
6 Months	1.0000 (1.0000 to 1.0000)	0.8612 (0.6286 to 0.9531)	0.9865 (0.9079 to 0.9981)	0.8926 (0.8144 to 0.9390)	
8 Months	1.0000 (1.0000 to 1.0000)	0.8612 (0.6286 to 0.9531)	0.9865 (0.9079 to 0.9981)	0.8926 (0.8144 to 0.9390)	
10 Months	1.0000 (1.0000 to 1.0000)	0.8612 (0.6286 to 0.9531)	0.9682 (0.8769 to 0.9921)	0.8926 (0.8144 to 0.9390)	
12 Months	1.0000 (1.0000 to 1.0000)	0.8612 (0.6286 to 0.9531)	0.9682 (0.8769 to 0.9921)	0.8802 (0.7982 to 0.9303)	
14 Months	1.0000 (1.0000 to 1.0000)	0.8612 (0.6286 to 0.9531)	0.9682 (0.8769 to 0.9921)	0.8802 (0.7982 to 0.9303)	
16 Months	1.0000 (1.0000 to 1.0000)	0.8612 (0.6286 to 0.9531)	0.9682 (0.8769 to 0.9921)	0.8802 (0.7982 to 0.9303)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.14 Treatment emergent severe adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	31	18	73	94	
4 Months	27	17	72	89	
6 Months	20	15	64	80	
8 Months	20	13	57	79	
10 Months	20	12	53	77	
12 Months	17	10	46	67	
14 Months	13	7	32	47	
16 Months	7	1	15	21	
Neutropenia (days)					
Number (%) of events	11 (32.4)	12 (52.2)	22 (28.9)	48 (46.6)	0.7095
Number (%) of patients censored	23 (67.6)	11 (47.8)	54 (71.1)	55 (53.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.0370 (0.5914 to NC)	0.7556 (0.4928 to 0.8542)	3.0883 (1.4127 to NC)	0.8542 (0.7556 to 1.4784)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_care_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.3 Treatment emergent adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	71	72	48	63	
4 Months	64	66	43	58	
6 Months	57	59	38	51	
8 Months	52	52	32	49	
10 Months	50	48	29	44	
12 Months	45	44	23	39	
14 Months	26	28	14	29	
16 Months	13	11	6	15	
Febrile neutropenia (days)					
Number (%) of events	3 (3.4)	10 (12.3)	0 (0.0)	8 (11.3)	0.9887
Number (%) of patients censored	85 (96.6)	71 (87.7)	61 (100.0)	63 (88.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.3 Treatment emergent adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0274		0.0092	
Hazard ratio (95% CI) vs Pd	-	3.85 (1.06 to 13.99)		NC	
P-value	-	0.0406		0.9930	
Hazard ratio inverted (95% CI) vs IPd	0.26 (0.07 to 0.94)				
Events probability (95% CI)[b]					
2 Months	0.9770 (0.9112 to 0.9942)	0.9001 (0.8102 to 0.9488)	1.0000 (1.0000 to 1.0000)	0.9153 (0.8211 to 0.9610)	
4 Months	0.9770 (0.9112 to 0.9942)	0.9001 (0.8102 to 0.9488)	1.0000 (1.0000 to 1.0000)	0.9007 (0.8030 to 0.9514)	
6 Months	0.9770 (0.9112 to 0.9942)	0.8869 (0.7939 to 0.9395)	1.0000 (1.0000 to 1.0000)	0.8860 (0.7848 to 0.9413)	
8 Months	0.9770 (0.9112 to 0.9942)	0.8869 (0.7939 to 0.9395)	1.0000 (1.0000 to 1.0000)	0.8860 (0.7848 to 0.9413)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.3 Treatment emergent adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.9615 (0.8839 to 0.9876)	0.8869 (0.7939 to 0.9395)	1.0000 (1.0000 to 1.0000)	0.8860 (0.7848 to 0.9413)	
12 Months	0.9615 (0.8839 to 0.9876)	0.8692 (0.7691 to 0.9278)	1.0000 (1.0000 to 1.0000)	0.8860 (0.7848 to 0.9413)	
14 Months	0.9615 (0.8839 to 0.9876)	0.8692 (0.7691 to 0.9278)	1.0000 (1.0000 to 1.0000)	0.8860 (0.7848 to 0.9413)	
16 Months	0.9615 (0.8839 to 0.9876)	0.8692 (0.7691 to 0.9278)	1.0000 (1.0000 to 1.0000)	0.8860 (0.7848 to 0.9413)	
Number of patients at risk[b]					
2 Months	84	71	56	64	
4 Months	79	68	53	61	
6 Months	70	61	46	53	
8 Months	65	57	40	53	
10 Months	62	55	38	52	
12 Months	55	47	31	47	
14 Months	35	32	19	32	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.3 Treatment emergent adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	17	12	9	14	
Headache (days)					
Number (%) of events	6 (6.8)	7 (8.6)	2 (3.3)	8 (11.3)	0.1757
Number (%) of patients censored	82 (93.2)	74 (91.4)	59 (96.7)	63 (88.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7372		0.0500	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.40 to 3.58)		6.16 (0.77 to 49.33)	
P-value	-	0.7379		0.0865	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.5 Treatment emergent serious adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	0 (0.0)	3 (2.0)	10 (6.7)	0.9997
Number (%) of patients censored	2 (100.0)	2 (100.0)	144 (98.0)	140 (93.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0583	
Hazard ratio (95% CI) vs Pd	-	NC		3.25 (0.89 to 11.80)	
P-value	-			0.0737	
Events probability (95% CI)[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.5 Treatment emergent serious adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.9464 (0.8956 to 0.9728)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.9394 (0.8868 to 0.9680)	
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.9394 (0.8868 to 0.9680)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.9394 (0.8868 to 0.9680)	
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9760 (0.9262 to 0.9923)	0.9394 (0.8868 to 0.9680)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9760 (0.9262 to 0.9923)	0.9301 (0.8734 to 0.9619)	
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9760 (0.9262 to 0.9923)	0.9301 (0.8734 to 0.9619)	
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9760 (0.9262 to 0.9923)	0.9301 (0.8734 to 0.9619)	

Number of patients at risk[b]

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.5 Treatment emergent serious adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	2	2	138	139	
4 Months	2	2	130	130	
6 Months	2	2	114	117	
8 Months	2	2	103	112	
10 Months	1	2	99	108	
12 Months	1	1	85	96	
14 Months	1	0	53	65	
16 Months	0	0	26	27	
Pneumonia (days)					
Number (%) of events	0 (0.0)	0 (0.0)	23 (15.6)	23 (15.3)	1.0000
Number (%) of patients censored	2 (100.0)	2 (100.0)	124 (84.4)	127 (84.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.12 Treatment emergent severe adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	0 (0.0)	3 (2.0)	18 (12.0)	0.9995
Number (%) of patients censored	2 (100.0)	2 (100.0)	144 (98.0)	132 (88.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0011	
Hazard ratio (95% CI) vs Pd	-	NC		6.00 (1.77 to 20.38)	
P-value	-			0.0040	
Hazard ratio inverted (95% CI) vs IPd			0.17 (0.05 to 0.57)		

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.12 Treatment emergent severe adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.9061 (0.8465 to 0.9433)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.8991 (0.8383 to 0.9379)	
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.8850 (0.8215 to 0.9269)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.8850 (0.8215 to 0.9269)	
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9760 (0.9262 to 0.9923)	0.8850 (0.8215 to 0.9269)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9760 (0.9262 to 0.9923)	0.8760 (0.8100 to 0.9201)	
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9760 (0.9262 to 0.9923)	0.8760 (0.8100 to 0.9201)	
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9760 (0.9262 to 0.9923)	0.8760 (0.8100 to 0.9201)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.12 Treatment emergent severe adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	2	2	138	133	
4 Months	2	2	130	127	
6 Months	2	2	114	112	
8 Months	2	2	103	108	
10 Months	1	2	99	105	
12 Months	1	1	85	93	
14 Months	1	0	53	64	
16 Months	0	0	26	26	
Neutropenia (days)					
Number (%) of events	0 (0.0)	1 (50.0)	48 (32.7)	68 (45.3)	0.9848
Number (%) of patients censored	2 (100.0)	1 (50.0)	99 (67.3)	82 (54.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	2.0370 (2.0370 to NC)	1.9384 (0.9528 to 4.9938)	0.8542 (0.7556 to 1.0185)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.3 Treatment emergent adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	76	94	34	26	
4 Months	70	86	29	25	
6 Months	60	76	28	24	
8 Months	52	68	25	23	
10 Months	50	60	23	22	
12 Months	42	53	20	21	
14 Months	24	36	10	14	
16 Months	12	15	5	6	
Febrile neutropenia (days)					
Number (%) of events	1 (1.0)	12 (11.7)	1 (2.5)	5 (15.6)	0.2377
Number (%) of patients censored	97 (99.0)	91 (88.3)	39 (97.5)	27 (84.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.6571 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_semm_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.3 Treatment emergent adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0028		0.0469	
Hazard ratio (95% CI) vs Pd	-	11.58 (1.51 to 89.05)		6.59 (0.77 to 56.40)	
P-value	-	0.0186		0.0853	
Hazard ratio inverted (95% CI) vs IPd	0.09 (0.01 to 0.66)				
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9217 (0.8496 to 0.9601)	0.9744 (0.8316 to 0.9963)	0.8426 (0.6622 to 0.9313)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9118 (0.8374 to 0.9531)	0.9744 (0.8316 to 0.9963)	0.8426 (0.6622 to 0.9313)	
6 Months	1.0000 (1.0000 to 1.0000)	0.8916 (0.8127 to 0.9385)	0.9744 (0.8316 to 0.9963)	0.8426 (0.6622 to 0.9313)	
8 Months	1.0000 (1.0000 to 1.0000)	0.8916 (0.8127 to 0.9385)	0.9744 (0.8316 to 0.9963)	0.8426 (0.6622 to 0.9313)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_semm_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.3 Treatment emergent adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.9851 (0.8987 to 0.9979)	0.8916 (0.8127 to 0.9385)	0.9744 (0.8316 to 0.9963)	0.8426 (0.6622 to 0.9313)	
12 Months	0.9851 (0.8987 to 0.9979)	0.8783 (0.7949 to 0.9292)	0.9744 (0.8316 to 0.9963)	0.8426 (0.6622 to 0.9313)	
14 Months	0.9851 (0.8987 to 0.9979)	0.8783 (0.7949 to 0.9292)	0.9744 (0.8316 to 0.9963)	0.8426 (0.6622 to 0.9313)	
16 Months	0.9851 (0.8987 to 0.9979)	0.8783 (0.7949 to 0.9292)	0.9744 (0.8316 to 0.9963)	0.8426 (0.6622 to 0.9313)	
Number of patients at risk[b]					
2 Months	94	94	37	26	
4 Months	91	90	33	26	
6 Months	76	80	32	25	
8 Months	69	76	28	25	
10 Months	66	73	27	25	
12 Months	57	63	23	23	
14 Months	35	44	13	14	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_semm_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.3 Treatment emergent adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	17	17	7	5	
Headache (days)					
Number (%) of events	7 (7.1)	11 (10.7)	1 (2.5)	2 (6.3)	0.9647
Number (%) of patients censored	91 (92.9)	92 (89.3)	39 (97.5)	30 (93.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3529		0.4691	
Hazard ratio (95% CI) vs Pd	-	1.60 (0.59 to 4.32)		2.36 (0.21 to 26.08)	
P-value	-	0.3573		0.4826	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_semm_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.6 Treatment emergent serious adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	1 (1.0)	6 (5.8)	1 (2.5)	4 (12.5)	0.9967
Number (%) of patients censored	97 (99.0)	97 (94.2)	39 (97.5)	28 (87.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.6571 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0725		0.0996	
Hazard ratio (95% CI) vs Pd	-	5.58 (0.67 to 46.37)		5.20 (0.58 to 46.53)	
P-value	-	0.1113		0.1404	
Events probability (95% CI)[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_semm_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.6 Treatment emergent serious adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	0.9608 (0.8989 to 0.9851)	0.9744 (0.8316 to 0.9963)	0.8750 (0.7004 to 0.9512)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9508 (0.8858 to 0.9792)	0.9744 (0.8316 to 0.9963)	0.8750 (0.7004 to 0.9512)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9508 (0.8858 to 0.9792)	0.9744 (0.8316 to 0.9963)	0.8750 (0.7004 to 0.9512)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9508 (0.8858 to 0.9792)	0.9744 (0.8316 to 0.9963)	0.8750 (0.7004 to 0.9512)	
10 Months	0.9851 (0.8987 to 0.9979)	0.9508 (0.8858 to 0.9792)	0.9744 (0.8316 to 0.9963)	0.8750 (0.7004 to 0.9512)	
12 Months	0.9851 (0.8987 to 0.9979)	0.9370 (0.8639 to 0.9715)	0.9744 (0.8316 to 0.9963)	0.8750 (0.7004 to 0.9512)	
14 Months	0.9851 (0.8987 to 0.9979)	0.9370 (0.8639 to 0.9715)	0.9744 (0.8316 to 0.9963)	0.8750 (0.7004 to 0.9512)	
16 Months	0.9851 (0.8987 to 0.9979)	0.9370 (0.8639 to 0.9715)	0.9744 (0.8316 to 0.9963)	0.8750 (0.7004 to 0.9512)	

Number of patients at risk[b]

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_semm_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.6 Treatment emergent serious adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	94	98	37	27	
4 Months	91	92	33	26	
6 Months	76	84	32	25	
8 Months	69	79	28	25	
10 Months	66	75	27	25	
12 Months	57	65	23	23	
14 Months	35	44	13	14	
16 Months	17	17	7	5	
Pneumonia (days)					
Number (%) of events	20 (20.4)	17 (16.5)	3 (7.5)	5 (15.6)	0.4684
Number (%) of patients censored	78 (79.6)	86 (83.5)	37 (92.5)	27 (84.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (2.8255 to NC)	NC (6.3409 to NC)	NC (NC to NC)	NC (2.8583 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_semm_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.14 Treatment emergent severe adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	1 (1.0)	12 (11.7)	1 (2.5)	5 (15.6)	0.2377
Number (%) of patients censored	97 (99.0)	91 (88.3)	39 (97.5)	27 (84.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.6571 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0028		0.0469	
Hazard ratio (95% CI) vs Pd	-	11.58 (1.51 to 89.05)		6.59 (0.77 to 56.40)	
P-value	-	0.0186		0.0853	
Hazard ratio inverted (95% CI) vs IPd	0.09 (0.01 to 0.66)				

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_semm_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.14 Treatment emergent severe adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9217 (0.8496 to 0.9601)	0.9744 (0.8316 to 0.9963)	0.8426 (0.6622 to 0.9313)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9118 (0.8374 to 0.9531)	0.9744 (0.8316 to 0.9963)	0.8426 (0.6622 to 0.9313)	
6 Months	1.0000 (1.0000 to 1.0000)	0.8916 (0.8127 to 0.9385)	0.9744 (0.8316 to 0.9963)	0.8426 (0.6622 to 0.9313)	
8 Months	1.0000 (1.0000 to 1.0000)	0.8916 (0.8127 to 0.9385)	0.9744 (0.8316 to 0.9963)	0.8426 (0.6622 to 0.9313)	
10 Months	0.9851 (0.8987 to 0.9979)	0.8916 (0.8127 to 0.9385)	0.9744 (0.8316 to 0.9963)	0.8426 (0.6622 to 0.9313)	
12 Months	0.9851 (0.8987 to 0.9979)	0.8783 (0.7949 to 0.9292)	0.9744 (0.8316 to 0.9963)	0.8426 (0.6622 to 0.9313)	
14 Months	0.9851 (0.8987 to 0.9979)	0.8783 (0.7949 to 0.9292)	0.9744 (0.8316 to 0.9963)	0.8426 (0.6622 to 0.9313)	
16 Months	0.9851 (0.8987 to 0.9979)	0.8783 (0.7949 to 0.9292)	0.9744 (0.8316 to 0.9963)	0.8426 (0.6622 to 0.9313)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.14 Treatment emergent severe adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	94	94	37	26	
4 Months	91	90	33	26	
6 Months	76	80	32	25	
8 Months	69	76	28	25	
10 Months	66	73	27	25	
12 Months	57	63	23	23	
14 Months	35	44	13	14	
16 Months	17	17	7	5	
Neutropenia (days)					
Number (%) of events	31 (31.6)	46 (44.7)	13 (32.5)	19 (59.4)	0.2653
Number (%) of patients censored	67 (68.4)	57 (55.3)	27 (67.5)	13 (40.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.8255 (0.9856 to NC)	0.8542 (0.7556 to 1.4456)	1.5441 (0.7556 to NC)	0.8049 (0.5257 to 0.8542)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_semm_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.3 Treatment emergent adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	75	92	43	42	
4 Months	69	84	37	39	
6 Months	59	74	35	35	
8 Months	51	66	32	34	
10 Months	49	58	29	33	
12 Months	41	51	26	31	
14 Months	23	35	16	22	
16 Months	11	15	7	11	
Febrile neutropenia (days)					
Number (%) of events	1 (1.0)	12 (11.9)	2 (3.9)	6 (12.0)	0.3085
Number (%) of patients censored	96 (99.0)	89 (88.1)	49 (96.1)	44 (88.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.3 Treatment emergent adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0026		0.1370	
Hazard ratio (95% CI) vs Pd	-	11.70 (1.52 to 90.01)		3.16 (0.64 to 15.65)	
P-value	-	0.0181		0.1591	
Hazard ratio inverted (95% CI) vs IPd	0.09 (0.01 to 0.66)				
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9202 (0.8467 to 0.9593)	0.9592 (0.8465 to 0.9896)	0.8791 (0.7504 to 0.9438)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9101 (0.8343 to 0.9522)	0.9592 (0.8465 to 0.9896)	0.8791 (0.7504 to 0.9438)	
6 Months	1.0000 (1.0000 to 1.0000)	0.8894 (0.8091 to 0.9372)	0.9592 (0.8465 to 0.9896)	0.8791 (0.7504 to 0.9438)	
8 Months	1.0000 (1.0000 to 1.0000)	0.8894 (0.8091 to 0.9372)	0.9592 (0.8465 to 0.9896)	0.8791 (0.7504 to 0.9438)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.3 Treatment emergent adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.9848 (0.8973 to 0.9979)	0.8894 (0.8091 to 0.9372)	0.9592 (0.8465 to 0.9896)	0.8791 (0.7504 to 0.9438)	
12 Months	0.9848 (0.8973 to 0.9979)	0.8757 (0.7907 to 0.9277)	0.9592 (0.8465 to 0.9896)	0.8791 (0.7504 to 0.9438)	
14 Months	0.9848 (0.8973 to 0.9979)	0.8757 (0.7907 to 0.9277)	0.9592 (0.8465 to 0.9896)	0.8791 (0.7504 to 0.9438)	
16 Months	0.9848 (0.8973 to 0.9979)	0.8757 (0.7907 to 0.9277)	0.9592 (0.8465 to 0.9896)	0.8791 (0.7504 to 0.9438)	
Number of patients at risk[b]					
2 Months	93	92	46	42	
4 Months	90	88	41	40	
6 Months	75	78	40	35	
8 Months	68	74	36	35	
10 Months	65	71	34	35	
12 Months	56	61	29	32	
14 Months	34	43	19	21	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.3 Treatment emergent adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	16	17	9	9	
Headache (days)					
Number (%) of events	7 (7.2)	11 (10.9)	1 (2.0)	4 (8.0)	0.4693
Number (%) of patients censored	90 (92.8)	90 (89.1)	50 (98.0)	46 (92.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3425		0.1826	
Hazard ratio (95% CI) vs Pd	-	1.61 (0.60 to 4.36)		3.97 (0.44 to 35.51)	
P-value	-	0.3471		0.2176	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.7 Treatment emergent serious adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	1 (1.0)	6 (5.9)	2 (3.9)	4 (8.0)	0.4503
Number (%) of patients censored	96 (99.0)	95 (94.1)	49 (96.1)	46 (92.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0704		0.3899	
Hazard ratio (95% CI) vs Pd	-	5.64 (0.68 to 46.85)		2.07 (0.38 to 11.31)	
P-value	-	0.1092		0.4004	
Events probability (95% CI)[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.7 Treatment emergent serious adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	0.9600 (0.8969 to 0.9848)	0.9592 (0.8465 to 0.9896)	0.9200 (0.8007 to 0.9692)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9498 (0.8836 to 0.9788)	0.9592 (0.8465 to 0.9896)	0.9200 (0.8007 to 0.9692)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9498 (0.8836 to 0.9788)	0.9592 (0.8465 to 0.9896)	0.9200 (0.8007 to 0.9692)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9498 (0.8836 to 0.9788)	0.9592 (0.8465 to 0.9896)	0.9200 (0.8007 to 0.9692)	
10 Months	0.9848 (0.8973 to 0.9979)	0.9498 (0.8836 to 0.9788)	0.9592 (0.8465 to 0.9896)	0.9200 (0.8007 to 0.9692)	
12 Months	0.9848 (0.8973 to 0.9979)	0.9356 (0.8610 to 0.9708)	0.9592 (0.8465 to 0.9896)	0.9200 (0.8007 to 0.9692)	
14 Months	0.9848 (0.8973 to 0.9979)	0.9356 (0.8610 to 0.9708)	0.9592 (0.8465 to 0.9896)	0.9200 (0.8007 to 0.9692)	
16 Months	0.9848 (0.8973 to 0.9979)	0.9356 (0.8610 to 0.9708)	0.9592 (0.8465 to 0.9896)	0.9200 (0.8007 to 0.9692)	

Number of patients at risk[b]

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.7 Treatment emergent serious adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	93	96	46	44	
4 Months	90	90	41	41	
6 Months	75	82	40	36	
8 Months	68	77	36	36	
10 Months	65	73	34	36	
12 Months	56	63	29	33	
14 Months	34	43	19	22	
16 Months	16	17	9	10	
Pneumonia (days)					
Number (%) of events	20 (20.6)	17 (16.8)	3 (5.9)	6 (12.0)	0.2096
Number (%) of patients censored	77 (79.4)	84 (83.2)	48 (94.1)	44 (88.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (2.8255 to NC)	NC (6.3409 to NC)	NC (NC to NC)	NC (11.6304 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.15 Treatment emergent severe adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	1 (1.0)	12 (11.9)	2 (3.9)	6 (12.0)	0.3085
Number (%) of patients censored	96 (99.0)	89 (88.1)	49 (96.1)	44 (88.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0026		0.1370	
Hazard ratio (95% CI) vs Pd	-	11.70 (1.52 to 90.01)		3.16 (0.64 to 15.65)	
P-value	-	0.0181		0.1591	
Hazard ratio inverted (95% CI) vs IPd	0.09 (0.01 to 0.66)				

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.15 Treatment emergent severe adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9202 (0.8467 to 0.9593)	0.9592 (0.8465 to 0.9896)	0.8791 (0.7504 to 0.9438)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9101 (0.8343 to 0.9522)	0.9592 (0.8465 to 0.9896)	0.8791 (0.7504 to 0.9438)	
6 Months	1.0000 (1.0000 to 1.0000)	0.8894 (0.8091 to 0.9372)	0.9592 (0.8465 to 0.9896)	0.8791 (0.7504 to 0.9438)	
8 Months	1.0000 (1.0000 to 1.0000)	0.8894 (0.8091 to 0.9372)	0.9592 (0.8465 to 0.9896)	0.8791 (0.7504 to 0.9438)	
10 Months	0.9848 (0.8973 to 0.9979)	0.8894 (0.8091 to 0.9372)	0.9592 (0.8465 to 0.9896)	0.8791 (0.7504 to 0.9438)	
12 Months	0.9848 (0.8973 to 0.9979)	0.8757 (0.7907 to 0.9277)	0.9592 (0.8465 to 0.9896)	0.8791 (0.7504 to 0.9438)	
14 Months	0.9848 (0.8973 to 0.9979)	0.8757 (0.7907 to 0.9277)	0.9592 (0.8465 to 0.9896)	0.8791 (0.7504 to 0.9438)	
16 Months	0.9848 (0.8973 to 0.9979)	0.8757 (0.7907 to 0.9277)	0.9592 (0.8465 to 0.9896)	0.8791 (0.7504 to 0.9438)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.15 Treatment emergent severe adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	93	92	46	42	
4 Months	90	88	41	40	
6 Months	75	78	40	35	
8 Months	68	74	36	35	
10 Months	65	71	34	35	
12 Months	56	61	29	32	
14 Months	34	43	19	21	
16 Months	16	17	9	9	
Neutropenia (days)					
Number (%) of events	31 (32.0)	44 (43.6)	17 (33.3)	24 (48.0)	0.8177
Number (%) of patients censored	66 (68.0)	57 (56.4)	34 (66.7)	26 (52.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.8255 (0.9856 to NC)	0.8542 (0.7556 to 1.9384)	1.4127 (0.7885 to NC)	0.8542 (0.5585 to 1.4127)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.2 Treatment emergent adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	7	14	112	121	
4 Months	4	13	103	111	
6 Months	3	11	92	99	
8 Months	1	10	83	91	
10 Months	1	10	78	82	
12 Months	1	8	67	75	
14 Months	1	7	39	50	
16 Months	0	5	19	21	
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	1 (7.1)	3 (2.2)	17 (12.3)	0.9906
Number (%) of patients censored	10 (100.0)	13 (92.9)	136 (97.8)	121 (87.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (1.8727 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.2 Treatment emergent adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4227		0.0013	
Hazard ratio (95% CI) vs Pd	-	NC		5.91 (1.73 to 20.16)	
P-value	-	0.9985		0.0046	
Hazard ratio inverted (95% CI) vs IPd			0.17 (0.05 to 0.58)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9851 (0.9416 to 0.9962)	0.9053 (0.8424 to 0.9439)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9851 (0.9416 to 0.9962)	0.8977 (0.8334 to 0.9381)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9851 (0.9416 to 0.9962)	0.8822 (0.8149 to 0.9262)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9851 (0.9416 to 0.9962)	0.8822 (0.8149 to 0.9262)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.2 Treatment emergent adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9751 (0.9240 to 0.9920)	0.8822 (0.8149 to 0.9262)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9751 (0.9240 to 0.9920)	0.8724 (0.8024 to 0.9189)	
14 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9751 (0.9240 to 0.9920)	0.8724 (0.8024 to 0.9189)	
16 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9751 (0.9240 to 0.9920)	0.8724 (0.8024 to 0.9189)	
Number of patients at risk[b]					
2 Months	9	13	131	122	
4 Months	7	13	125	116	
6 Months	5	11	111	103	
8 Months	2	10	103	100	
10 Months	2	10	98	97	
12 Months	2	8	84	86	
14 Months	2	7	52	57	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.2 Treatment emergent adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0	5	26	21	
Headache (days)					
Number (%) of events	0 (0.0)	1 (7.1)	8 (5.8)	14 (10.1)	0.9897
Number (%) of patients censored	10 (100.0)	13 (92.9)	131 (94.2)	124 (89.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (1.9055 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4227		0.1544	
Hazard ratio (95% CI) vs Pd	-	NC		1.91 (0.77 to 4.74)	
P-value	-	0.9985		0.1617	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.4 Treatment emergent serious adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	0 (0.0)	3 (2.2)	10 (7.2)	0.9996
Number (%) of patients censored	10 (100.0)	14 (100.0)	136 (97.8)	128 (92.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0489	
Hazard ratio (95% CI) vs Pd	-	NC		3.39 (0.93 to 12.30)	
P-value	-			0.0640	
Events probability (95% CI)[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.4 Treatment emergent serious adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9851 (0.9416 to 0.9962)	0.9417 (0.8867 to 0.9704)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9851 (0.9416 to 0.9962)	0.9341 (0.8771 to 0.9651)	
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9851 (0.9416 to 0.9962)	0.9341 (0.8771 to 0.9651)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9851 (0.9416 to 0.9962)	0.9341 (0.8771 to 0.9651)	
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9751 (0.9240 to 0.9920)	0.9341 (0.8771 to 0.9651)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9751 (0.9240 to 0.9920)	0.9240 (0.8628 to 0.9586)	
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9751 (0.9240 to 0.9920)	0.9240 (0.8628 to 0.9586)	
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9751 (0.9240 to 0.9920)	0.9240 (0.8628 to 0.9586)	

Number of patients at risk[b]

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.4 Treatment emergent serious adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	9	14	131	127	
4 Months	7	13	125	119	
6 Months	5	11	111	108	
8 Months	2	10	103	104	
10 Months	2	10	98	100	
12 Months	2	8	84	89	
14 Months	2	7	52	58	
16 Months	0	5	26	22	
Pneumonia (days)					
Number (%) of events	0 (0.0)	2 (14.3)	23 (16.5)	21 (15.2)	0.9885
Number (%) of patients censored	10 (100.0)	12 (85.7)	116 (83.5)	117 (84.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (1.0185 to NC)	NC (5.6838 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.10 Treatment emergent severe adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	1 (7.1)	3 (2.2)	17 (12.3)	0.9906
Number (%) of patients censored	10 (100.0)	13 (92.9)	136 (97.8)	121 (87.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (1.8727 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4227		0.0013	
Hazard ratio (95% CI) vs Pd	-	NC		5.91 (1.73 to 20.16)	
P-value	-	0.9985		0.0046	
Hazard ratio inverted (95% CI) vs IPd			0.17 (0.05 to 0.58)		

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.10 Treatment emergent severe adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9851 (0.9416 to 0.9962)	0.9053 (0.8424 to 0.9439)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9851 (0.9416 to 0.9962)	0.8977 (0.8334 to 0.9381)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9851 (0.9416 to 0.9962)	0.8822 (0.8149 to 0.9262)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9851 (0.9416 to 0.9962)	0.8822 (0.8149 to 0.9262)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9751 (0.9240 to 0.9920)	0.8822 (0.8149 to 0.9262)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9751 (0.9240 to 0.9920)	0.8724 (0.8024 to 0.9189)	
14 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9751 (0.9240 to 0.9920)	0.8724 (0.8024 to 0.9189)	
16 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	0.9751 (0.9240 to 0.9920)	0.8724 (0.8024 to 0.9189)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.10 Treatment emergent severe adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	9	13	131	122	
4 Months	7	13	125	116	
6 Months	5	11	111	103	
8 Months	2	10	103	100	
10 Months	2	10	98	97	
12 Months	2	8	84	86	
14 Months	2	7	52	57	
16 Months	0	5	26	21	
Neutropenia (days)					
Number (%) of events	1 (10.0)	7 (50.0)	47 (33.8)	62 (44.9)	0.2459
Number (%) of patients censored	9 (90.0)	7 (50.0)	92 (66.2)	76 (55.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (0.7556 to NC)	0.8542 (0.5257 to 2.0370)	1.9384 (0.9528 to 4.6653)	0.8542 (0.7556 to 1.0185)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.2 Treatment emergent adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	77	78	36	47	
4 Months	72	73	30	43	
6 Months	68	67	24	38	
8 Months	62	62	19	34	
10 Months	58	57	18	30	
12 Months	51	49	15	29	
14 Months	30	33	8	20	
16 Months	13	16	4	9	
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	8 (9.3)	3 (6.4)	9 (16.7)	0.9913
Number (%) of patients censored	94 (100.0)	78 (90.7)	44 (93.6)	45 (83.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.8727 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.2 Treatment emergent adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0029		0.1333	
Hazard ratio (95% CI) vs Pd	-	NC		2.62 (0.71 to 9.68)	
P-value	-	0.9928		0.1485	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9302 (0.8513 to 0.9680)	0.9556 (0.8338 to 0.9887)	0.8704 (0.7472 to 0.9360)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9302 (0.8513 to 0.9680)	0.9556 (0.8338 to 0.9887)	0.8514 (0.7248 to 0.9228)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9182 (0.8359 to 0.9601)	0.9556 (0.8338 to 0.9887)	0.8325 (0.7028 to 0.9091)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9182 (0.8359 to 0.9601)	0.9556 (0.8338 to 0.9887)	0.8325 (0.7028 to 0.9091)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9182 (0.8359 to 0.9601)	0.9202 (0.7653 to 0.9745)	0.8325 (0.7028 to 0.9091)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.2 Treatment emergent adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
12 Months	1.0000 (1.0000 to 1.0000)	0.9033 (0.8154 to 0.9506)	0.9202 (0.7653 to 0.9745)	0.8325 (0.7028 to 0.9091)	
14 Months	1.0000 (1.0000 to 1.0000)	0.9033 (0.8154 to 0.9506)	0.9202 (0.7653 to 0.9745)	0.8325 (0.7028 to 0.9091)	
16 Months	1.0000 (1.0000 to 1.0000)	0.9033 (0.8154 to 0.9506)	0.9202 (0.7653 to 0.9745)	0.8325 (0.7028 to 0.9091)	
Number of patients at risk[b]					
2 Months	91	79	42	47	
4 Months	87	77	39	45	
6 Months	79	71	33	39	
8 Months	73	69	28	37	
10 Months	70	68	26	35	
12 Months	62	58	22	32	
14 Months	37	41	15	20	
16 Months	17	18	7	8	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.5 Treatment emergent serious adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	5 (5.8)	3 (6.4)	5 (9.3)	0.9923
Number (%) of patients censored	94 (100.0)	81 (94.2)	44 (93.6)	49 (90.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0199		0.6307	
Hazard ratio (95% CI) vs Pd	-	NC		1.42 (0.34 to 5.94)	
P-value	-	0.9943		0.6325	
Events probability (95% CI)[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_crcl_s_t_x.rtf (16FEB2021 22:48)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.5 Treatment emergent serious adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	0.9535 (0.8808 to 0.9823)	0.9556 (0.8338 to 0.9887)	0.9259 (0.8146 to 0.9715)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9535 (0.8808 to 0.9823)	0.9556 (0.8338 to 0.9887)	0.9066 (0.7900 to 0.9601)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9535 (0.8808 to 0.9823)	0.9556 (0.8338 to 0.9887)	0.9066 (0.7900 to 0.9601)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9535 (0.8808 to 0.9823)	0.9556 (0.8338 to 0.9887)	0.9066 (0.7900 to 0.9601)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9535 (0.8808 to 0.9823)	0.9202 (0.7653 to 0.9745)	0.9066 (0.7900 to 0.9601)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9386 (0.8579 to 0.9741)	0.9202 (0.7653 to 0.9745)	0.9066 (0.7900 to 0.9601)	
14 Months	1.0000 (1.0000 to 1.0000)	0.9386 (0.8579 to 0.9741)	0.9202 (0.7653 to 0.9745)	0.9066 (0.7900 to 0.9601)	
16 Months	1.0000 (1.0000 to 1.0000)	0.9386 (0.8579 to 0.9741)	0.9202 (0.7653 to 0.9745)	0.9066 (0.7900 to 0.9601)	

Number of patients at risk[b]

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.5 Treatment emergent serious adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	91	81	42	50	
4 Months	87	79	39	45	
6 Months	79	74	33	40	
8 Months	73	72	28	37	
10 Months	70	70	26	35	
12 Months	62	60	22	32	
14 Months	37	41	15	20	
16 Months	17	18	7	8	
Pneumonia (days)					
Number (%) of events	12 (12.8)	9 (10.5)	11 (23.4)	14 (25.9)	0.6345
Number (%) of patients censored	82 (87.2)	77 (89.5)	36 (76.6)	40 (74.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.6756 to NC)	6.2752 (2.7269 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.11 Treatment emergent severe adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	8 (9.3)	3 (6.4)	9 (16.7)	0.9913
Number (%) of patients censored	94 (100.0)	78 (90.7)	44 (93.6)	45 (83.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.8727 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0029		0.1333	
Hazard ratio (95% CI) vs Pd	-	NC		2.62 (0.71 to 9.68)	
P-value	-	0.9928		0.1485	
Events probability (95% CI)[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_crcl_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.11 Treatment emergent severe adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	0.9302 (0.8513 to 0.9680)	0.9556 (0.8338 to 0.9887)	0.8704 (0.7472 to 0.9360)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9302 (0.8513 to 0.9680)	0.9556 (0.8338 to 0.9887)	0.8514 (0.7248 to 0.9228)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9182 (0.8359 to 0.9601)	0.9556 (0.8338 to 0.9887)	0.8325 (0.7028 to 0.9091)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9182 (0.8359 to 0.9601)	0.9556 (0.8338 to 0.9887)	0.8325 (0.7028 to 0.9091)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9182 (0.8359 to 0.9601)	0.9202 (0.7653 to 0.9745)	0.8325 (0.7028 to 0.9091)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9033 (0.8154 to 0.9506)	0.9202 (0.7653 to 0.9745)	0.8325 (0.7028 to 0.9091)	
14 Months	1.0000 (1.0000 to 1.0000)	0.9033 (0.8154 to 0.9506)	0.9202 (0.7653 to 0.9745)	0.8325 (0.7028 to 0.9091)	
16 Months	1.0000 (1.0000 to 1.0000)	0.9033 (0.8154 to 0.9506)	0.9202 (0.7653 to 0.9745)	0.8325 (0.7028 to 0.9091)	

Number of patients at risk[b]

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.11 Treatment emergent severe adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	91	79	42	47	
4 Months	87	77	39	45	
6 Months	79	71	33	39	
8 Months	73	69	28	37	
10 Months	70	68	26	35	
12 Months	62	58	22	32	
14 Months	37	41	15	20	
16 Months	17	18	7	8	
Neutropenia (days)					
Number (%) of events	29 (30.9)	43 (50.0)	18 (38.3)	23 (42.6)	0.1891
Number (%) of patients censored	65 (69.1)	43 (50.0)	29 (61.7)	31 (57.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.8255 (0.9199 to NC)	0.8214 (0.6242 to 0.9856)	1.4456 (0.5914 to 3.3840)	0.8542 (0.7556 to 1.4784)	
Median (95% CI)	NC (NC to NC)	9.3306 (1.9384 to NC)	NC (2.9569 to NC)	NC (1.4784 to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.2 Treatment emergent adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	0 (0.0)	3 (2.0)	18 (12.0)	0.9995
Number (%) of patients censored	2 (100.0)	2 (100.0)	144 (98.0)	132 (88.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0010	
Hazard ratio (95% CI) vs Pd	-	NC		6.02 (1.77 to 20.42)	
P-value	-			0.0040	
Hazard ratio inverted (95% CI) vs IPd			0.17 (0.05 to 0.56)		
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.2 Treatment emergent adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.9061 (0.8465 to 0.9433)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.8991 (0.8383 to 0.9379)	
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.8850 (0.8215 to 0.9269)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.8850 (0.8215 to 0.9269)	
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9761 (0.9265 to 0.9923)	0.8850 (0.8215 to 0.9269)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9761 (0.9265 to 0.9923)	0.8759 (0.8098 to 0.9201)	
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9761 (0.9265 to 0.9923)	0.8759 (0.8098 to 0.9201)	
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9761 (0.9265 to 0.9923)	0.8759 (0.8098 to 0.9201)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.2 Treatment emergent adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	2	2	138	133	
4 Months	2	2	130	127	
6 Months	1	2	115	112	
8 Months	0	2	105	108	
10 Months	0	2	100	105	
12 Months	0	2	86	92	
14 Months	0	2	54	62	
16 Months	0	0	26	26	
Headache (days)					
Number (%) of events	1 (50.0)	0 (0.0)	7 (4.8)	15 (10.0)	0.9903
Number (%) of patients censored	1 (50.0)	2 (100.0)	140 (95.2)	135 (90.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.9528 (0.9528 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (0.9528 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (0.9528 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.4 Treatment emergent serious adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	0 (0.0)	3 (2.0)	10 (6.7)	0.9997
Number (%) of patients censored	2 (100.0)	2 (100.0)	144 (98.0)	140 (93.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0577	
Hazard ratio (95% CI) vs Pd	-	NC		3.25 (0.90 to 11.82)	
P-value	-			0.0731	
Events probability (95% CI)[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.4 Treatment emergent serious adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.9464 (0.8956 to 0.9728)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.9394 (0.8868 to 0.9680)	
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.9394 (0.8868 to 0.9680)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.9394 (0.8868 to 0.9680)	
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9761 (0.9265 to 0.9923)	0.9394 (0.8868 to 0.9680)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9761 (0.9265 to 0.9923)	0.9300 (0.8732 to 0.9619)	
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9761 (0.9265 to 0.9923)	0.9300 (0.8732 to 0.9619)	
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9761 (0.9265 to 0.9923)	0.9300 (0.8732 to 0.9619)	

Number of patients at risk[b]

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.4 Treatment emergent serious adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	2	2	138	139	
4 Months	2	2	130	130	
6 Months	1	2	115	117	
8 Months	0	2	105	112	
10 Months	0	2	100	108	
12 Months	0	2	86	95	
14 Months	0	2	54	63	
16 Months	0	0	26	27	
Pneumonia (days)					
Number (%) of events	0 (0.0)	0 (0.0)	23 (15.6)	23 (15.3)	1.0000
Number (%) of patients censored	2 (100.0)	2 (100.0)	124 (84.4)	127 (84.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.10 Treatment emergent severe adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	0 (0.0)	0 (0.0)	3 (2.0)	18 (12.0)	0.9995
Number (%) of patients censored	2 (100.0)	2 (100.0)	144 (98.0)	132 (88.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.0010	
Hazard ratio (95% CI) vs Pd	-	NC		6.02 (1.77 to 20.42)	
P-value	-			0.0040	
Hazard ratio inverted (95% CI) vs IPd			0.17 (0.05 to 0.56)		

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.10 Treatment emergent severe adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.9061 (0.8465 to 0.9433)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.8991 (0.8383 to 0.9379)	
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.8850 (0.8215 to 0.9269)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9858 (0.9445 to 0.9964)	0.8850 (0.8215 to 0.9269)	
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9761 (0.9265 to 0.9923)	0.8850 (0.8215 to 0.9269)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9761 (0.9265 to 0.9923)	0.8759 (0.8098 to 0.9201)	
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9761 (0.9265 to 0.9923)	0.8759 (0.8098 to 0.9201)	
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9761 (0.9265 to 0.9923)	0.8759 (0.8098 to 0.9201)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.10 Treatment emergent severe adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	2	2	138	133	
4 Months	2	2	130	127	
6 Months	1	2	115	112	
8 Months	0	2	105	108	
10 Months	0	2	100	105	
12 Months	0	2	86	92	
14 Months	0	2	54	62	
16 Months	0	0	26	26	
Neutropenia (days)					
Number (%) of events	1 (50.0)	0 (0.0)	47 (32.0)	69 (46.0)	0.9827
Number (%) of patients censored	1 (50.0)	2 (100.0)	100 (68.0)	81 (54.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.1643 (0.1643 to NC)	NC (NC to NC)	2.0370 (0.9856 to 4.9938)	0.8542 (0.7556 to 1.0185)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.3 Treatment emergent adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	88	104	31	31	
4 Months	80	96	27	28	
6 Months	72	85	23	25	
8 Months	64	80	20	21	
10 Months	59	72	20	20	
12 Months	50	65	18	18	
14 Months	31	47	9	10	
16 Months	13	23	6	3	
Febrile neutropenia (days)					
Number (%) of events	3 (2.7)	12 (10.3)	0 (0.0)	6 (17.1)	0.9911
Number (%) of patients censored	108 (97.3)	105 (89.7)	38 (100.0)	29 (82.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.5585 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.3 Treatment emergent adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0275		0.0088	
Hazard ratio (95% CI) vs Pd	-	3.76 (1.06 to 13.32)		NC	
P-value	-	0.0403		0.9938	
Hazard ratio inverted (95% CI) vs IPd	0.27 (0.08 to 0.94)				
Events probability (95% CI)[b]					
2 Months	0.9811 (0.9267 to 0.9952)	0.9310 (0.8668 to 0.9649)	1.0000 (1.0000 to 1.0000)	0.8286 (0.6577 to 0.9191)	
4 Months	0.9811 (0.9267 to 0.9952)	0.9222 (0.8559 to 0.9588)	1.0000 (1.0000 to 1.0000)	0.8286 (0.6577 to 0.9191)	
6 Months	0.9811 (0.9267 to 0.9952)	0.9043 (0.8339 to 0.9459)	1.0000 (1.0000 to 1.0000)	0.8286 (0.6577 to 0.9191)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.3 Treatment emergent adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.9811 (0.9267 to 0.9952)	0.9043 (0.8339 to 0.9459)	1.0000 (1.0000 to 1.0000)	0.8286 (0.6577 to 0.9191)	
10 Months	0.9677 (0.9014 to 0.9897)	0.9043 (0.8339 to 0.9459)	1.0000 (1.0000 to 1.0000)	0.8286 (0.6577 to 0.9191)	
12 Months	0.9677 (0.9014 to 0.9897)	0.8929 (0.8186 to 0.9379)	1.0000 (1.0000 to 1.0000)	0.8286 (0.6577 to 0.9191)	
14 Months	0.9677 (0.9014 to 0.9897)	0.8929 (0.8186 to 0.9379)	1.0000 (1.0000 to 1.0000)	0.8286 (0.6577 to 0.9191)	
16 Months	0.9677 (0.9014 to 0.9897)	0.8929 (0.8186 to 0.9379)	1.0000 (1.0000 to 1.0000)	0.8286 (0.6577 to 0.9191)	
Number of patients at risk[b]					
2 Months	103	107	37	28	
4 Months	97	103	35	26	
6 Months	85	90	31	24	
8 Months	77	87	28	23	
10 Months	72	84	28	23	
12 Months	61	75	25	19	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.3 Treatment emergent adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	39	52	15	12	
16 Months	17	23	9	3	
Headache (days)					
Number (%) of events	5 (4.5)	7 (6.0)	3 (7.9)	8 (22.9)	0.4824
Number (%) of patients censored	106 (95.5)	110 (94.0)	35 (92.1)	27 (77.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	12.5503 (5.0595 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4882		0.0935	
Hazard ratio (95% CI) vs Pd	-	1.54 (0.45 to 5.26)		2.95 (0.78 to 11.13)	
P-value	-	0.4916		0.1100	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.5 Treatment emergent serious adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	3 (2.7)	6 (5.1)	0 (0.0)	4 (11.4)	0.9927
Number (%) of patients censored	108 (97.3)	111 (94.9)	38 (100.0)	31 (88.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.6571 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3881		0.0349	
Hazard ratio (95% CI) vs Pd	-	1.82 (0.46 to 7.30)		NC	
P-value	-	0.3952		0.9949	
Events probability (95% CI)[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.5 Treatment emergent serious adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9811 (0.9267 to 0.9952)	0.9655 (0.9107 to 0.9869)	1.0000 (1.0000 to 1.0000)	0.8857 (0.7236 to 0.9555)	
4 Months	0.9811 (0.9267 to 0.9952)	0.9567 (0.8992 to 0.9818)	1.0000 (1.0000 to 1.0000)	0.8857 (0.7236 to 0.9555)	
6 Months	0.9811 (0.9267 to 0.9952)	0.9567 (0.8992 to 0.9818)	1.0000 (1.0000 to 1.0000)	0.8857 (0.7236 to 0.9555)	
8 Months	0.9811 (0.9267 to 0.9952)	0.9567 (0.8992 to 0.9818)	1.0000 (1.0000 to 1.0000)	0.8857 (0.7236 to 0.9555)	
10 Months	0.9677 (0.9014 to 0.9897)	0.9567 (0.8992 to 0.9818)	1.0000 (1.0000 to 1.0000)	0.8857 (0.7236 to 0.9555)	
12 Months	0.9677 (0.9014 to 0.9897)	0.9449 (0.8806 to 0.9751)	1.0000 (1.0000 to 1.0000)	0.8857 (0.7236 to 0.9555)	
14 Months	0.9677 (0.9014 to 0.9897)	0.9449 (0.8806 to 0.9751)	1.0000 (1.0000 to 1.0000)	0.8857 (0.7236 to 0.9555)	
16 Months	0.9677 (0.9014 to 0.9897)	0.9449 (0.8806 to 0.9751)	1.0000 (1.0000 to 1.0000)	0.8857 (0.7236 to 0.9555)	
Number of patients at risk[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_refr4_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.5 Treatment emergent serious adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	103	111	37	30	
4 Months	97	105	35	27	
6 Months	85	94	31	25	
8 Months	77	90	28	24	
10 Months	72	86	28	24	
12 Months	61	77	25	20	
14 Months	39	53	15	12	
16 Months	17	24	9	3	
Pneumonia (days)					
Number (%) of events	17 (15.3)	19 (16.2)	6 (15.8)	4 (11.4)	0.6050
Number (%) of patients censored	94 (84.7)	98 (83.8)	32 (84.2)	31 (88.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (5.6838 to NC)	NC (11.6304 to NC)	NC (2.6283 to NC)	NC (6.2752 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_refr4_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.12 Treatment emergent severe adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	3 (2.7)	12 (10.3)	0 (0.0)	6 (17.1)	0.9911
Number (%) of patients censored	108 (97.3)	105 (89.7)	38 (100.0)	29 (82.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.5585 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0275		0.0088	
Hazard ratio (95% CI) vs Pd	-	3.76 (1.06 to 13.32)		NC	
P-value	-	0.0403		0.9938	
Hazard ratio inverted (95% CI) vs IPd	0.27 (0.08 to 0.94)				

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.12 Treatment emergent severe adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9811 (0.9267 to 0.9952)	0.9310 (0.8668 to 0.9649)	1.0000 (1.0000 to 1.0000)	0.8286 (0.6577 to 0.9191)	
4 Months	0.9811 (0.9267 to 0.9952)	0.9222 (0.8559 to 0.9588)	1.0000 (1.0000 to 1.0000)	0.8286 (0.6577 to 0.9191)	
6 Months	0.9811 (0.9267 to 0.9952)	0.9043 (0.8339 to 0.9459)	1.0000 (1.0000 to 1.0000)	0.8286 (0.6577 to 0.9191)	
8 Months	0.9811 (0.9267 to 0.9952)	0.9043 (0.8339 to 0.9459)	1.0000 (1.0000 to 1.0000)	0.8286 (0.6577 to 0.9191)	
10 Months	0.9677 (0.9014 to 0.9897)	0.9043 (0.8339 to 0.9459)	1.0000 (1.0000 to 1.0000)	0.8286 (0.6577 to 0.9191)	
12 Months	0.9677 (0.9014 to 0.9897)	0.8929 (0.8186 to 0.9379)	1.0000 (1.0000 to 1.0000)	0.8286 (0.6577 to 0.9191)	
14 Months	0.9677 (0.9014 to 0.9897)	0.8929 (0.8186 to 0.9379)	1.0000 (1.0000 to 1.0000)	0.8286 (0.6577 to 0.9191)	
16 Months	0.9677 (0.9014 to 0.9897)	0.8929 (0.8186 to 0.9379)	1.0000 (1.0000 to 1.0000)	0.8286 (0.6577 to 0.9191)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.12 Treatment emergent severe adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	103	107	37	28	
4 Months	97	103	35	26	
6 Months	85	90	31	24	
8 Months	77	87	28	23	
10 Months	72	84	28	23	
12 Months	61	75	25	19	
14 Months	39	52	15	12	
16 Months	17	23	9	3	
Neutropenia (days)					
Number (%) of events	38 (34.2)	54 (46.2)	10 (26.3)	15 (42.9)	0.4372
Number (%) of patients censored	73 (65.8)	63 (53.8)	28 (73.7)	20 (57.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.4127 (0.7885 to 3.3840)	0.8542 (0.7556 to 1.0185)	4.9938 (1.4456 to NC)	0.7556 (0.5257 to 2.1027)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.2 Treatment emergent adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	112	129	7	6	
4 Months	102	118	5	6	
6 Months	90	104	5	6	
8 Months	81	98	3	3	
10 Months	76	89	3	3	
12 Months	65	80	3	3	
14 Months	39	55	1	2	
16 Months	18	26	1	0	
Febrile neutropenia (days)					
Number (%) of events	3 (2.1)	17 (11.7)	0 (0.0)	1 (14.3)	0.9930
Number (%) of patients censored	137 (97.9)	128 (88.3)	9 (100.0)	6 (85.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.3039 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.3039 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.2 Treatment emergent adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0020		0.2568	
Hazard ratio (95% CI) vs Pd	-	5.57 (1.63 to 19.02)		NC	
P-value	-	0.0061		0.9984	
Hazard ratio inverted (95% CI) vs IPd	0.18 (0.05 to 0.61)				
Events probability (95% CI)[b]					
2 Months	0.9851 (0.9416 to 0.9962)	0.9028 (0.8414 to 0.9413)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9851 (0.9416 to 0.9962)	0.8956 (0.8329 to 0.9357)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9851 (0.9416 to 0.9962)	0.8883 (0.8241 to 0.9300)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
8 Months	0.9851 (0.9416 to 0.9962)	0.8883 (0.8241 to 0.9300)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.2 Treatment emergent adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.9744 (0.9212 to 0.9918)	0.8883 (0.8241 to 0.9300)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
12 Months	0.9744 (0.9212 to 0.9918)	0.8788 (0.8119 to 0.9231)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
14 Months	0.9744 (0.9212 to 0.9918)	0.8788 (0.8119 to 0.9231)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
16 Months	0.9744 (0.9212 to 0.9918)	0.8788 (0.8119 to 0.9231)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
Number of patients at risk[b]					
2 Months	131	128	9	7	
4 Months	123	122	9	7	
6 Months	107	108	9	6	
8 Months	96	105	9	5	
10 Months	91	102	9	5	
12 Months	78	89	8	5	
14 Months	49	61	5	3	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.2 Treatment emergent adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	24	26	2	0	
Headache (days)					
Number (%) of events	7 (5.0)	13 (9.0)	1 (11.1)	2 (28.6)	0.7585
Number (%) of patients censored	133 (95.0)	132 (91.0)	8 (88.9)	5 (71.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.7823 to NC)	8.0164 (5.6181 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.7823 to NC)	NC (5.6181 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.0164 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1695		0.3245	
Hazard ratio (95% CI) vs Pd	-	1.95 (0.74 to 5.12)		3.15 (0.28 to 35.09)	
P-value	-	0.1775		0.3502	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.4 Treatment emergent serious adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	3 (2.1)	10 (6.9)	0 (0.0)	0 (0.0)	0.9997
Number (%) of patients censored	137 (97.9)	135 (93.1)	9 (100.0)	7 (100.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0632			
Hazard ratio (95% CI) vs Pd	-	3.18 (0.88 to 11.56)		NC	
P-value	-	0.0788			
Events probability (95% CI)[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.4 Treatment emergent serious adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9851 (0.9416 to 0.9962)	0.9445 (0.8921 to 0.9718)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9851 (0.9416 to 0.9962)	0.9373 (0.8829 to 0.9669)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9851 (0.9416 to 0.9962)	0.9373 (0.8829 to 0.9669)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
8 Months	0.9851 (0.9416 to 0.9962)	0.9373 (0.8829 to 0.9669)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
10 Months	0.9744 (0.9212 to 0.9918)	0.9373 (0.8829 to 0.9669)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
12 Months	0.9744 (0.9212 to 0.9918)	0.9276 (0.8690 to 0.9606)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
14 Months	0.9744 (0.9212 to 0.9918)	0.9276 (0.8690 to 0.9606)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
16 Months	0.9744 (0.9212 to 0.9918)	0.9276 (0.8690 to 0.9606)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	

Number of patients at risk[b]

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.4 Treatment emergent serious adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	131	134	9	7	
4 Months	123	125	9	7	
6 Months	107	112	9	7	
8 Months	96	109	9	5	
10 Months	91	105	9	5	
12 Months	78	92	8	5	
14 Months	49	62	5	3	
16 Months	24	27	2	0	
Pneumonia (days)					
Number (%) of events	21 (15.0)	22 (15.2)	2 (22.2)	1 (14.3)	0.7585
Number (%) of patients censored	119 (85.0)	123 (84.8)	7 (77.8)	6 (85.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.1971 to NC)	NC (0.2628 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.1971 to NC)	NC (0.2628 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_refr1_s_t_x.rtf (16FEB2021 22:49)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.10 Treatment emergent severe adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	3 (2.1)	17 (11.7)	0 (0.0)	1 (14.3)	0.9930
Number (%) of patients censored	137 (97.9)	128 (88.3)	9 (100.0)	6 (85.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.3039 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.3039 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0020		0.2568	
Hazard ratio (95% CI) vs Pd	-	5.57 (1.63 to 19.02)		NC	
P-value	-	0.0061		0.9984	
Hazard ratio inverted (95% CI) vs IPd	0.18 (0.05 to 0.61)				

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_refr1_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.10 Treatment emergent severe adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9851 (0.9416 to 0.9962)	0.9028 (0.8414 to 0.9413)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9851 (0.9416 to 0.9962)	0.8956 (0.8329 to 0.9357)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9851 (0.9416 to 0.9962)	0.8883 (0.8241 to 0.9300)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
8 Months	0.9851 (0.9416 to 0.9962)	0.8883 (0.8241 to 0.9300)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
10 Months	0.9744 (0.9212 to 0.9918)	0.8883 (0.8241 to 0.9300)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
12 Months	0.9744 (0.9212 to 0.9918)	0.8788 (0.8119 to 0.9231)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
14 Months	0.9744 (0.9212 to 0.9918)	0.8788 (0.8119 to 0.9231)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
16 Months	0.9744 (0.9212 to 0.9918)	0.8788 (0.8119 to 0.9231)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.10 Treatment emergent severe adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	131	128	9	7	
4 Months	123	122	9	7	
6 Months	107	108	9	6	
8 Months	96	105	9	5	
10 Months	91	102	9	5	
12 Months	78	89	8	5	
14 Months	49	61	5	3	
16 Months	24	26	2	0	
Neutropenia (days)					
Number (%) of events	43 (30.7)	65 (44.8)	5 (55.6)	4 (57.1)	0.5738
Number (%) of patients censored	97 (69.3)	80 (55.2)	4 (44.4)	3 (42.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.8255 (0.9856 to 7.6222)	0.8542 (0.7556 to 1.0185)	0.9856 (0.5914 to 4.6653)	0.7228 (0.5585 to 9.3306)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.3 Treatment emergent adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	72	84	47	51	
4 Months	66	74	41	50	
6 Months	59	65	36	45	
8 Months	52	59	32	42	
10 Months	52	54	27	38	
12 Months	45	52	23	31	
14 Months	28	33	12	24	
16 Months	12	13	7	13	
Febrile neutropenia (days)					
Number (%) of events	3 (3.4)	13 (14.3)	0 (0.0)	5 (8.2)	0.9893
Number (%) of patients censored	84 (96.6)	78 (85.7)	62 (100.0)	56 (91.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.3 Treatment emergent adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0120		0.0272	
Hazard ratio (95% CI) vs Pd	-	4.36 (1.24 to 15.30)		NC	
P-value	-	0.0215		0.9944	
Hazard ratio inverted (95% CI) vs IPd	0.23 (0.07 to 0.80)				
Events probability (95% CI)[b]					
2 Months	0.9762 (0.9081 to 0.9940)	0.8669 (0.7774 to 0.9221)	1.0000 (1.0000 to 1.0000)	0.9672 (0.8752 to 0.9917)	
4 Months	0.9762 (0.9081 to 0.9940)	0.8669 (0.7774 to 0.9221)	1.0000 (1.0000 to 1.0000)	0.9505 (0.8544 to 0.9838)	
6 Months	0.9762 (0.9081 to 0.9940)	0.8669 (0.7774 to 0.9221)	1.0000 (1.0000 to 1.0000)	0.9166 (0.8111 to 0.9644)	
8 Months	0.9762 (0.9081 to 0.9940)	0.8669 (0.7774 to 0.9221)	1.0000 (1.0000 to 1.0000)	0.9166 (0.8111 to 0.9644)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.3 Treatment emergent adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.9602 (0.8801 to 0.9872)	0.8669 (0.7774 to 0.9221)	1.0000 (1.0000 to 1.0000)	0.9166 (0.8111 to 0.9644)	
12 Months	0.9602 (0.8801 to 0.9872)	0.8519 (0.7579 to 0.9115)	1.0000 (1.0000 to 1.0000)	0.9166 (0.8111 to 0.9644)	
14 Months	0.9602 (0.8801 to 0.9872)	0.8519 (0.7579 to 0.9115)	1.0000 (1.0000 to 1.0000)	0.9166 (0.8111 to 0.9644)	
16 Months	0.9602 (0.8801 to 0.9872)	0.8519 (0.7579 to 0.9115)	1.0000 (1.0000 to 1.0000)	0.9166 (0.8111 to 0.9644)	
Number of patients at risk[b]					
2 Months	81	77	59	58	
4 Months	77	73	55	56	
6 Months	69	65	47	49	
8 Months	61	63	44	47	
10 Months	60	62	40	45	
12 Months	52	56	34	38	
14 Months	33	37	21	27	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.3 Treatment emergent adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	15	14	11	12	
Headache (days)					
Number (%) of events	5 (5.7)	10 (11.0)	3 (4.8)	5 (8.2)	0.6611
Number (%) of patients censored	82 (94.3)	81 (89.0)	59 (95.2)	56 (91.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1450		0.5450	
Hazard ratio (95% CI) vs Pd	-	2.31 (0.72 to 7.37)		1.55 (0.37 to 6.49)	
P-value	-	0.1569		0.5482	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.7 Treatment emergent serious adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	3 (3.4)	8 (8.8)	0 (0.0)	2 (3.3)	0.9915
Number (%) of patients censored	84 (96.6)	83 (91.2)	62 (100.0)	59 (96.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1431		0.1645	
Hazard ratio (95% CI) vs Pd	-	2.60 (0.69 to 9.79)		NC	
P-value	-	0.1585		0.9964	
Events probability (95% CI)[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.7 Treatment emergent serious adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9762 (0.9081 to 0.9940)	0.9223 (0.8440 to 0.9622)	1.0000 (1.0000 to 1.0000)	0.9836 (0.8893 to 0.9977)	
4 Months	0.9762 (0.9081 to 0.9940)	0.9223 (0.8440 to 0.9622)	1.0000 (1.0000 to 1.0000)	0.9669 (0.8742 to 0.9916)	
6 Months	0.9762 (0.9081 to 0.9940)	0.9223 (0.8440 to 0.9622)	1.0000 (1.0000 to 1.0000)	0.9669 (0.8742 to 0.9916)	
8 Months	0.9762 (0.9081 to 0.9940)	0.9223 (0.8440 to 0.9622)	1.0000 (1.0000 to 1.0000)	0.9669 (0.8742 to 0.9916)	
10 Months	0.9602 (0.8801 to 0.9872)	0.9223 (0.8440 to 0.9622)	1.0000 (1.0000 to 1.0000)	0.9669 (0.8742 to 0.9916)	
12 Months	0.9602 (0.8801 to 0.9872)	0.9070 (0.8215 to 0.9527)	1.0000 (1.0000 to 1.0000)	0.9669 (0.8742 to 0.9916)	
14 Months	0.9602 (0.8801 to 0.9872)	0.9070 (0.8215 to 0.9527)	1.0000 (1.0000 to 1.0000)	0.9669 (0.8742 to 0.9916)	
16 Months	0.9602 (0.8801 to 0.9872)	0.9070 (0.8215 to 0.9527)	1.0000 (1.0000 to 1.0000)	0.9669 (0.8742 to 0.9916)	
Number of patients at risk[b]					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.7 Treatment emergent serious adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	81	82	59	59	
4 Months	77	75	55	57	
6 Months	69	67	47	52	
8 Months	61	65	44	49	
10 Months	60	64	40	46	
12 Months	52	58	34	39	
14 Months	33	37	21	28	
16 Months	15	14	11	13	
Pneumonia (days)					
Number (%) of events	12 (13.8)	13 (14.3)	11 (17.7)	10 (16.4)	0.7851
Number (%) of patients censored	75 (86.2)	78 (85.7)	51 (82.3)	51 (83.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (8.5092 to NC)	NC (4.1396 to NC)	NC (4.7310 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.16 Treatment emergent severe adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Febrile neutropenia (days)					
Number (%) of events	3 (3.4)	13 (14.3)	0 (0.0)	5 (8.2)	0.9893
Number (%) of patients censored	84 (96.6)	78 (85.7)	62 (100.0)	56 (91.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0120		0.0272	
Hazard ratio (95% CI) vs Pd	-	4.36 (1.24 to 15.30)		NC	
P-value	-	0.0215		0.9944	
Hazard ratio inverted (95% CI) vs IPd	0.23 (0.07 to 0.80)				

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_llen_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.16 Treatment emergent severe adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9762 (0.9081 to 0.9940)	0.8669 (0.7774 to 0.9221)	1.0000 (1.0000 to 1.0000)	0.9672 (0.8752 to 0.9917)	
4 Months	0.9762 (0.9081 to 0.9940)	0.8669 (0.7774 to 0.9221)	1.0000 (1.0000 to 1.0000)	0.9505 (0.8544 to 0.9838)	
6 Months	0.9762 (0.9081 to 0.9940)	0.8669 (0.7774 to 0.9221)	1.0000 (1.0000 to 1.0000)	0.9166 (0.8111 to 0.9644)	
8 Months	0.9762 (0.9081 to 0.9940)	0.8669 (0.7774 to 0.9221)	1.0000 (1.0000 to 1.0000)	0.9166 (0.8111 to 0.9644)	
10 Months	0.9602 (0.8801 to 0.9872)	0.8669 (0.7774 to 0.9221)	1.0000 (1.0000 to 1.0000)	0.9166 (0.8111 to 0.9644)	
12 Months	0.9602 (0.8801 to 0.9872)	0.8519 (0.7579 to 0.9115)	1.0000 (1.0000 to 1.0000)	0.9166 (0.8111 to 0.9644)	
14 Months	0.9602 (0.8801 to 0.9872)	0.8519 (0.7579 to 0.9115)	1.0000 (1.0000 to 1.0000)	0.9166 (0.8111 to 0.9644)	
16 Months	0.9602 (0.8801 to 0.9872)	0.8519 (0.7579 to 0.9115)	1.0000 (1.0000 to 1.0000)	0.9166 (0.8111 to 0.9644)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.16 Treatment emergent severe adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	81	77	59	58	
4 Months	77	73	55	56	
6 Months	69	65	47	49	
8 Months	61	63	44	47	
10 Months	60	62	40	45	
12 Months	52	56	34	38	
14 Months	33	37	21	27	
16 Months	15	14	11	12	
Neutropenia (days)					
Number (%) of events	27 (31.0)	41 (45.1)	21 (33.9)	28 (45.9)	0.7359
Number (%) of patients censored	60 (69.0)	50 (54.9)	41 (66.1)	33 (54.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.9055 (0.7885 to NC)	0.8214 (0.6899 to 1.4127)	2.0370 (0.9856 to 4.6653)	0.9199 (0.7556 to 1.4784)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	63	48	47	57	25	27	
4 Months	58	45	42	55	23	22	
6 Months	49	40	39	50	17	21	
8 Months	44	36	36	48	16	21	
10 Months	42	34	35	44	14	20	
12 Months	37	31	30	38	10	18	
14 Months	22	19	19	25	7	14	
16 Months	12	10	8	11	4	4	
Neutropenia (days)							
Number (%) of events	19 (27.9)	24 (44.4)	18 (34.0)	30 (45.5)	13 (46.4)	17 (53.1)	0.5666
Number (%) of patients censored	49 (72.1)	30 (55.6)	35 (66.0)	36 (54.5)	15 (53.6)	15 (46.9)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	4.9938 (1.1499 to NC)	0.8214 (0.5914 to 1.9384)	1.8398 (0.7556 to NC)	0.9856 (0.7885 to 1.9055)	0.7721 (0.2300 to 4.3039)	0.7885 (0.5257 to 0.9199)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (1.9384 to NC)	NC (4.5010 to NC)	NC (3.0554 to NC)	NC (0.9856 to NC)	4.4353 (0.8214 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0310		0.2848		0.7130	
Hazard ratio (95% CI) vs Pd	-	1.92 (1.05 to 3.51)		1.37 (0.77 to 2.46)		1.15 (0.56 to 2.36)	
P-value	-	0.0341		0.2868		0.7132	
Hazard ratio inverted (95% CI) vs IPd	0.52 (0.29 to 0.95)						
Events probability (95% CI)[b]							
2 Months	0.8209 (0.7062 to 0.8941)	0.6286 (0.4854 to 0.7421)	0.7236 (0.5782 to 0.8261)	0.6465 (0.5175 to 0.7491)	0.6429 (0.4381 to 0.7894)	0.5313 (0.3471 to 0.6852)	
4 Months	0.7750 (0.6547 to 0.8578)	0.5511 (0.4085 to 0.6727)	0.6615 (0.5127 to 0.7744)	0.6157 (0.4864 to 0.7215)	0.6027 (0.3976 to 0.7573)	0.5313 (0.3471 to 0.6852)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.7209 (0.5930 to 0.8147)	0.5511 (0.4085 to 0.6727)	0.6402 (0.4907 to 0.7562)	0.6157 (0.4864 to 0.7215)	0.5130 (0.3089 to 0.6844)	0.4958 (0.3137 to 0.6541)	
8 Months	0.7003 (0.5692 to 0.7984)	0.5511 (0.4085 to 0.6727)	0.6402 (0.4907 to 0.7562)	0.5805 (0.4501 to 0.6903)	0.5130 (0.3089 to 0.6844)	0.4958 (0.3137 to 0.6541)	
10 Months	0.7003 (0.5692 to 0.7984)	0.5511 (0.4085 to 0.6727)	0.6402 (0.4907 to 0.7562)	0.5418 (0.4101 to 0.6561)	0.5130 (0.3089 to 0.6844)	0.4958 (0.3137 to 0.6541)	
12 Months	0.7003 (0.5692 to 0.7984)	0.5511 (0.4085 to 0.6727)	0.6402 (0.4907 to 0.7562)	0.5418 (0.4101 to 0.6561)	0.5130 (0.3089 to 0.6844)	0.4545 (0.2737 to 0.6188)	
14 Months	0.7003 (0.5692 to 0.7984)	0.5511 (0.4085 to 0.6727)	0.6402 (0.4907 to 0.7562)	0.5117 (0.3750 to 0.6328)	0.5130 (0.3089 to 0.6844)	0.4545 (0.2737 to 0.6188)	
16 Months	0.7003 (0.5692 to 0.7984)	0.5511 (0.4085 to 0.6727)	0.6402 (0.4907 to 0.7562)	0.5117 (0.3750 to 0.6328)	0.5130 (0.3089 to 0.6844)	0.4545 (0.2737 to 0.6188)	
Number of patients at risk[b]							
2 Months	55	33	36	42	18	17	
4 Months	48	26	31	40	15	15	
6 Months	38	23	29	35	11	12	
8 Months	34	20	26	33	9	12	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	32	18	26	27	9	12	
12 Months	30	16	23	25	6	10	
14 Months	20	12	15	15	3	7	
16 Months	14	4	7	7	2	3	
Oedema peripheral (days)							
Number (%) of events	6 (8.8)	6 (11.1)	7 (13.2)	8 (12.1)	3 (10.7)	6 (18.8)	0.7936
Number (%) of patients censored	62 (91.2)	48 (88.9)	46 (86.8)	58 (87.9)	25 (89.3)	26 (81.3)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (9.5277 to NC)	NC (8.1150 to NC)	NC (NC to NC)	NC (1.0842 to NC)	NC (2.1355 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.7627		0.7180		0.5787	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.14 Treatment emergent severe adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	65	47	49	59	26	29	
4 Months	61	44	47	59	24	26	
6 Months	54	39	44	51	18	24	
8 Months	49	35	40	51	16	24	
10 Months	46	34	39	49	15	24	
12 Months	41	30	34	43	11	21	
14 Months	25	20	21	29	8	15	
16 Months	14	9	8	13	4	4	
Neutropenia (days)							
Number (%) of events	18 (26.5)	24 (44.4)	17 (32.1)	29 (43.9)	13 (46.4)	16 (50.0)	0.4497
Number (%) of patients censored	50 (73.5)	30 (55.6)	36 (67.9)	37 (56.1)	15 (53.6)	16 (50.0)	
Kaplan-Meier estimates of event in months							

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.14 Treatment emergent severe adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	4.9938 (1.1499 to NC)	0.8214 (0.5914 to 1.9384)	1.8398 (0.7556 to NC)	0.9856 (0.7885 to 2.7926)	0.7721 (0.2300 to 4.3039)	0.7885 (0.5257 to 0.9199)	
Median (95% CI)	NC (NC to NC)	NC (1.9384 to NC)	NC (NC to NC)	NC (6.0780 to NC)	NC (0.9856 to NC)	10.4476 (0.8214 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0214		0.2596		0.8460	
Hazard ratio (95% CI) vs Pd	-	2.02 (1.10 to 3.73)		1.41 (0.77 to 2.56)		1.08 (0.52 to 2.24)	
P-value	-	0.0242		0.2619		0.8464	
Hazard ratio inverted (95% CI) vs IPd	0.49 (0.27 to 0.91)						
Events probability (95% CI)[b]							
2 Months	0.8209 (0.7062 to 0.8941)	0.6286 (0.4854 to 0.7421)	0.7236 (0.5782 to 0.8261)	0.6612 (0.5323 to 0.7622)	0.6429 (0.4381 to 0.7894)	0.5313 (0.3471 to 0.6852)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.14 Treatment emergent severe adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	0.7750 (0.6547 to 0.8578)	0.5511 (0.4085 to 0.6727)	0.6615 (0.5127 to 0.7744)	0.6297 (0.5001 to 0.7343)	0.6027 (0.3976 to 0.7573)	0.5313 (0.3471 to 0.6852)	
6 Months	0.7389 (0.6132 to 0.8293)	0.5511 (0.4085 to 0.6727)	0.6615 (0.5127 to 0.7744)	0.6297 (0.5001 to 0.7343)	0.5130 (0.3089 to 0.6844)	0.5313 (0.3471 to 0.6852)	
8 Months	0.7184 (0.5891 to 0.8133)	0.5511 (0.4085 to 0.6727)	0.6615 (0.5127 to 0.7744)	0.5937 (0.4626 to 0.7029)	0.5130 (0.3089 to 0.6844)	0.5313 (0.3471 to 0.6852)	
10 Months	0.7184 (0.5891 to 0.8133)	0.5511 (0.4085 to 0.6727)	0.6615 (0.5127 to 0.7744)	0.5541 (0.4212 to 0.6682)	0.5130 (0.3089 to 0.6844)	0.5313 (0.3471 to 0.6852)	
12 Months	0.7184 (0.5891 to 0.8133)	0.5511 (0.4085 to 0.6727)	0.6615 (0.5127 to 0.7744)	0.5541 (0.4212 to 0.6682)	0.5130 (0.3089 to 0.6844)	0.4870 (0.3015 to 0.6494)	
14 Months	0.7184 (0.5891 to 0.8133)	0.5511 (0.4085 to 0.6727)	0.6615 (0.5127 to 0.7744)	0.5233 (0.3848 to 0.6446)	0.5130 (0.3089 to 0.6844)	0.4870 (0.3015 to 0.6494)	
16 Months	0.7184 (0.5891 to 0.8133)	0.5511 (0.4085 to 0.6727)	0.6615 (0.5127 to 0.7744)	0.5233 (0.3848 to 0.6446)	0.5130 (0.3089 to 0.6844)	0.4870 (0.3015 to 0.6494)	
Number of patients at risk[b]							
2 Months	55	33	36	42	18	17	
4 Months	48	26	31	40	15	15	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_age_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.14 Treatment emergent severe adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	39	23	30	35	11	13	
8 Months	35	20	27	33	9	13	
10 Months	33	18	27	27	9	12	
12 Months	30	16	24	25	6	10	
14 Months	20	12	15	15	3	7	
16 Months	14	4	7	7	2	3	
Pneumonia (days)							
Number (%) of events	14 (20.6)	7 (13.0)	6 (11.3)	14 (21.2)	2 (7.1)	4 (12.5)	0.2340
Number (%) of patients censored	54 (79.4)	47 (87.0)	47 (88.7)	52 (78.8)	26 (92.9)	28 (87.5)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (2.7598 to NC)	NC (2.6283 to NC)	NC (5.6838 to NC)	NC (5.1253 to NC)	NC (1.6756 to NC)	NC (2.8583 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_age_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.2 Treatment emergent adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	89	89	46	43	
4 Months	81	80	42	42	
6 Months	70	74	35	37	
8 Months	66	71	30	34	
10 Months	65	66	26	32	
12 Months	53	60	24	27	
14 Months	33	41	15	17	
16 Months	14	18	10	7	
Neutropenia (days)					
Number (%) of events	35 (35.0)	46 (45.5)	15 (30.6)	25 (49.0)	0.4629
Number (%) of patients censored	65 (65.0)	55 (54.5)	34 (69.4)	26 (51.0)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_plne_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.2 Treatment emergent adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	1.5441 (0.7885 to 4.9938)	0.8542 (0.7556 to 1.4456)	2.4312 (0.7885 to NC)	0.8214 (0.5914 to 1.0185)	
Median (95% CI)	NC (NC to NC)	NC (2.7926 to NC)	NC (NC to NC)	13.8645 (1.0185 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1431		0.0498	
Hazard ratio (95% CI) vs Pd	-	1.39 (0.89 to 2.15)		1.88 (0.99 to 3.57)	
P-value	-	0.1449		0.0536	
Events probability (95% CI)[b]					
2 Months	0.7447 (0.6459 to 0.8197)	0.6301 (0.5277 to 0.7163)	0.7708 (0.6245 to 0.8660)	0.5876 (0.4405 to 0.7083)	
4 Months	0.6905 (0.5879 to 0.7725)	0.5891 (0.4861 to 0.6783)	0.7279 (0.5779 to 0.8320)	0.5471 (0.4009 to 0.6716)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_plne_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.2 Treatment emergent adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.6421 (0.5360 to 0.7299)	0.5782 (0.4750 to 0.6682)	0.6817 (0.5278 to 0.7947)	0.5471 (0.4009 to 0.6716)	
8 Months	0.6292 (0.5223 to 0.7186)	0.5528 (0.4484 to 0.6453)	0.6817 (0.5278 to 0.7947)	0.5471 (0.4009 to 0.6716)	
10 Months	0.6292 (0.5223 to 0.7186)	0.5244 (0.4185 to 0.6199)	0.6817 (0.5278 to 0.7947)	0.5471 (0.4009 to 0.6716)	
12 Months	0.6292 (0.5223 to 0.7186)	0.5244 (0.4185 to 0.6199)	0.6817 (0.5278 to 0.7947)	0.5197 (0.3720 to 0.6484)	
14 Months	0.6292 (0.5223 to 0.7186)	0.5244 (0.4185 to 0.6199)	0.6817 (0.5278 to 0.7947)	0.4677 (0.3046 to 0.6153)	
16 Months	0.6292 (0.5223 to 0.7186)	0.5244 (0.4185 to 0.6199)	0.6817 (0.5278 to 0.7947)	0.4677 (0.3046 to 0.6153)	
Number of patients at risk[b]					
2 Months	72	63	37	29	
4 Months	62	54	32	27	
6 Months	52	46	26	24	
8 Months	47	43	22	22	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.2 Treatment emergent adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	47	37	20	20	
12 Months	40	35	19	16	
14 Months	25	25	13	9	
16 Months	15	12	8	2	
Oedema peripheral (days)					
Number (%) of events	11 (11.0)	12 (11.9)	5 (10.2)	8 (15.7)	0.6683
Number (%) of patients censored	89 (89.0)	89 (88.1)	44 (89.8)	43 (84.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.1992 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9918		0.6204	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.12 Treatment emergent severe adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	92	87	48	48	
4 Months	87	81	45	48	
6 Months	78	72	38	42	
8 Months	72	71	33	39	
10 Months	70	69	30	38	
12 Months	59	62	27	32	
14 Months	37	42	17	22	
16 Months	16	18	10	8	
Neutropenia (days)					
Number (%) of events	34 (34.0)	44 (43.6)	14 (28.6)	25 (49.0)	0.3485
Number (%) of patients censored	66 (66.0)	57 (56.4)	35 (71.4)	26 (51.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.5441 (0.7885 to 4.9938)	0.8542 (0.7556 to 1.8398)	2.4312 (0.7885 to NC)	0.8214 (0.5914 to 1.0185)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_plne_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.12 Treatment emergent severe adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (3.0554 to NC)	NC (NC to NC)	13.8645 (1.0185 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1738		0.0324	
Hazard ratio (95% CI) vs Pd	-	1.36 (0.87 to 2.13)		2.02 (1.05 to 3.88)	
P-value	-	0.1756		0.0360	
Hazard ratio inverted (95% CI) vs IPd			0.50 (0.26 to 0.96)		
Events probability (95% CI)[b]					
2 Months	0.7447 (0.6459 to 0.8197)	0.6397 (0.5373 to 0.7252)	0.7708 (0.6245 to 0.8660)	0.5876 (0.4405 to 0.7083)	
4 Months	0.6905 (0.5879 to 0.7725)	0.5980 (0.4948 to 0.6869)	0.7279 (0.5779 to 0.8320)	0.5471 (0.4009 to 0.6716)	
6 Months	0.6542 (0.5488 to 0.7407)	0.5980 (0.4948 to 0.6869)	0.7052 (0.5532 to 0.8138)	0.5471 (0.4009 to 0.6716)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.12 Treatment emergent severe adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.6413 (0.5350 to 0.7295)	0.5723 (0.4676 to 0.6638)	0.7052 (0.5532 to 0.8138)	0.5471 (0.4009 to 0.6716)	
10 Months	0.6413 (0.5350 to 0.7295)	0.5430 (0.4361 to 0.6380)	0.7052 (0.5532 to 0.8138)	0.5471 (0.4009 to 0.6716)	
12 Months	0.6413 (0.5350 to 0.7295)	0.5430 (0.4361 to 0.6380)	0.7052 (0.5532 to 0.8138)	0.5197 (0.3720 to 0.6484)	
14 Months	0.6413 (0.5350 to 0.7295)	0.5430 (0.4361 to 0.6380)	0.7052 (0.5532 to 0.8138)	0.4677 (0.3046 to 0.6153)	
16 Months	0.6413 (0.5350 to 0.7295)	0.5430 (0.4361 to 0.6380)	0.7052 (0.5532 to 0.8138)	0.4677 (0.3046 to 0.6153)	
Number of patients at risk[b]					
2 Months	72	63	37	29	
4 Months	62	54	32	27	
6 Months	53	47	27	24	
8 Months	48	44	23	22	
10 Months	48	37	21	20	
12 Months	40	35	20	16	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.12 Treatment emergent severe adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	25	25	13	9	
16 Months	15	12	8	2	
Pneumonia (days)					
Number (%) of events	13 (13.0)	16 (15.8)	9 (18.4)	9 (17.6)	0.6248
Number (%) of patients censored	87 (87.0)	85 (84.2)	40 (81.6)	42 (82.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.6304 to NC)	NC (2.0370 to NC)	NC (4.2710 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6248		0.7914	
Hazard ratio (95% CI) vs Pd	-	1.20 (0.58 to 2.49)		0.88 (0.35 to 2.22)	
P-value	-	0.6253		0.7910	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.3 Treatment emergent adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.9242 (0.8273 to 0.9677)	0.8652 (0.7683 to 0.9235)	0.8685 (0.7600 to 0.9302)	0.8085 (0.6871 to 0.8866)	
Number of patients at risk[b]					
2 Months	61	78	74	54	
4 Months	57	73	66	49	
6 Months	50	66	55	45	
8 Months	49	63	47	42	
10 Months	46	58	45	40	
12 Months	37	50	40	37	
14 Months	23	31	25	27	
16 Months	14	16	10	9	
Neutropenia (days)					
Number (%) of events	19 (27.9)	36 (40.9)	31 (38.3)	35 (54.7)	0.8255
Number (%) of patients censored	49 (72.1)	52 (59.1)	50 (61.7)	29 (45.3)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.3 Treatment emergent adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	3.3840 (1.1170 to NC)	0.9856 (0.7556 to 2.0370)	1.1499 (0.7228 to 4.3039)	0.8214 (0.5585 to 0.9199)	
Median (95% CI)	NC (NC to NC)	NC (3.0554 to NC)	NC (4.9938 to NC)	6.0780 (0.9528 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0605		0.0873	
Hazard ratio (95% CI) vs Pd	-	1.69 (0.97 to 2.95)		1.52 (0.94 to 2.47)	
P-value	-	0.0636		0.0896	
Events probability (95% CI)[b]					
2 Months	0.8060 (0.6894 to 0.8824)	0.6663 (0.5566 to 0.7547)	0.7085 (0.5946 to 0.7958)	0.5469 (0.4176 to 0.6590)	
4 Months	0.7442 (0.6211 to 0.8326)	0.6065 (0.4952 to 0.7006)	0.6681 (0.5518 to 0.7606)	0.5313 (0.4025 to 0.6443)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_sex_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.3 Treatment emergent adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.7096 (0.5827 to 0.8043)	0.6065 (0.4952 to 0.7006)	0.6066 (0.4864 to 0.7070)	0.5141 (0.3857 to 0.6284)	
8 Months	0.7096 (0.5827 to 0.8043)	0.6065 (0.4952 to 0.7006)	0.5888 (0.4671 to 0.6917)	0.4728 (0.3437 to 0.5914)	
10 Months	0.7096 (0.5827 to 0.8043)	0.5754 (0.4618 to 0.6734)	0.5888 (0.4671 to 0.6917)	0.4728 (0.3437 to 0.5914)	
12 Months	0.7096 (0.5827 to 0.8043)	0.5754 (0.4618 to 0.6734)	0.5888 (0.4671 to 0.6917)	0.4503 (0.3209 to 0.5712)	
14 Months	0.7096 (0.5827 to 0.8043)	0.5754 (0.4618 to 0.6734)	0.5888 (0.4671 to 0.6917)	0.4128 (0.2768 to 0.5437)	
16 Months	0.7096 (0.5827 to 0.8043)	0.5754 (0.4618 to 0.6734)	0.5888 (0.4671 to 0.6917)	0.4128 (0.2768 to 0.5437)	
Number of patients at risk[b]					
2 Months	54	57	55	35	
4 Months	47	50	47	31	
6 Months	40	44	38	26	
8 Months	38	43	31	22	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.3 Treatment emergent adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	36	36	31	21	
12 Months	30	32	29	19	
14 Months	21	23	17	11	
16 Months	14	10	9	4	
Oedema peripheral (days)					
Number (%) of events	7 (10.3)	12 (13.6)	9 (11.1)	8 (12.5)	0.7237
Number (%) of patients censored	61 (89.7)	76 (86.4)	72 (88.9)	56 (87.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (10.7762 to NC)	NC (NC to NC)	NC (9.5277 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6311		0.9630	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_sex_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.15 Treatment emergent severe adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	64	76	76	59	
4 Months	61	74	71	55	
6 Months	55	64	61	50	
8 Months	53	62	52	48	
10 Months	50	59	50	48	
12 Months	41	52	45	42	
14 Months	27	34	27	30	
16 Months	15	15	11	11	
Neutropenia (days)					
Number (%) of events	18 (26.5)	36 (40.9)	30 (37.0)	33 (51.6)	0.6608
Number (%) of patients censored	50 (73.5)	52 (59.1)	51 (63.0)	31 (48.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	3.3840 (1.1170 to NC)	0.9856 (0.7556 to 2.0370)	1.1499 (0.7228 to 4.3039)	0.8214 (0.5585 to 0.9199)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_sex_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.15 Treatment emergent severe adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (3.0554 to NC)	NC (7.6222 to NC)	10.4476 (0.9528 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0413		0.1223	
Hazard ratio (95% CI) vs Pd	-	1.79 (1.02 to 3.15)		1.47 (0.90 to 2.42)	
P-value	-	0.0442		0.1247	
Hazard ratio inverted (95% CI) vs IPd	0.56 (0.32 to 0.99)				
Events probability (95% CI)[b]					
2 Months	0.8060 (0.6894 to 0.8824)	0.6663 (0.5566 to 0.7547)	0.7085 (0.5946 to 0.7958)	0.5621 (0.4322 to 0.6732)	
4 Months	0.7442 (0.6211 to 0.8326)	0.6065 (0.4952 to 0.7006)	0.6681 (0.5518 to 0.7606)	0.5460 (0.4165 to 0.6583)	
6 Months	0.7269 (0.6017 to 0.8185)	0.6065 (0.4952 to 0.7006)	0.6218 (0.5023 to 0.7205)	0.5460 (0.4165 to 0.6583)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_sex_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.15 Treatment emergent severe adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.7269 (0.6017 to 0.8185)	0.6065 (0.4952 to 0.7006)	0.6041 (0.4829 to 0.7054)	0.5039 (0.3726 to 0.6213)	
10 Months	0.7269 (0.6017 to 0.8185)	0.5754 (0.4618 to 0.6734)	0.6041 (0.4829 to 0.7054)	0.5039 (0.3726 to 0.6213)	
12 Months	0.7269 (0.6017 to 0.8185)	0.5754 (0.4618 to 0.6734)	0.6041 (0.4829 to 0.7054)	0.4799 (0.3474 to 0.6006)	
14 Months	0.7269 (0.6017 to 0.8185)	0.5754 (0.4618 to 0.6734)	0.6041 (0.4829 to 0.7054)	0.4399 (0.2986 to 0.5724)	
16 Months	0.7269 (0.6017 to 0.8185)	0.5754 (0.4618 to 0.6734)	0.6041 (0.4829 to 0.7054)	0.4399 (0.2986 to 0.5724)	
Number of patients at risk[b]					
2 Months	54	57	55	35	
4 Months	47	50	47	31	
6 Months	41	44	39	27	
8 Months	39	43	32	23	
10 Months	37	36	32	21	
12 Months	30	32	30	19	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.15 Treatment emergent severe adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	21	23	17	11	
16 Months	14	10	9	4	
Pneumonia (days)					
Number (%) of events	9 (13.2)	17 (19.3)	13 (16.0)	8 (12.5)	0.2608
Number (%) of patients censored	59 (86.8)	71 (80.7)	68 (84.0)	56 (87.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (5.9795 to NC)	NC (4.3696 to NC)	NC (11.6304 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3589		0.4919	
Hazard ratio (95% CI) vs Pd	-	1.46 (0.65 to 3.27)		0.74 (0.30 to 1.77)	
P-value	-	0.3617		0.4936	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_sex_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.2 Treatment emergent adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	111	100	17	23	
4 Months	100	93	17	22	
6 Months	84	84	17	22	
8 Months	75	80	17	20	
10 Months	71	74	16	19	
12 Months	63	66	12	16	
14 Months	44	42	2	12	
16 Months	21	19	1	5	
Neutropenia (days)					
Number (%) of events	42 (34.4)	49 (42.2)	6 (31.6)	18 (75.0)	0.0330
Number (%) of patients censored	80 (65.6)	67 (57.8)	13 (68.4)	6 (25.0)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_race_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.2 Treatment emergent adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	1.4456 (0.7885 to 4.3039)	0.8542 (0.7556 to 1.4456)	4.6653 (1.1499 to NC)	0.6571 (0.2300 to 0.8542)	
Median (95% CI)	NC (NC to NC)	NC (7.4908 to NC)	NC (4.6653 to NC)	1.4456 (0.7228 to 9.3306)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	10.4476 (2.7926 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2559		0.0015	
Hazard ratio (95% CI) vs Pd	-	1.27 (0.84 to 1.92)		4.05 (1.60 to 10.27)	
P-value	-	0.2569		0.0033	
Hazard ratio inverted (95% CI) vs IPd			0.25 (0.10 to 0.63)		
Events probability (95% CI)[b]					
2 Months	0.7413 (0.6530 to 0.8104)	0.6379 (0.5434 to 0.7179)	0.7895 (0.5319 to 0.9153)	0.4545 (0.2515 to 0.6374)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.2 Treatment emergent adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	0.6795 (0.5871 to 0.7555)	0.6116 (0.5166 to 0.6935)	0.7895 (0.5319 to 0.9153)	0.3636 (0.1783 to 0.5524)	
6 Months	0.6395 (0.5444 to 0.7199)	0.6116 (0.5166 to 0.6935)	0.7368 (0.4789 to 0.8810)	0.3182 (0.1447 to 0.5075)	
8 Months	0.6395 (0.5444 to 0.7199)	0.5908 (0.4948 to 0.6747)	0.6802 (0.4214 to 0.8421)	0.3182 (0.1447 to 0.5075)	
10 Months	0.6395 (0.5444 to 0.7199)	0.5790 (0.4822 to 0.6641)	0.6802 (0.4214 to 0.8421)	0.2727 (0.1132 to 0.4608)	
12 Months	0.6395 (0.5444 to 0.7199)	0.5790 (0.4822 to 0.6641)	0.6802 (0.4214 to 0.8421)	0.2273 (0.0841 to 0.4121)	
14 Months	0.6395 (0.5444 to 0.7199)	0.5615 (0.4614 to 0.6501)	0.6802 (0.4214 to 0.8421)	0.2273 (0.0841 to 0.4121)	
16 Months	0.6395 (0.5444 to 0.7199)	0.5615 (0.4614 to 0.6501)	0.6802 (0.4214 to 0.8421)	0.2273 (0.0841 to 0.4121)	
Number of patients at risk[b]					
2 Months	88	74	15	10	
4 Months	74	67	15	8	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.2 Treatment emergent adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	61	60	14	7	
8 Months	54	55	12	7	
10 Months	52	48	12	6	
12 Months	48	45	9	3	
14 Months	33	29	3	2	
16 Months	20	13	1	0	
Oedema peripheral (days)					
Number (%) of events	14 (11.5)	14 (12.1)	2 (10.5)	6 (25.0)	0.2497
Number (%) of patients censored	108 (88.5)	102 (87.9)	17 (89.5)	18 (75.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.3799 to NC)	8.9692 (2.0370 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.9692 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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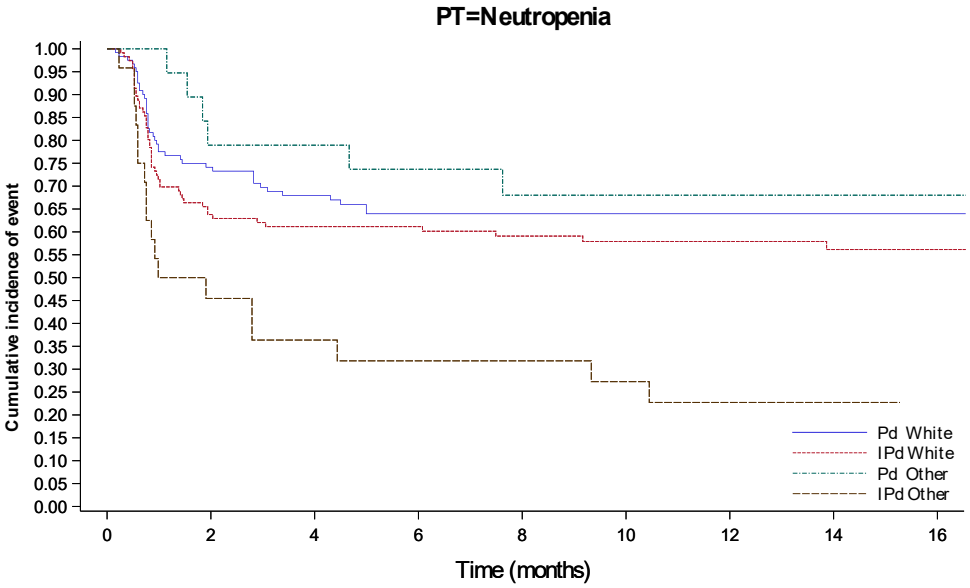
16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.3 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group according to race - Safety population



Number at Risk

Pd White	122	88	74	61	54	52	48	33	20
IPd White	116	74	67	60	55	48	45	29	13
Pd Other	19	15	15	14	12	12	9	3	1
IPd Other	24	10	8	7	7	6	3	2	0

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.12 Treatment emergent severe adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	114	104	19	22	
4 Months	107	101	19	21	
6 Months	93	90	19	20	
8 Months	83	87	18	19	
10 Months	79	84	17	19	
12 Months	71	73	13	17	
14 Months	49	48	3	13	
16 Months	23	21	1	5	
Neutropenia (days)					
Number (%) of events	41 (33.6)	49 (42.2)	6 (31.6)	17 (70.8)	0.0537
Number (%) of patients censored	81 (66.4)	67 (57.8)	13 (68.4)	7 (29.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.4456 (0.7885 to 4.3039)	0.8542 (0.7556 to 1.4456)	4.6653 (1.1499 to NC)	0.6571 (0.2300 to 0.8542)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_race_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.12 Treatment emergent severe adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (7.4908 to NC)	NC (4.6653 to NC)	1.4456 (0.7228 to 10.4476)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.7926 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2107		0.0034	
Hazard ratio (95% CI) vs Pd	-	1.30 (0.86 to 1.97)		3.71 (1.45 to 9.47)	
P-value	-	0.2121		0.0061	
Hazard ratio inverted (95% CI) vs IPd			0.27 (0.11 to 0.69)		
Events probability (95% CI)[b]					
2 Months	0.7413 (0.6530 to 0.8104)	0.6379 (0.5434 to 0.7179)	0.7895 (0.5319 to 0.9153)	0.4545 (0.2515 to 0.6374)	
4 Months	0.6795 (0.5871 to 0.7555)	0.6116 (0.5166 to 0.6935)	0.7895 (0.5319 to 0.9153)	0.3636 (0.1783 to 0.5524)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.12 Treatment emergent severe adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.6495 (0.5550 to 0.7288)	0.6116 (0.5166 to 0.6935)	0.7368 (0.4789 to 0.8810)	0.3636 (0.1783 to 0.5524)	
8 Months	0.6495 (0.5550 to 0.7288)	0.5908 (0.4948 to 0.6747)	0.6802 (0.4214 to 0.8421)	0.3636 (0.1783 to 0.5524)	
10 Months	0.6495 (0.5550 to 0.7288)	0.5790 (0.4822 to 0.6641)	0.6802 (0.4214 to 0.8421)	0.3117 (0.1379 to 0.5037)	
12 Months	0.6495 (0.5550 to 0.7288)	0.5790 (0.4822 to 0.6641)	0.6802 (0.4214 to 0.8421)	0.2597 (0.1012 to 0.4523)	
14 Months	0.6495 (0.5550 to 0.7288)	0.5615 (0.4614 to 0.6501)	0.6802 (0.4214 to 0.8421)	0.2597 (0.1012 to 0.4523)	
16 Months	0.6495 (0.5550 to 0.7288)	0.5615 (0.4614 to 0.6501)	0.6802 (0.4214 to 0.8421)	0.2597 (0.1012 to 0.4523)	
Number of patients at risk[b]					
2 Months	88	74	15	10	
4 Months	74	67	15	8	
6 Months	62	60	14	8	
8 Months	55	55	12	8	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.12 Treatment emergent severe adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	53	48	12	6	
12 Months	49	45	9	3	
14 Months	33	29	3	2	
16 Months	20	13	1	0	
Pneumonia (days)					
Number (%) of events	19 (15.6)	21 (18.1)	3 (15.8)	4 (16.7)	0.9944
Number (%) of patients censored	103 (84.4)	95 (81.9)	16 (84.2)	20 (83.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (6.3409 to NC)	NC (1.5770 to NC)	NC (0.2300 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7602		0.8901	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.3 Treatment emergent adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	2	4	118	112	
4 Months	2	4	110	104	
6 Months	1	4	95	96	
8 Months	1	4	86	90	
10 Months	1	4	81	83	
12 Months	0	3	69	73	
14 Months	0	3	42	49	
16 Months	0	1	21	22	
Neutropenia (days)					
Number (%) of events	1 (33.3)	2 (50.0)	45 (34.6)	59 (46.1)	0.8143
Number (%) of patients censored	2 (66.7)	2 (50.0)	85 (65.4)	69 (53.9)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.3 Treatment emergent adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	5.0267 (NC to NC)	1.9220 (0.7885 to NC)	1.9384 (0.8871 to 4.5010)	0.8378 (0.7228 to 0.9856)	
Median (95% CI)	5.0267 (NC to NC)	NC (0.7885 to NC)	NC (NC to NC)	NC (2.7926 to NC)	
75% quantile (95% CI)	5.0267 (NC to NC)	NC (0.7885 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9358		0.0495	
Hazard ratio (95% CI) vs Pd	-	1.10 (0.10 to 12.24)		1.47 (1.00 to 2.17)	
P-value	-	0.9358		0.0509	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.7436 (0.6588 to 0.8103)	0.6091 (0.5189 to 0.6875)	
4 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.6869 (0.5986 to 0.7597)	0.5849 (0.4944 to 0.6648)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.3 Treatment emergent adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.6513 (0.5608 to 0.7277)	0.5766 (0.4859 to 0.6569)	
8 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.6411 (0.5498 to 0.7187)	0.5670 (0.4759 to 0.6481)	
10 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.6411 (0.5498 to 0.7187)	0.5456 (0.4533 to 0.6287)	
12 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.6411 (0.5498 to 0.7187)	0.5347 (0.4419 to 0.6188)	
14 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.6411 (0.5498 to 0.7187)	0.5174 (0.4216 to 0.6049)	
16 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.6411 (0.5498 to 0.7187)	0.5174 (0.4216 to 0.6049)	
Number of patients at risk[b]					
2 Months	2	3	95	77	
4 Months	2	2	82	70	
6 Months	0	2	70	62	
8 Months	0	2	61	58	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.3 Treatment emergent adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0	2	59	50	
12 Months	0	2	52	44	
14 Months	0	2	33	27	
16 Months	0	0	20	12	
Oedema peripheral (days)					
Number (%) of events	0 (0.0)	1 (25.0)	13 (10.0)	18 (14.1)	0.9884
Number (%) of patients censored	3 (100.0)	3 (75.0)	117 (90.0)	110 (85.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.6899 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (0.6899 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.6899 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.4779	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.11 Treatment emergent severe adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	2	3	123	116	
4 Months	2	3	117	112	
6 Months	1	3	104	100	
8 Months	1	3	93	96	
10 Months	1	3	88	93	
12 Months	0	3	76	81	
14 Months	0	3	48	55	
16 Months	0	1	23	24	
Neutropenia (days)					
Number (%) of events	0 (0.0)	2 (50.0)	44 (33.8)	58 (45.3)	0.9850
Number (%) of patients censored	3 (100.0)	2 (50.0)	86 (66.2)	70 (54.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	1.9220 (0.7885 to NC)	1.9384 (0.8871 to 4.6653)	0.8378 (0.7228 to 0.9856)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.11 Treatment emergent severe adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (0.7885 to NC)	NC (NC to NC)	NC (2.7926 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.7885 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2807		0.0483	
Hazard ratio (95% CI) vs Pd	-	NC		1.48 (1.00 to 2.19)	
P-value	-	0.9979		0.0498	
Hazard ratio inverted (95% CI) vs IPd			0.68 (0.46 to 1.00)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.7436 (0.6588 to 0.8103)	0.6091 (0.5189 to 0.6875)	
4 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.6869 (0.5986 to 0.7597)	0.5849 (0.4944 to 0.6648)	
6 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.6602 (0.5702 to 0.7358)	0.5849 (0.4944 to 0.6648)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.11 Treatment emergent severe adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.6501 (0.5592 to 0.7268)	0.5753 (0.4844 to 0.6560)	
10 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.6501 (0.5592 to 0.7268)	0.5536 (0.4613 to 0.6364)	
12 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.6501 (0.5592 to 0.7268)	0.5426 (0.4496 to 0.6264)	
14 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.6501 (0.5592 to 0.7268)	0.5251 (0.4289 to 0.6125)	
16 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.6501 (0.5592 to 0.7268)	0.5251 (0.4289 to 0.6125)	
Number of patients at risk[b]					
2 Months	2	3	95	77	
4 Months	2	2	82	70	
6 Months	1	2	71	63	
8 Months	1	2	62	59	
10 Months	1	2	60	50	
12 Months	0	2	53	44	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.11 Treatment emergent severe adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0	2	33	27	
16 Months	0	0	20	12	
Pneumonia (days)					
Number (%) of events	0 (0.0)	1 (25.0)	20 (15.4)	24 (18.8)	0.9854
Number (%) of patients censored	3 (100.0)	3 (75.0)	110 (84.6)	104 (81.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (2.0698 to NC)	NC (NC to NC)	NC (6.3409 to NC)	
Median (95% CI)	NC (NC to NC)	NC (2.0698 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (2.0698 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4795		0.5637	
Hazard ratio (95% CI) vs Pd	-	NC		1.19 (0.66 to 2.16)	
P-value	-	0.9985		0.5642	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_ethn_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
4 Months	56	44	18	22	4	4	14	19	31	33	
6 Months	52	39	13	19	4	4	14	19	22	30	
8 Months	45	37	12	17	4	4	14	18	21	29	
10 Months	45	35	10	16	4	3	13	18	19	26	
12 Months	40	32	9	14	2	2	10	15	16	24	
14 Months	29	19	6	8	1	0	1	11	11	20	
16 Months	13	6	2	3	0	0	1	5	8	11	
Neutropenia (days)											
Number (%) of events	19 (25.7)	23 (41.8)	10 (50.0)	14 (50.0)	3 (60.0)	4 (57.1)	6 (40.0)	15 (71.4)	12 (34.3)	15 (36.6)	0.4254
Number (%) of patients censored	55 (74.3)	32 (58.2)	10 (50.0)	14 (50.0)	2 (40.0)	3 (42.9)	9 (60.0)	6 (28.6)	23 (65.7)	26 (63.4)	
Kaplan-Meier estimates of event in months											

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_greg_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
25% quantile (95% CI)	4.9938 (0.7556 to NC)	0.8542 (0.5585 to 1.8398)	0.7885 (0.5257 to 3.0883)	0.8049 (0.3285 to 1.0185)	2.8255 (1.4127 to NC)	0.8542 (0.5585 to 4.4353)	1.9384 (1.1499 to NC)	0.7228 (0.2300 to 0.8542)	2.8255 (0.7885 to NC)	1.9384 (0.7885 to NC)	
Median (95% CI)	NC (NC to NC)	NC (1.8398 to NC)	4.3039 (0.7885 to NC)	7.4908 (0.8542 to NC)	5.0267 (1.4127 to NC)	4.4353 (0.5585 to NC)	NC (1.8398 to NC)	1.9055 (0.7228 to 10.4476)	NC (3.3840 to NC)	NC (6.0780 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.3039 to NC)	NC (NC to NC)	NC (1.4127 to NC)	NC (3.0554 to NC)	NC (NC to NC)	NC (2.7926 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.0694		0.9872		0.9275		0.0259		0.9381	
Hazard ratio (95% CI) vs Pd	-	1.74 (0.95 to 3.20)		1.01 (0.45 to 2.27)		1.07 (0.24 to 4.81)		2.82 (1.09 to 7.31)		1.03 (0.48 to 2.20)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_greg_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
P-value	-	0.0730		0.9872		0.9278		0.0328		0.9382	
Hazard ratio inverted (95% CI) vs IPd							0.35 (0.14 to 0.92)				
Events probability (95% CI)[b]											
2 Months	0.7780 (0.6634 to 0.8577)	0.6111 (0.4683 to 0.7264)	0.6316 (0.3790 to 0.8044)	0.5357 (0.3381 to 0.6982)	0.8000 (0.2038 to 0.9692)	0.7143 (0.2582 to 0.9198)	0.7333 (0.4362 to 0.8905)	0.4714 (0.2513 to 0.6640)	0.7714 (0.5946 to 0.8785)	0.7317 (0.5681 to 0.8415)	
4 Months	0.7636 (0.6475 to 0.8459)	0.5926 (0.4500 to 0.7097)	0.5263 (0.2872 to 0.7188)	0.5357 (0.3381 to 0.6982)	0.6000 (0.1257 to 0.8818)	0.5714 (0.1719 to 0.8371)	0.7333 (0.4362 to 0.8905)	0.3667 (0.1686 to 0.5681)	0.6789 (0.4948 to 0.8080)	0.6821 (0.5161 to 0.8014)	
6 Months	0.7297 (0.6086 to 0.8188)	0.5926 (0.4500 to 0.7097)	0.4678 (0.2373 to 0.6696)	0.5357 (0.3381 to 0.6982)	0.4000 (0.0520 to 0.7528)	0.4286 (0.0978 to 0.7344)	0.6667 (0.3753 to 0.8456)	0.3667 (0.1686 to 0.5681)	0.6431 (0.4559 to 0.7803)	0.6821 (0.5161 to 0.8014)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_greg_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
8 Months	0.7297 (0.6086 to 0.8188)	0.5926 (0.4500 to 0.7097)	0.4678 (0.2373 to 0.6696)	0.4911 (0.2948 to 0.6610)	0.4000 (0.0520 to 0.7528)	0.4286 (0.0978 to 0.7344)	0.6000 (0.3176 to 0.7965)	0.3667 (0.1686 to 0.5681)	0.6431 (0.4559 to 0.7803)	0.6548 (0.4872 to 0.7793)	
10 Months	0.7297 (0.6086 to 0.8188)	0.5644 (0.4183 to 0.6870)	0.4678 (0.2373 to 0.6696)	0.4911 (0.2948 to 0.6610)	0.4000 (0.0520 to 0.7528)	0.4286 (0.0978 to 0.7344)	0.6000 (0.3176 to 0.7965)	0.3143 (0.1314 to 0.5168)	0.6431 (0.4559 to 0.7803)	0.6548 (0.4872 to 0.7793)	
12 Months	0.7297 (0.6086 to 0.8188)	0.5644 (0.4183 to 0.6870)	0.4678 (0.2373 to 0.6696)	0.4911 (0.2948 to 0.6610)	0.4000 (0.0520 to 0.7528)	0.4286 (0.0978 to 0.7344)	0.6000 (0.3176 to 0.7965)	0.2619 (0.0972 to 0.4630)	0.6431 (0.4559 to 0.7803)	0.6548 (0.4872 to 0.7793)	
14 Months	0.7297 (0.6086 to 0.8188)	0.5644 (0.4183 to 0.6870)	0.4678 (0.2373 to 0.6696)	0.4911 (0.2948 to 0.6610)	0.4000 (0.0520 to 0.7528)	0.4286 (0.0978 to 0.7344)	0.6000 (0.3176 to 0.7965)	0.2619 (0.0972 to 0.4630)	0.6431 (0.4559 to 0.7803)	0.6163 (0.4415 to 0.7508)	
16 Months	0.7297 (0.6086 to 0.8188)	0.5644 (0.4183 to 0.6870)	0.4678 (0.2373 to 0.6696)	0.4911 (0.2948 to 0.6610)	0.4000 (0.0520 to 0.7528)	0.4286 (0.0978 to 0.7344)	0.6000 (0.3176 to 0.7965)	0.2619 (0.0972 to 0.4630)	0.6431 (0.4559 to 0.7803)	0.6163 (0.4415 to 0.7508)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_greg_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Number of patients at risk[b]											
2 Months	55	33	12	15	4	5	11	9	27	30	
4 Months	48	29	10	14	3	4	11	7	22	27	
6 Months	43	24	7	12	2	2	10	7	16	25	
8 Months	37	23	7	10	2	2	9	7	14	23	
10 Months	37	20	7	9	2	2	9	6	12	20	
12 Months	33	18	7	8	1	2	7	3	11	20	
14 Months	24	12	4	5	0	0	2	2	8	15	
16 Months	13	4	2	2	0	0	1	0	7	8	
Oedema peripheral (days)											
Number (%) of events	6 (8.1)	5 (9.1)	4 (20.0)	2 (7.1)	0 (0.0)	2 (28.6)	1 (6.7)	5 (23.8)	5 (14.3)	6 (14.6)	0.4641

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_greg_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.10 Treatment emergent severe adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
14 Months	31	20	9	12	1	1	2	12	11	19	
16 Months	14	6	3	4	0	1	1	5	8	10	
Neutropenia (days)											
Number (%) of events	19 (25.7)	22 (40.0)	10 (50.0)	14 (50.0)	2 (40.0)	3 (42.9)	6 (40.0)	15 (71.4)	11 (31.4)	15 (36.6)	0.5421
Number (%) of patients censored	55 (74.3)	33 (60.0)	10 (50.0)	14 (50.0)	3 (60.0)	4 (57.1)	9 (60.0)	6 (28.6)	24 (68.6)	26 (63.4)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	4.9938 (0.7556 to NC)	0.8542 (0.5585 to 1.9384)	0.7885 (0.5257 to 3.0883)	0.8049 (0.3285 to 1.0185)	2.8255 (1.4127 to NC)	0.8542 (0.5585 to NC)	1.9384 (1.1499 to NC)	0.7228 (0.2300 to 0.8542)	2.8255 (0.7885 to NC)	1.9384 (0.7885 to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.10 Treatment emergent severe adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Median (95% CI)	NC (NC to NC)	NC (1.9384 to NC)	4.3039 (0.7885 to NC)	7.4908 (0.8542 to NC)	NC (1.4127 to NC)	NC (0.5585 to NC)	NC (1.8398 to NC)	1.9055 (0.7228 to 10.4476)	NC (3.3840 to NC)	NC (6.0780 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.3039 to NC)	NC (NC to NC)	NC (1.4127 to NC)	NC (3.0554 to NC)	NC (NC to NC)	NC (2.7926 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.1004		0.9872		0.8631		0.0259		0.7518	
Hazard ratio (95% CI) vs Pd	-	1.66 (0.90 to 3.08)		1.01 (0.45 to 2.27)		1.17 (0.19 to 7.05)		2.82 (1.09 to 7.31)		1.13 (0.52 to 2.47)	
P-value	-	0.1041		0.9872		0.8632		0.0328		0.7519	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_greg_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.10 Treatment emergent severe adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=35)**	**IPd (N=41)**	**p-value of treatment-by-subgroup interaction[c]**
Hazard ratio inverted (95% CI) vs IPd							0.35 (0.14 to 0.92)				
Events probability (95% CI)[b]											
2 Months	0.7780 (0.6634 to 0.8577)	0.6286 (0.4854 to 0.7421)	0.6316 (0.3790 to 0.8044)	0.5357 (0.3381 to 0.6982)	0.8000 (0.2038 to 0.9692)	0.7143 (0.2582 to 0.9198)	0.7333 (0.4362 to 0.8905)	0.4714 (0.2513 to 0.6640)	0.7714 (0.5946 to 0.8785)	0.7317 (0.5681 to 0.8415)	
4 Months	0.7636 (0.6475 to 0.8459)	0.6095 (0.4663 to 0.7253)	0.5263 (0.2872 to 0.7188)	0.5357 (0.3381 to 0.6982)	0.6000 (0.1257 to 0.8818)	0.5714 (0.1719 to 0.8371)	0.7333 (0.4362 to 0.8905)	0.3667 (0.1686 to 0.5681)	0.6789 (0.4948 to 0.8080)	0.6821 (0.5161 to 0.8014)	
6 Months	0.7297 (0.6086 to 0.8188)	0.6095 (0.4663 to 0.7253)	0.4678 (0.2373 to 0.6696)	0.5357 (0.3381 to 0.6982)	0.6000 (0.1257 to 0.8818)	0.5714 (0.1719 to 0.8371)	0.6667 (0.3753 to 0.8456)	0.3667 (0.1686 to 0.5681)	0.6789 (0.4948 to 0.8080)	0.6821 (0.5161 to 0.8014)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_greg_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.10 Treatment emergent severe adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
8 Months	0.7297 (0.6086 to 0.8188)	0.6095 (0.4663 to 0.7253)	0.4678 (0.2373 to 0.6696)	0.4911 (0.2948 to 0.6610)	0.6000 (0.1257 to 0.8818)	0.5714 (0.1719 to 0.8371)	0.6000 (0.3176 to 0.7965)	0.3667 (0.1686 to 0.5681)	0.6789 (0.4948 to 0.8080)	0.6548 (0.4872 to 0.7793)	
10 Months	0.7297 (0.6086 to 0.8188)	0.5805 (0.4330 to 0.7023)	0.4678 (0.2373 to 0.6696)	0.4911 (0.2948 to 0.6610)	0.6000 (0.1257 to 0.8818)	0.5714 (0.1719 to 0.8371)	0.6000 (0.3176 to 0.7965)	0.3143 (0.1314 to 0.5168)	0.6789 (0.4948 to 0.8080)	0.6548 (0.4872 to 0.7793)	
12 Months	0.7297 (0.6086 to 0.8188)	0.5805 (0.4330 to 0.7023)	0.4678 (0.2373 to 0.6696)	0.4911 (0.2948 to 0.6610)	0.6000 (0.1257 to 0.8818)	0.5714 (0.1719 to 0.8371)	0.6000 (0.3176 to 0.7965)	0.2619 (0.0972 to 0.4630)	0.6789 (0.4948 to 0.8080)	0.6548 (0.4872 to 0.7793)	
14 Months	0.7297 (0.6086 to 0.8188)	0.5805 (0.4330 to 0.7023)	0.4678 (0.2373 to 0.6696)	0.4911 (0.2948 to 0.6610)	0.6000 (0.1257 to 0.8818)	0.5714 (0.1719 to 0.8371)	0.6000 (0.3176 to 0.7965)	0.2619 (0.0972 to 0.4630)	0.6789 (0.4948 to 0.8080)	0.6163 (0.4415 to 0.7508)	
16 Months	0.7297 (0.6086 to 0.8188)	0.5805 (0.4330 to 0.7023)	0.4678 (0.2373 to 0.6696)	0.4911 (0.2948 to 0.6610)	0.6000 (0.1257 to 0.8818)	0.5714 (0.1719 to 0.8371)	0.6000 (0.3176 to 0.7965)	0.2619 (0.0972 to 0.4630)	0.6789 (0.4948 to 0.8080)	0.6163 (0.4415 to 0.7508)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.10 Treatment emergent severe adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Number of patients at risk[b]											
2 Months	55	33	12	15	4	5	11	9	27	30	
4 Months	48	29	10	14	3	4	11	7	22	27	
6 Months	43	24	7	12	3	3	10	7	17	25	
8 Months	37	23	7	10	3	3	9	7	15	23	
10 Months	37	20	7	9	3	2	9	6	13	20	
12 Months	33	18	7	8	1	2	7	3	12	20	
14 Months	24	12	4	5	0	0	2	2	8	15	
16 Months	13	4	2	2	0	0	1	0	7	8	
Pneumonia (days)											
Number (%) of events	5 (6.8)	3 (5.5)	5 (25.0)	6 (21.4)	2 (40.0)	1 (14.3)	3 (20.0)	4 (19.0)	7 (20.0)	11 (26.8)	0.8655

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.3 Treatment emergent adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	84	65	51	67	
4 Months	73	58	50	64	
6 Months	66	52	39	59	
8 Months	58	49	38	56	
10 Months	56	46	35	52	
12 Months	49	41	28	46	
14 Months	34	25	14	33	
16 Months	15	9	9	16	
Neutropenia (days)					
Number (%) of events	25 (26.6)	33 (42.9)	25 (45.5)	38 (50.7)	0.3315
Number (%) of patients censored	69 (73.4)	44 (57.1)	30 (54.5)	37 (49.3)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.3 Treatment emergent adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	4.9938 (0.9528 to NC)	0.9528 (0.7556 to 2.0370)	1.4456 (0.7885 to 2.8255)	0.7885 (0.6242 to 0.9528)	
Median (95% CI)	NC (NC to NC)	NC (2.8912 to NC)	NC (2.8255 to NC)	9.3306 (1.0185 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0349		0.4257	
Hazard ratio (95% CI) vs Pd	-	1.74 (1.03 to 2.92)		1.23 (0.74 to 2.03)	
P-value	-	0.0372		0.4265	
Hazard ratio inverted (95% CI) vs IPd	0.58 (0.34 to 0.97)				
Events probability (95% CI)[b]					
2 Months	0.8044 (0.7076 to 0.8720)	0.6579 (0.5397 to 0.7526)	0.6669 (0.5246 to 0.7754)	0.5727 (0.4530 to 0.6755)	
4 Months	0.7699 (0.6691 to 0.8435)	0.6053 (0.4864 to 0.7049)	0.5907 (0.4475 to 0.7084)	0.5441 (0.4245 to 0.6490)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.3 Treatment emergent adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.7179 (0.6108 to 0.8003)	0.5912 (0.4720 to 0.6921)	0.5492 (0.4059 to 0.6714)	0.5441 (0.4245 to 0.6490)	
8 Months	0.7179 (0.6108 to 0.8003)	0.5912 (0.4720 to 0.6921)	0.5263 (0.3828 to 0.6511)	0.5130 (0.3933 to 0.6204)	
10 Months	0.7179 (0.6108 to 0.8003)	0.5721 (0.4511 to 0.6759)	0.5263 (0.3828 to 0.6511)	0.4953 (0.3752 to 0.6044)	
12 Months	0.7179 (0.6108 to 0.8003)	0.5721 (0.4511 to 0.6759)	0.5263 (0.3828 to 0.6511)	0.4770 (0.3566 to 0.5878)	
14 Months	0.7179 (0.6108 to 0.8003)	0.5449 (0.4180 to 0.6553)	0.5263 (0.3828 to 0.6511)	0.4770 (0.3566 to 0.5878)	
16 Months	0.7179 (0.6108 to 0.8003)	0.5449 (0.4180 to 0.6553)	0.5263 (0.3828 to 0.6511)	0.4770 (0.3566 to 0.5878)	
Number of patients at risk[b]					
2 Months	73	50	36	42	
4 Months	63	43	31	38	
6 Months	54	35	24	35	
8 Months	46	33	23	32	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.3 Treatment emergent adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	44	30	23	27	
12 Months	39	28	20	23	
14 Months	27	18	11	16	
16 Months	15	7	8	7	
Oedema peripheral (days)					
Number (%) of events	8 (8.5)	12 (15.6)	8 (14.5)	8 (10.7)	0.1489
Number (%) of patients censored	86 (91.5)	65 (84.4)	47 (85.5)	67 (89.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (8.9692 to NC)	NC (4.2710 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2125		0.4039	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.11 Treatment emergent severe adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	88	66	52	69	
4 Months	81	61	51	68	
6 Months	74	53	42	61	
8 Months	63	51	42	59	
10 Months	61	51	39	56	
12 Months	53	45	33	49	
14 Months	36	29	18	35	
16 Months	16	10	10	16	
Neutropenia (days)					
Number (%) of events	23 (24.5)	31 (40.3)	25 (45.5)	38 (50.7)	0.3197
Number (%) of patients censored	71 (75.5)	46 (59.7)	30 (54.5)	37 (49.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	4.9938 (0.9528 to NC)	0.9528 (0.7556 to 2.1027)	1.4456 (0.7885 to 2.8255)	0.7885 (0.6242 to 0.9528)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.11 Treatment emergent severe adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (3.0554 to NC)	NC (2.8255 to NC)	9.3306 (1.0185 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0367		0.4257	
Hazard ratio (95% CI) vs Pd	-	1.76 (1.03 to 3.03)		1.23 (0.74 to 2.03)	
P-value	-	0.0392		0.4265	
Hazard ratio inverted (95% CI) vs IPd	0.57 (0.33 to 0.97)				
Events probability (95% CI)[b]					
2 Months	0.8044 (0.7076 to 0.8720)	0.6705 (0.5526 to 0.7639)	0.6669 (0.5246 to 0.7754)	0.5727 (0.4530 to 0.6755)	
4 Months	0.7699 (0.6691 to 0.8435)	0.6169 (0.4977 to 0.7158)	0.5907 (0.4475 to 0.7084)	0.5441 (0.4245 to 0.6490)	
6 Months	0.7438 (0.6394 to 0.8221)	0.6169 (0.4977 to 0.7158)	0.5492 (0.4059 to 0.6714)	0.5441 (0.4245 to 0.6490)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.11 Treatment emergent severe adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.7438 (0.6394 to 0.8221)	0.6169 (0.4977 to 0.7158)	0.5263 (0.3828 to 0.6511)	0.5130 (0.3933 to 0.6204)	
10 Months	0.7438 (0.6394 to 0.8221)	0.5970 (0.4752 to 0.6993)	0.5263 (0.3828 to 0.6511)	0.4953 (0.3752 to 0.6044)	
12 Months	0.7438 (0.6394 to 0.8221)	0.5970 (0.4752 to 0.6993)	0.5263 (0.3828 to 0.6511)	0.4770 (0.3566 to 0.5878)	
14 Months	0.7438 (0.6394 to 0.8221)	0.5686 (0.4397 to 0.6784)	0.5263 (0.3828 to 0.6511)	0.4770 (0.3566 to 0.5878)	
16 Months	0.7438 (0.6394 to 0.8221)	0.5686 (0.4397 to 0.6784)	0.5263 (0.3828 to 0.6511)	0.4770 (0.3566 to 0.5878)	
Number of patients at risk[b]					
2 Months	73	50	36	42	
4 Months	63	43	31	38	
6 Months	56	36	24	35	
8 Months	48	34	23	32	
10 Months	46	30	23	27	
12 Months	40	28	20	23	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.11 Treatment emergent severe adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	27	18	11	16	
16 Months	15	7	8	7	
Pneumonia (days)					
Number (%) of events	10 (10.6)	7 (9.1)	12 (21.8)	18 (24.0)	0.6707
Number (%) of patients censored	84 (89.4)	70 (90.9)	43 (78.2)	57 (76.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.9384 to NC)	11.6304 (3.9754 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6947		0.8584	
Hazard ratio (95% CI) vs Pd	-	0.82 (0.31 to 2.17)		1.07 (0.51 to 2.22)	
P-value	-	0.6952		0.8593	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.2 Treatment emergent adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	122	121	13	11	
4 Months	111	114	12	8	
6 Months	96	104	9	7	
8 Months	88	98	8	7	
10 Months	84	91	7	7	
12 Months	72	81	5	6	
14 Months	45	55	3	3	
16 Months	22	23	2	2	
Neutropenia (days)					
Number (%) of events	45 (33.3)	63 (46.3)	5 (35.7)	8 (50.0)	0.8565
Number (%) of patients censored	90 (66.7)	73 (53.7)	9 (64.3)	8 (50.0)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_ecog_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.2 Treatment emergent adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	2.8255 (0.9856 to 4.9938)	0.8542 (0.7556 to 0.9856)	0.6899 (0.2300 to NC)	0.9856 (0.5257 to 6.0780)	
Median (95% CI)	NC (NC to NC)	NC (2.7926 to NC)	NC (0.6242 to NC)	7.6222 (0.8214 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.0780 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0256		0.5231	
Hazard ratio (95% CI) vs Pd	-	1.54 (1.05 to 2.26)		1.44 (0.47 to 4.41)	
P-value	-	0.0268		0.5253	
Hazard ratio inverted (95% CI) vs IPd	0.65 (0.44 to 0.95)				
Events probability (95% CI)[b]					
2 Months	0.7648 (0.6827 to 0.8284)	0.6100 (0.5226 to 0.6862)	0.6429 (0.3433 to 0.8331)	0.6667 (0.3753 to 0.8456)	
4 Months	0.7093 (0.6230 to 0.7793)	0.5722 (0.4844 to 0.6505)	0.6429 (0.3433 to 0.8331)	0.6000 (0.3176 to 0.7965)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.2 Treatment emergent adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.6561 (0.5662 to 0.7319)	0.5643 (0.4765 to 0.6431)	0.6429 (0.3433 to 0.8331)	0.6000 (0.3176 to 0.7965)	
8 Months	0.6460 (0.5552 to 0.7229)	0.5552 (0.4671 to 0.6346)	0.6429 (0.3433 to 0.8331)	0.5000 (0.2176 to 0.7298)	
10 Months	0.6460 (0.5552 to 0.7229)	0.5452 (0.4564 to 0.6254)	0.6429 (0.3433 to 0.8331)	0.4000 (0.1397 to 0.6528)	
12 Months	0.6460 (0.5552 to 0.7229)	0.5349 (0.4456 to 0.6161)	0.6429 (0.3433 to 0.8331)	0.4000 (0.1397 to 0.6528)	
14 Months	0.6460 (0.5552 to 0.7229)	0.5204 (0.4291 to 0.6039)	0.6429 (0.3433 to 0.8331)	0.4000 (0.1397 to 0.6528)	
16 Months	0.6460 (0.5552 to 0.7229)	0.5204 (0.4291 to 0.6039)	0.6429 (0.3433 to 0.8331)	0.4000 (0.1397 to 0.6528)	
Number of patients at risk[b]					
2 Months	100	82	9	10	
4 Months	86	73	8	8	
6 Months	71	64	7	6	
8 Months	62	60	7	5	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.2 Treatment emergent adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	60	53	7	4	
12 Months	54	47	5	4	
14 Months	35	33	3	1	
16 Months	20	14	3	0	
Oedema peripheral (days)					
Number (%) of events	16 (11.9)	17 (12.5)	0 (0.0)	3 (18.8)	0.9865
Number (%) of patients censored	119 (88.1)	119 (87.5)	14 (100.0)	13 (81.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.6899 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.8111 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8350		0.0696	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.11 Treatment emergent severe adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	126	123	14	12	
4 Months	119	119	13	10	
6 Months	106	107	10	7	
8 Months	96	103	9	7	
10 Months	92	100	8	7	
12 Months	80	88	6	6	
14 Months	50	61	4	3	
16 Months	23	24	3	2	
Neutropenia (days)					
Number (%) of events	43 (31.9)	62 (45.6)	5 (35.7)	7 (43.8)	0.6471
Number (%) of patients censored	92 (68.1)	74 (54.4)	9 (64.3)	9 (56.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.8255 (0.9856 to 4.9938)	0.8542 (0.7556 to 0.9856)	0.6899 (0.2300 to NC)	1.4784 (0.5257 to 9.1663)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.11 Treatment emergent severe adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (2.7926 to NC)	NC (0.6242 to NC)	9.1663 (0.8214 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.0780 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0188		0.6977	
Hazard ratio (95% CI) vs Pd	-	1.59 (1.08 to 2.34)		1.26 (0.40 to 3.98)	
P-value	-	0.0199		0.6983	
Hazard ratio inverted (95% CI) vs IPd	0.63 (0.43 to 0.93)				
Events probability (95% CI)[b]					
2 Months	0.7648 (0.6827 to 0.8284)	0.6100 (0.5226 to 0.6862)	0.6429 (0.3433 to 0.8331)	0.7333 (0.4362 to 0.8905)	
4 Months	0.7093 (0.6230 to 0.7793)	0.5722 (0.4844 to 0.6505)	0.6429 (0.3433 to 0.8331)	0.6600 (0.3647 to 0.8427)	
6 Months	0.6739 (0.5850 to 0.7478)	0.5722 (0.4844 to 0.6505)	0.6429 (0.3433 to 0.8331)	0.6600 (0.3647 to 0.8427)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.11 Treatment emergent severe adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.6638 (0.5740 to 0.7390)	0.5631 (0.4750 to 0.6421)	0.6429 (0.3433 to 0.8331)	0.5500 (0.2437 to 0.7763)	
10 Months	0.6638 (0.5740 to 0.7390)	0.5529 (0.4641 to 0.6328)	0.6429 (0.3433 to 0.8331)	0.4400 (0.1543 to 0.6972)	
12 Months	0.6638 (0.5740 to 0.7390)	0.5424 (0.4531 to 0.6234)	0.6429 (0.3433 to 0.8331)	0.4400 (0.1543 to 0.6972)	
14 Months	0.6638 (0.5740 to 0.7390)	0.5278 (0.4363 to 0.6112)	0.6429 (0.3433 to 0.8331)	0.4400 (0.1543 to 0.6972)	
16 Months	0.6638 (0.5740 to 0.7390)	0.5278 (0.4363 to 0.6112)	0.6429 (0.3433 to 0.8331)	0.4400 (0.1543 to 0.6972)	
Number of patients at risk[b]					
2 Months	100	82	9	10	
4 Months	86	73	8	8	
6 Months	73	65	7	6	
8 Months	64	61	7	5	
10 Months	62	53	7	4	
12 Months	55	47	5	4	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.11 Treatment emergent severe adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	35	33	3	1	
16 Months	20	14	3	0	
Pneumonia (days)					
Number (%) of events	19 (14.1)	23 (16.9)	3 (21.4)	2 (12.5)	0.5060
Number (%) of patients censored	116 (85.9)	113 (83.1)	11 (78.6)	14 (87.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.6304 to NC)	NC (0.2628 to NC)	NC (1.0185 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.7741 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6480		0.6004	
Hazard ratio (95% CI) vs Pd	-	1.15 (0.63 to 2.12)		0.62 (0.10 to 3.73)	
P-value	-	0.6482		0.6037	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	45	47	41	41	17	22	
8 Months	44	46	35	39	15	19	
10 Months	43	44	32	35	14	18	
12 Months	39	39	24	31	12	16	
14 Months	24	25	15	21	9	11	
16 Months	13	13	7	7	4	5	
Neutropenia (days)							
Number (%) of events	16 (31.4)	31 (49.2)	17 (30.9)	25 (47.2)	17 (42.5)	15 (45.5)	0.4136
Number (%) of patients censored	35 (68.6)	32 (50.8)	38 (69.1)	28 (52.8)	23 (57.5)	18 (54.5)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	3.0883 (0.7556 to NC)	0.8542 (0.7556 to 1.9384)	2.8255 (0.9199 to NC)	0.8542 (0.5914 to 0.9856)	0.9856 (0.5257 to 2.9569)	0.7721 (0.5257 to 1.4784)	
Median (95% CI)	NC (NC to NC)	13.8645 (2.1027 to NC)	NC (NC to NC)	NC (0.9856 to NC)	NC (1.4456 to NC)	NC (0.8214 to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0496		0.0567		0.9180	
Hazard ratio (95% CI) vs Pd	-	1.82 (0.99 to 3.33)		1.81 (0.97 to 3.35)		1.04 (0.52 to 2.08)	
P-value	-	0.0530		0.0603		0.9179	
Events probability (95% CI)[b]							
2 Months	0.7843 (0.6445 to 0.8743)	0.6349 (0.5036 to 0.7402)	0.7950 (0.6603 to 0.8809)	0.6038 (0.4596 to 0.7207)	0.6333 (0.4606 to 0.7641)	0.5625 (0.3759 to 0.7130)	
4 Months	0.7451 (0.6019 to 0.8432)	0.5702 (0.4388 to 0.6817)	0.7382 (0.5982 to 0.8358)	0.5641 (0.4203 to 0.6852)	0.5667 (0.3903 to 0.7097)	0.5625 (0.3759 to 0.7130)	
6 Months	0.7048 (0.5588 to 0.8104)	0.5702 (0.4388 to 0.6817)	0.6759 (0.5306 to 0.7850)	0.5425 (0.3985 to 0.6659)	0.5231 (0.3420 to 0.6761)	0.5625 (0.3759 to 0.7130)	
8 Months	0.6841 (0.5369 to 0.7931)	0.5309 (0.3984 to 0.6467)	0.6759 (0.5306 to 0.7850)	0.5425 (0.3985 to 0.6659)	0.5231 (0.3420 to 0.6761)	0.5625 (0.3759 to 0.7130)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_seiss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.6841 (0.5369 to 0.7931)	0.5096 (0.3766 to 0.6279)	0.6759 (0.5306 to 0.7850)	0.5123 (0.3653 to 0.6413)	0.5231 (0.3420 to 0.6761)	0.5625 (0.3759 to 0.7130)	
12 Months	0.6841 (0.5369 to 0.7931)	0.5096 (0.3766 to 0.6279)	0.6759 (0.5306 to 0.7850)	0.5123 (0.3653 to 0.6413)	0.5231 (0.3420 to 0.6761)	0.5192 (0.3306 to 0.6784)	
14 Months	0.6841 (0.5369 to 0.7931)	0.4756 (0.3365 to 0.6023)	0.6759 (0.5306 to 0.7850)	0.5123 (0.3653 to 0.6413)	0.5231 (0.3420 to 0.6761)	0.5192 (0.3306 to 0.6784)	
16 Months	0.6841 (0.5369 to 0.7931)	0.4756 (0.3365 to 0.6023)	0.6759 (0.5306 to 0.7850)	0.5123 (0.3653 to 0.6413)	0.5231 (0.3420 to 0.6761)	0.5192 (0.3306 to 0.6784)	
Number of patients at risk[b]							
2 Months	40	40	42	31	24	18	
4 Months	37	35	39	26	16	17	
6 Months	35	29	30	22	11	16	
8 Months	32	27	25	21	10	14	
10 Months	32	24	23	17	10	13	
12 Months	30	20	18	17	9	11	
14 Months	19	13	12	11	7	7	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_seiss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	15	7	5	5	3	2	
Oedema peripheral (days)							
Number (%) of events	4 (7.8)	12 (19.0)	5 (9.1)	6 (11.3)	6 (15.0)	1 (3.0)	0.0665
Number (%) of patients censored	47 (92.2)	51 (81.0)	50 (90.9)	47 (88.7)	34 (85.0)	32 (97.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (7.8850 to NC)	NC (NC to NC)	NC (10.1191 to NC)	NC (1.7741 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0887		0.8122		0.0611	
Hazard ratio (95% CI) vs Pd	-	2.58 (0.83 to 8.00)		1.15 (0.35 to 3.79)		0.17 (0.02 to 1.40)	
P-value	-	0.1009		0.8123		0.0992	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.10 Treatment emergent severe adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	50	56	52	47	35	29	
4 Months	49	56	52	43	29	27	
6 Months	49	50	45	39	20	22	
8 Months	46	49	40	38	17	20	
10 Months	44	47	38	38	16	19	
12 Months	41	41	29	33	14	17	
14 Months	26	27	18	23	10	11	
16 Months	15	12	7	8	4	6	
Neutropenia (days)							
Number (%) of events	16 (31.4)	31 (49.2)	15 (27.3)	23 (43.4)	17 (42.5)	15 (45.5)	0.4083
Number (%) of patients censored	35 (68.6)	32 (50.8)	40 (72.7)	30 (56.6)	23 (57.5)	18 (54.5)	
Kaplan-Meier estimates of event in months							

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.10 Treatment emergent severe adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	3.0883 (0.7556 to NC)	0.8542 (0.7556 to 1.9384)	2.8255 (0.9199 to NC)	0.8542 (0.5914 to 1.4127)	0.9856 (0.5257 to 2.9569)	0.7721 (0.5257 to 1.4784)	
Median (95% CI)	NC (NC to NC)	13.8645 (2.1027 to NC)	NC (NC to NC)	NC (0.9856 to NC)	NC (1.4456 to NC)	NC (0.8214 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0496		0.0579		0.9180	
Hazard ratio (95% CI) vs Pd	-	1.82 (0.99 to 3.33)		1.86 (0.97 to 3.57)		1.04 (0.52 to 2.08)	
P-value	-	0.0530		0.0619		0.9179	
Events probability (95% CI)[b]							
2 Months	0.7843 (0.6445 to 0.8743)	0.6349 (0.5036 to 0.7402)	0.7950 (0.6603 to 0.8809)	0.6226 (0.4784 to 0.7376)	0.6333 (0.4606 to 0.7641)	0.5625 (0.3759 to 0.7130)	
4 Months	0.7451 (0.6019 to 0.8432)	0.5702 (0.4388 to 0.6817)	0.7382 (0.5982 to 0.8358)	0.5818 (0.4370 to 0.7016)	0.5667 (0.3903 to 0.7097)	0.5625 (0.3759 to 0.7130)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.10 Treatment emergent severe adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.7048 (0.5588 to 0.8104)	0.5702 (0.4388 to 0.6817)	0.7182 (0.5765 to 0.8197)	0.5818 (0.4370 to 0.7016)	0.5231 (0.3420 to 0.6761)	0.5625 (0.3759 to 0.7130)	
8 Months	0.6841 (0.5369 to 0.7931)	0.5309 (0.3984 to 0.6467)	0.7182 (0.5765 to 0.8197)	0.5818 (0.4370 to 0.7016)	0.5231 (0.3420 to 0.6761)	0.5625 (0.3759 to 0.7130)	
10 Months	0.6841 (0.5369 to 0.7931)	0.5096 (0.3766 to 0.6279)	0.7182 (0.5765 to 0.8197)	0.5495 (0.3994 to 0.6765)	0.5231 (0.3420 to 0.6761)	0.5625 (0.3759 to 0.7130)	
12 Months	0.6841 (0.5369 to 0.7931)	0.5096 (0.3766 to 0.6279)	0.7182 (0.5765 to 0.8197)	0.5495 (0.3994 to 0.6765)	0.5231 (0.3420 to 0.6761)	0.5192 (0.3306 to 0.6784)	
14 Months	0.6841 (0.5369 to 0.7931)	0.4756 (0.3365 to 0.6023)	0.7182 (0.5765 to 0.8197)	0.5495 (0.3994 to 0.6765)	0.5231 (0.3420 to 0.6761)	0.5192 (0.3306 to 0.6784)	
16 Months	0.6841 (0.5369 to 0.7931)	0.4756 (0.3365 to 0.6023)	0.7182 (0.5765 to 0.8197)	0.5495 (0.3994 to 0.6765)	0.5231 (0.3420 to 0.6761)	0.5192 (0.3306 to 0.6784)	
Number of patients at risk[b]							
2 Months	40	40	42	31	24	18	
4 Months	37	35	39	26	16	17	
6 Months	35	29	32	23	11	16	
8 Months	32	27	27	22	10	14	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.10 Treatment emergent severe adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	32	24	25	17	10	13	
12 Months	30	20	19	17	9	11	
14 Months	19	13	12	11	7	7	
16 Months	15	7	5	5	3	2	
Pneumonia (days)							
Number (%) of events	4 (7.8)	11 (17.5)	11 (20.0)	7 (13.2)	7 (17.5)	7 (21.2)	0.2048
Number (%) of patients censored	47 (92.2)	52 (82.5)	44 (80.0)	46 (86.8)	33 (82.5)	26 (78.8)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (5.8809 to NC)	NC (1.9384 to NC)	NC (6.7351 to NC)	NC (1.6756 to NC)	NC (1.0185 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1196		0.3248		0.8553	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.2 Treatment emergent adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Neutropenia (days)							
Number (%) of events	8 (25.8)	18 (46.2)	33 (34.0)	47 (48.0)	9 (42.9)	6 (40.0)	0.5138
Number (%) of patients censored	23 (74.2)	21 (53.8)	64 (66.0)	51 (52.0)	12 (57.1)	9 (60.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	7.6222 (0.6899 to NC)	1.4456 (0.6242 to 3.0554)	2.8255 (0.9856 to 4.9938)	0.8214 (0.7228 to 0.9856)	0.9856 (0.2300 to 3.3840)	0.7556 (0.4928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (2.1027 to NC)	NC (NC to NC)	NC (1.9055 to NC)	NC (0.9856 to NC)	NC (0.5257 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0970		0.0364		0.9066	
Hazard ratio (95% CI) vs Pd	-	2.00 (0.87 to 4.60)		1.60 (1.03 to 2.50)		0.94 (0.33 to 2.64)	
P-value	-	0.1038		0.0381		0.9072	
Hazard ratio inverted (95% CI) vs IPd			0.62 (0.40 to 0.97)				

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.2 Treatment emergent adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]							
2 Months	0.8065 (0.6191 to 0.9080)	0.6923 (0.5223 to 0.8121)	0.7678 (0.6691 to 0.8406)	0.5915 (0.4875 to 0.6813)	0.6015 (0.3588 to 0.7772)	0.5714 (0.2840 to 0.7797)	
4 Months	0.7742 (0.5840 to 0.8854)	0.6133 (0.4424 to 0.7460)	0.7133 (0.6102 to 0.7936)	0.5600 (0.4559 to 0.6517)	0.5263 (0.2784 to 0.7246)	0.5714 (0.2840 to 0.7797)	
6 Months	0.7742 (0.5840 to 0.8854)	0.6133 (0.4424 to 0.7460)	0.6408 (0.5328 to 0.7301)	0.5490 (0.4449 to 0.6414)	0.5263 (0.2784 to 0.7246)	0.5714 (0.2840 to 0.7797)	
8 Months	0.7419 (0.5497 to 0.8617)	0.5841 (0.4128 to 0.7213)	0.6408 (0.5328 to 0.7301)	0.5362 (0.4318 to 0.6298)	0.5263 (0.2784 to 0.7246)	0.5714 (0.2840 to 0.7797)	
10 Months	0.7419 (0.5497 to 0.8617)	0.5549 (0.3839 to 0.6961)	0.6408 (0.5328 to 0.7301)	0.5213 (0.4159 to 0.6166)	0.5263 (0.2784 to 0.7246)	0.5714 (0.2840 to 0.7797)	
12 Months	0.7419 (0.5497 to 0.8617)	0.5549 (0.3839 to 0.6961)	0.6408 (0.5328 to 0.7301)	0.5064 (0.4002 to 0.6032)	0.5263 (0.2784 to 0.7246)	0.5714 (0.2840 to 0.7797)	
14 Months	0.7419 (0.5497 to 0.8617)	0.5087 (0.3307 to 0.6617)	0.6408 (0.5328 to 0.7301)	0.5064 (0.4002 to 0.6032)	0.5263 (0.2784 to 0.7246)	0.5714 (0.2840 to 0.7797)	
16 Months	0.7419 (0.5497 to 0.8617)	0.5087 (0.3307 to 0.6617)	0.6408 (0.5328 to 0.7301)	0.5064 (0.4002 to 0.6032)	0.5263 (0.2784 to 0.7246)	0.5714 (0.2840 to 0.7797)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.2 Treatment emergent adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	25	27	72	57	12	8	
4 Months	24	23	64	51	6	7	
6 Months	24	21	50	43	4	6	
8 Months	22	20	43	41	4	4	
10 Months	22	19	41	35	4	3	
12 Months	21	17	34	31	4	3	
14 Months	12	10	22	21	4	3	
16 Months	10	6	12	8	1	0	
Oedema peripheral (days)							
Number (%) of events	0 (0.0)	7 (17.9)	13 (13.4)	12 (12.2)	3 (14.3)	1 (6.7)	0.7938
Number (%) of patients censored	31 (100.0)	32 (82.1)	84 (86.6)	86 (87.8)	18 (85.7)	14 (93.3)	
Kaplan-Meier estimates of event in months							

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.13 Treatment emergent severe adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	30	33	93	90	17	12	
4 Months	30	33	90	85	12	11	
6 Months	30	31	79	74	7	9	
8 Months	29	31	70	72	6	7	
10 Months	29	31	65	70	6	6	
12 Months	27	28	54	60	5	6	
14 Months	16	17	34	41	4	6	
16 Months	10	9	15	15	1	2	
Neutropenia (days)							
Number (%) of events	8 (25.8)	18 (46.2)	31 (32.0)	45 (45.9)	9 (42.9)	6 (40.0)	0.5266
Number (%) of patients censored	23 (74.2)	21 (53.8)	66 (68.0)	53 (54.1)	12 (57.1)	9 (60.0)	
Kaplan-Meier estimates of event in months							

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.13 Treatment emergent severe adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	7.6222 (0.6899 to NC)	1.4456 (0.6242 to 3.0554)	2.8255 (0.9856 to NC)	0.8214 (0.7228 to 0.9856)	0.9856 (0.2300 to 3.3840)	0.7556 (0.4928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (2.1027 to NC)	NC (NC to NC)	NC (1.9384 to NC)	NC (0.9856 to NC)	NC (0.5257 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.0970		0.0348		0.9066	
Hazard ratio (95% CI) vs Pd	-	2.00 (0.87 to 4.60)		1.63 (1.03 to 2.58)		0.94 (0.33 to 2.64)	
P-value	-	0.1038		0.0366		0.9072	
Hazard ratio inverted (95% CI) vs IPd			0.61 (0.39 to 0.97)				
Events probability (95% CI)[b]							
2 Months	0.8065 (0.6191 to 0.9080)	0.6923 (0.5223 to 0.8121)	0.7678 (0.6691 to 0.8406)	0.6013 (0.4973 to 0.6906)	0.6015 (0.3588 to 0.7772)	0.5714 (0.2840 to 0.7797)	
4 Months	0.7742 (0.5840 to 0.8854)	0.6133 (0.4424 to 0.7460)	0.7133 (0.6102 to 0.7936)	0.5693 (0.4650 to 0.6607)	0.5263 (0.2784 to 0.7246)	0.5714 (0.2840 to 0.7797)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.13 Treatment emergent severe adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.7742 (0.5840 to 0.8854)	0.6133 (0.4424 to 0.7460)	0.6650 (0.5584 to 0.7516)	0.5693 (0.4650 to 0.6607)	0.5263 (0.2784 to 0.7246)	0.5714 (0.2840 to 0.7797)	
8 Months	0.7419 (0.5497 to 0.8617)	0.5841 (0.4128 to 0.7213)	0.6650 (0.5584 to 0.7516)	0.5564 (0.4515 to 0.6490)	0.5263 (0.2784 to 0.7246)	0.5714 (0.2840 to 0.7797)	
10 Months	0.7419 (0.5497 to 0.8617)	0.5549 (0.3839 to 0.6961)	0.6650 (0.5584 to 0.7516)	0.5409 (0.4347 to 0.6356)	0.5263 (0.2784 to 0.7246)	0.5714 (0.2840 to 0.7797)	
12 Months	0.7419 (0.5497 to 0.8617)	0.5549 (0.3839 to 0.6961)	0.6650 (0.5584 to 0.7516)	0.5255 (0.4182 to 0.6219)	0.5263 (0.2784 to 0.7246)	0.5714 (0.2840 to 0.7797)	
14 Months	0.7419 (0.5497 to 0.8617)	0.5087 (0.3307 to 0.6617)	0.6650 (0.5584 to 0.7516)	0.5255 (0.4182 to 0.6219)	0.5263 (0.2784 to 0.7246)	0.5714 (0.2840 to 0.7797)	
16 Months	0.7419 (0.5497 to 0.8617)	0.5087 (0.3307 to 0.6617)	0.6650 (0.5584 to 0.7516)	0.5255 (0.4182 to 0.6219)	0.5263 (0.2784 to 0.7246)	0.5714 (0.2840 to 0.7797)	
Number of patients at risk[b]							
2 Months	25	27	72	57	12	8	
4 Months	24	23	64	51	6	7	
6 Months	24	21	52	44	4	6	
8 Months	22	20	45	42	4	4	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.13 Treatment emergent severe adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	22	19	43	35	4	3	
12 Months	21	17	35	31	4	3	
14 Months	12	10	22	21	4	3	
16 Months	10	6	12	8	1	0	
Pneumonia (days)							
Number (%) of events	1 (3.2)	4 (10.3)	15 (15.5)	17 (17.3)	6 (28.6)	4 (26.7)	0.5381
Number (%) of patients censored	30 (96.8)	35 (89.7)	82 (84.5)	81 (82.7)	15 (71.4)	11 (73.3)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (6.3409 to NC)	NC (5.6838 to NC)	NC (6.2752 to NC)	2.7598 (0.1314 to NC)	3.9754 (0.4600 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.7598 to NC)	NC (1.3142 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.2 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	18	9	85	104	
4 Months	15	6	77	99	
6 Months	10	5	65	92	
8 Months	10	4	61	89	
10 Months	10	3	58	83	
12 Months	10	3	48	72	
14 Months	9	2	32	49	
16 Months	4	0	16	22	
Neutropenia (days)					
Number (%) of events	7 (33.3)	6 (42.9)	28 (30.1)	57 (49.1)	0.7209
Number (%) of patients censored	14 (66.7)	8 (57.1)	65 (69.9)	59 (50.9)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.2 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	4.5010 (0.5914 to NC)	0.8542 (0.5585 to NC)	2.9569 (1.1499 to NC)	0.8378 (0.7556 to 0.9856)	
Median (95% CI)	NC (4.5010 to NC)	NC (0.8214 to NC)	NC (NC to NC)	10.4476 (2.0370 to NC)	
75% quantile (95% CI)	NC (4.9938 to NC)	NC (1.3799 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4557		0.0050	
Hazard ratio (95% CI) vs Pd	-	1.51 (0.51 to 4.50)		1.89 (1.20 to 2.97)	
P-value	-	0.4588		0.0058	
Hazard ratio inverted (95% CI) vs IPd			0.53 (0.34 to 0.83)		
Events probability (95% CI)[b]					
2 Months	0.8000 (0.5511 to 0.9198)	0.5385 (0.2477 to 0.7599)	0.7927 (0.6944 to 0.8624)	0.6034 (0.5084 to 0.6858)	
4 Months	0.8000 (0.5511 to 0.9198)	0.5385 (0.2477 to 0.7599)	0.7245 (0.6200 to 0.8048)	0.5593 (0.4641 to 0.6442)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.2 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.5333 (0.2422 to 0.7568)	0.5385 (0.2477 to 0.7599)	0.7002 (0.5936 to 0.7838)	0.5501 (0.4549 to 0.6355)	
8 Months	0.5333 (0.2422 to 0.7568)	0.5385 (0.2477 to 0.7599)	0.6862 (0.5780 to 0.7720)	0.5296 (0.4339 to 0.6163)	
10 Months	0.5333 (0.2422 to 0.7568)	0.5385 (0.2477 to 0.7599)	0.6862 (0.5780 to 0.7720)	0.5065 (0.4101 to 0.5951)	
12 Months	0.5333 (0.2422 to 0.7568)	0.5385 (0.2477 to 0.7599)	0.6862 (0.5780 to 0.7720)	0.4948 (0.3980 to 0.5842)	
14 Months	0.5333 (0.2422 to 0.7568)	0.5385 (0.2477 to 0.7599)	0.6862 (0.5780 to 0.7720)	0.4948 (0.3980 to 0.5842)	
16 Months	0.5333 (0.2422 to 0.7568)	0.5385 (0.2477 to 0.7599)	0.6862 (0.5780 to 0.7720)	0.4948 (0.3980 to 0.5842)	
Number of patients at risk[b]					
2 Months	16	7	72	70	
4 Months	13	6	62	61	
6 Months	6	4	55	54	
8 Months	6	3	47	50	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.2 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	6	2	45	43	
12 Months	6	2	41	37	
14 Months	6	2	28	26	
16 Months	4	0	15	11	
Oedema peripheral (days)					
Number (%) of events	1 (4.8)	3 (21.4)	8 (8.6)	14 (12.1)	0.3170
Number (%) of patients censored	20 (95.2)	11 (78.6)	85 (91.4)	102 (87.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (0.3285 to NC)	9.5277 (2.0370 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (9.5277 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (9.5277 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1211		0.5540	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.10 Treatment emergent severe adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	18	10	90	106	
4 Months	15	9	86	101	
6 Months	10	7	76	92	
8 Months	10	6	69	90	
10 Months	10	5	65	88	
12 Months	10	5	55	76	
14 Months	9	4	37	53	
16 Months	4	1	18	22	
Neutropenia (days)					
Number (%) of events	6 (28.6)	5 (35.7)	27 (29.0)	56 (48.3)	0.6847
Number (%) of patients censored	15 (71.4)	9 (64.3)	66 (71.0)	60 (51.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	4.9938 (0.5914 to NC)	0.8542 (0.5585 to NC)	2.9569 (1.1499 to NC)	0.8378 (0.7556 to 0.9856)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.10 Treatment emergent severe adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (4.9938 to NC)	NC (0.8214 to NC)	NC (NC to NC)	NC (2.0370 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5331		0.0045	
Hazard ratio (95% CI) vs Pd	-	1.46 (0.44 to 4.78)		1.92 (1.21 to 3.05)	
P-value	-	0.5355		0.0053	
Hazard ratio inverted (95% CI) vs IPd			0.52 (0.33 to 0.82)		
Events probability (95% CI)[b]					
2 Months	0.8000 (0.5511 to 0.9198)	0.6154 (0.3083 to 0.8184)	0.7927 (0.6944 to 0.8624)	0.6034 (0.5084 to 0.6858)	
4 Months	0.8000 (0.5511 to 0.9198)	0.6154 (0.3083 to 0.8184)	0.7245 (0.6200 to 0.8048)	0.5593 (0.4641 to 0.6442)	
6 Months	0.6222 (0.3226 to 0.8196)	0.6154 (0.3083 to 0.8184)	0.7125 (0.6069 to 0.7944)	0.5593 (0.4641 to 0.6442)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.10 Treatment emergent severe adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.6222 (0.3226 to 0.8196)	0.6154 (0.3083 to 0.8184)	0.6985 (0.5912 to 0.7827)	0.5388 (0.4431 to 0.6251)	
10 Months	0.6222 (0.3226 to 0.8196)	0.6154 (0.3083 to 0.8184)	0.6985 (0.5912 to 0.7827)	0.5154 (0.4186 to 0.6037)	
12 Months	0.6222 (0.3226 to 0.8196)	0.6154 (0.3083 to 0.8184)	0.6985 (0.5912 to 0.7827)	0.5034 (0.4062 to 0.5927)	
14 Months	0.6222 (0.3226 to 0.8196)	0.6154 (0.3083 to 0.8184)	0.6985 (0.5912 to 0.7827)	0.5034 (0.4062 to 0.5927)	
16 Months	0.6222 (0.3226 to 0.8196)	0.6154 (0.3083 to 0.8184)	0.6985 (0.5912 to 0.7827)	0.5034 (0.4062 to 0.5927)	
Number of patients at risk[b]					
2 Months	16	7	72	70	
4 Months	13	6	62	61	
6 Months	7	4	56	55	
8 Months	7	3	48	51	
10 Months	7	2	46	43	
12 Months	7	2	41	37	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.10 Treatment emergent severe adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	6	2	28	26	
16 Months	4	0	15	11	
Pneumonia (days)					
Number (%) of events	6 (28.6)	3 (21.4)	13 (14.0)	19 (16.4)	0.5704
Number (%) of patients censored	15 (71.4)	11 (78.6)	80 (86.0)	97 (83.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.2669 (0.1314 to NC)	NC (0.4600 to NC)	NC (NC to NC)	NC (11.6304 to NC)	
Median (95% CI)	NC (2.2669 to NC)	NC (1.3142 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6913		0.7361	
Hazard ratio (95% CI) vs Pd	-	0.76 (0.19 to 3.02)		1.13 (0.56 to 2.29)	
P-value	-	0.6923		0.7363	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_cyto_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.3 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	31	16	68	94	
4 Months	27	13	64	89	
6 Months	19	12	55	82	
8 Months	19	10	51	80	
10 Months	19	9	48	74	
12 Months	16	8	41	64	
14 Months	12	6	29	42	
16 Months	6	1	14	20	
Neutropenia (days)					
Number (%) of events	13 (38.2)	13 (56.5)	22 (28.9)	49 (47.6)	0.8732
Number (%) of patients censored	21 (61.8)	10 (43.5)	54 (71.1)	54 (52.4)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.3 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	2.0370 (0.5914 to 4.9938)	0.7556 (0.4928 to 0.8542)	3.0883 (1.4127 to NC)	0.8542 (0.7556 to 1.4784)	
Median (95% CI)	NC (4.5010 to NC)	0.9856 (0.7556 to NC)	NC (NC to NC)	NC (2.7926 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.9856 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0950		0.0114	
Hazard ratio (95% CI) vs Pd	-	1.91 (0.88 to 4.14)		1.89 (1.14 to 3.13)	
P-value	-	0.1007		0.0129	
Hazard ratio inverted (95% CI) vs IPd			0.53 (0.32 to 0.87)		
Events probability (95% CI)[b]					
2 Months	0.7590 (0.5753 to 0.8715)	0.4091 (0.2085 to 0.6007)	0.7988 (0.6885 to 0.8735)	0.6311 (0.5302 to 0.7160)	
4 Months	0.7274 (0.5411 to 0.8479)	0.4091 (0.2085 to 0.6007)	0.7299 (0.6132 to 0.8166)	0.5813 (0.4798 to 0.6698)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.3 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.5455 (0.3386 to 0.7124)	0.4091 (0.2085 to 0.6007)	0.7156 (0.5977 to 0.8045)	0.5709 (0.4693 to 0.6601)	
8 Months	0.5455 (0.3386 to 0.7124)	0.4091 (0.2085 to 0.6007)	0.6986 (0.5785 to 0.7905)	0.5476 (0.4453 to 0.6387)	
10 Months	0.5455 (0.3386 to 0.7124)	0.4091 (0.2085 to 0.6007)	0.6986 (0.5785 to 0.7905)	0.5215 (0.4182 to 0.6150)	
12 Months	0.5455 (0.3386 to 0.7124)	0.4091 (0.2085 to 0.6007)	0.6986 (0.5785 to 0.7905)	0.5081 (0.4044 to 0.6028)	
14 Months	0.5455 (0.3386 to 0.7124)	0.4091 (0.2085 to 0.6007)	0.6986 (0.5785 to 0.7905)	0.5081 (0.4044 to 0.6028)	
16 Months	0.5455 (0.3386 to 0.7124)	0.4091 (0.2085 to 0.6007)	0.6986 (0.5785 to 0.7905)	0.5081 (0.4044 to 0.6028)	
Number of patients at risk[b]					
2 Months	25	9	59	65	
4 Months	20	8	53	56	
6 Months	12	6	47	49	
8 Months	12	4	39	46	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.3 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	12	3	37	39	
12 Months	11	3	34	33	
14 Months	9	3	24	23	
16 Months	6	1	13	9	
Oedema peripheral (days)					
Number (%) of events	2 (5.9)	5 (21.7)	7 (9.2)	12 (11.7)	0.2518
Number (%) of patients censored	32 (94.1)	18 (78.3)	69 (90.8)	91 (88.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	9.5277 (2.0370 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (9.5277 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0933		0.7188	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.14 Treatment emergent severe adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	31	18	73	94	
4 Months	27	17	72	89	
6 Months	20	15	64	80	
8 Months	20	13	57	79	
10 Months	20	12	53	77	
12 Months	17	10	46	67	
14 Months	13	7	32	47	
16 Months	7	1	15	21	
Neutropenia (days)					
Number (%) of events	11 (32.4)	12 (52.2)	22 (28.9)	48 (46.6)	0.7095
Number (%) of patients censored	23 (67.6)	11 (47.8)	54 (71.1)	55 (53.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.0370 (0.5914 to NC)	0.7556 (0.4928 to 0.8542)	3.0883 (1.4127 to NC)	0.8542 (0.7556 to 1.4784)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.14 Treatment emergent severe adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (4.9938 to NC)	1.1828 (0.7556 to NC)	NC (NC to NC)	NC (2.7926 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (1.3799 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0852		0.0153	
Hazard ratio (95% CI) vs Pd	-	2.03 (0.89 to 4.62)		1.85 (1.12 to 3.06)	
P-value	-	0.0916		0.0170	
Hazard ratio inverted (95% CI) vs IPd			0.54 (0.33 to 0.90)		
Events probability (95% CI)[b]					
2 Months	0.7590 (0.5753 to 0.8715)	0.4545 (0.2444 to 0.6433)	0.7988 (0.6885 to 0.8735)	0.6311 (0.5302 to 0.7160)	
4 Months	0.7274 (0.5411 to 0.8479)	0.4545 (0.2444 to 0.6433)	0.7299 (0.6132 to 0.8166)	0.5813 (0.4798 to 0.6698)	
6 Months	0.6365 (0.4323 to 0.7839)	0.4545 (0.2444 to 0.6433)	0.7156 (0.5977 to 0.8045)	0.5813 (0.4798 to 0.6698)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.14 Treatment emergent severe adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.6365 (0.4323 to 0.7839)	0.4545 (0.2444 to 0.6433)	0.6986 (0.5785 to 0.7905)	0.5580 (0.4558 to 0.6485)	
10 Months	0.6365 (0.4323 to 0.7839)	0.4545 (0.2444 to 0.6433)	0.6986 (0.5785 to 0.7905)	0.5314 (0.4278 to 0.6246)	
12 Months	0.6365 (0.4323 to 0.7839)	0.4545 (0.2444 to 0.6433)	0.6986 (0.5785 to 0.7905)	0.5178 (0.4136 to 0.6122)	
14 Months	0.6365 (0.4323 to 0.7839)	0.4545 (0.2444 to 0.6433)	0.6986 (0.5785 to 0.7905)	0.5178 (0.4136 to 0.6122)	
16 Months	0.6365 (0.4323 to 0.7839)	0.4545 (0.2444 to 0.6433)	0.6986 (0.5785 to 0.7905)	0.5178 (0.4136 to 0.6122)	
Number of patients at risk[b]					
2 Months	25	9	59	65	
4 Months	20	8	53	56	
6 Months	14	6	47	50	
8 Months	14	4	39	47	
10 Months	14	3	37	39	
12 Months	12	3	34	33	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.14 Treatment emergent severe adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	9	3	24	23	
16 Months	6	1	13	9	
Pneumonia (days)					
Number (%) of events	6 (17.6)	5 (21.7)	13 (17.1)	16 (15.5)	0.6657
Number (%) of patients censored	28 (82.4)	18 (78.3)	63 (82.9)	87 (84.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (1.3799 to NC)	NC (0.4600 to NC)	NC (4.3696 to NC)	NC (11.6304 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7379		0.7274	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.37 to 4.01)		0.88 (0.42 to 1.83)	
P-value	-	0.7384		0.7276	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.3 Treatment emergent adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	82	71	53	61	
4 Months	73	66	50	56	
6 Months	62	60	43	51	
8 Months	58	54	38	51	
10 Months	55	50	36	48	
12 Months	48	44	29	43	
14 Months	30	27	18	31	
16 Months	15	12	9	13	
Neutropenia (days)					
Number (%) of events	28 (31.8)	34 (42.0)	22 (36.1)	37 (52.1)	0.9366
Number (%) of patients censored	60 (68.2)	47 (58.0)	39 (63.9)	34 (47.9)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.3 Treatment emergent adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	2.8255 (0.9528 to NC)	0.8214 (0.7228 to 1.9384)	1.5441 (0.6242 to 4.5010)	0.8542 (0.7556 to 1.0185)	
Median (95% CI)	NC (NC to NC)	NC (2.7926 to NC)	NC (4.5010 to NC)	9.3306 (1.4127 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1007		0.1430	
Hazard ratio (95% CI) vs Pd	-	1.52 (0.92 to 2.50)		1.48 (0.87 to 2.51)	
P-value	-	0.1032		0.1456	
Events probability (95% CI)[b]					
2 Months	0.7948 (0.6943 to 0.8654)	0.6498 (0.5346 to 0.7433)	0.6917 (0.5561 to 0.7934)	0.5775 (0.4543 to 0.6824)	
4 Months	0.7362 (0.6301 to 0.8162)	0.6113 (0.4953 to 0.7084)	0.6543 (0.5165 to 0.7616)	0.5342 (0.4118 to 0.6420)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.3 Treatment emergent adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.6813 (0.5696 to 0.7698)	0.6113 (0.4953 to 0.7084)	0.6153 (0.4757 to 0.7279)	0.5193 (0.3973 to 0.6281)	
8 Months	0.6658 (0.5524 to 0.7568)	0.5800 (0.4621 to 0.6808)	0.6153 (0.4757 to 0.7279)	0.5193 (0.3973 to 0.6281)	
10 Months	0.6658 (0.5524 to 0.7568)	0.5800 (0.4621 to 0.6808)	0.6153 (0.4757 to 0.7279)	0.4835 (0.3611 to 0.5955)	
12 Months	0.6658 (0.5524 to 0.7568)	0.5800 (0.4621 to 0.6808)	0.6153 (0.4757 to 0.7279)	0.4649 (0.3425 to 0.5784)	
14 Months	0.6658 (0.5524 to 0.7568)	0.5523 (0.4278 to 0.6604)	0.6153 (0.4757 to 0.7279)	0.4649 (0.3425 to 0.5784)	
16 Months	0.6658 (0.5524 to 0.7568)	0.5523 (0.4278 to 0.6604)	0.6153 (0.4757 to 0.7279)	0.4649 (0.3425 to 0.5784)	
Number of patients at risk[b]					
2 Months	69	51	40	41	
4 Months	59	45	35	36	
6 Months	47	40	31	30	
8 Months	43	35	26	30	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.3 Treatment emergent adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	41	31	26	26	
12 Months	38	28	21	23	
14 Months	26	20	12	14	
16 Months	16	7	7	7	
Oedema peripheral (days)					
Number (%) of events	11 (12.5)	9 (11.1)	5 (8.2)	11 (15.5)	0.3324
Number (%) of patients censored	77 (87.5)	72 (88.9)	56 (91.8)	60 (84.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (10.7762 to NC)	NC (NC to NC)	NC (9.1992 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6804		0.3344	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.12 Treatment emergent severe adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	84	71	56	64	
4 Months	79	68	53	61	
6 Months	70	61	46	53	
8 Months	65	57	40	53	
10 Months	62	55	38	52	
12 Months	55	47	31	47	
14 Months	35	32	19	32	
16 Months	17	12	9	14	
Neutropenia (days)					
Number (%) of events	27 (30.7)	34 (42.0)	21 (34.4)	35 (49.3)	0.8318
Number (%) of patients censored	61 (69.3)	47 (58.0)	40 (65.6)	36 (50.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.8255 (0.9528 to NC)	0.8214 (0.7228 to 1.9384)	1.5441 (0.6242 to 4.9938)	0.8542 (0.7556 to 1.0185)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.12 Treatment emergent severe adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (2.7926 to NC)	NC (4.9938 to NC)	10.4476 (1.4784 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0758		0.1680	
Hazard ratio (95% CI) vs Pd	-	1.57 (0.95 to 2.61)		1.46 (0.85 to 2.51)	
P-value	-	0.0784		0.1706	
Events probability (95% CI)[b]					
2 Months	0.7948 (0.6943 to 0.8654)	0.6498 (0.5346 to 0.7433)	0.6917 (0.5561 to 0.7934)	0.5909 (0.4675 to 0.6949)	
4 Months	0.7362 (0.6301 to 0.8162)	0.6113 (0.4953 to 0.7084)	0.6543 (0.5165 to 0.7616)	0.5466 (0.4234 to 0.6540)	
6 Months	0.6952 (0.5847 to 0.7817)	0.6113 (0.4953 to 0.7084)	0.6345 (0.4956 to 0.7447)	0.5466 (0.4234 to 0.6540)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.12 Treatment emergent severe adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.6798 (0.5674 to 0.7688)	0.5800 (0.4621 to 0.6808)	0.6345 (0.4956 to 0.7447)	0.5466 (0.4234 to 0.6540)	
10 Months	0.6798 (0.5674 to 0.7688)	0.5800 (0.4621 to 0.6808)	0.6345 (0.4956 to 0.7447)	0.5089 (0.3843 to 0.6205)	
12 Months	0.6798 (0.5674 to 0.7688)	0.5800 (0.4621 to 0.6808)	0.6345 (0.4956 to 0.7447)	0.4893 (0.3642 to 0.6030)	
14 Months	0.6798 (0.5674 to 0.7688)	0.5523 (0.4278 to 0.6604)	0.6345 (0.4956 to 0.7447)	0.4893 (0.3642 to 0.6030)	
16 Months	0.6798 (0.5674 to 0.7688)	0.5523 (0.4278 to 0.6604)	0.6345 (0.4956 to 0.7447)	0.4893 (0.3642 to 0.6030)	
Number of patients at risk[b]					
2 Months	69	51	40	41	
4 Months	59	45	35	36	
6 Months	48	40	32	31	
8 Months	44	35	27	31	
10 Months	42	31	27	26	
12 Months	38	28	22	23	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.12 Treatment emergent severe adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	26	20	12	14	
16 Months	16	7	7	7	
Pneumonia (days)					
Number (%) of events	13 (14.8)	11 (13.6)	9 (14.8)	14 (19.7)	0.6305
Number (%) of patients censored	75 (85.2)	70 (86.4)	52 (85.2)	57 (80.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (5.6838 to NC)	NC (NC to NC)	NC (2.6283 to NC)	NC (4.2710 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8474		0.6327	
Hazard ratio (95% CI) vs Pd	-	0.92 (0.41 to 2.06)		1.23 (0.53 to 2.83)	
P-value	-	0.8478		0.6333	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.2 Treatment emergent adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	2	2	133	130	
4 Months	2	2	121	120	
6 Months	2	2	103	109	
8 Months	2	2	94	103	
10 Months	1	2	90	96	
12 Months	1	1	76	86	
14 Months	1	0	47	58	
16 Months	0	0	24	25	
Neutropenia (days)					
Number (%) of events	0 (0.0)	1 (50.0)	50 (34.0)	70 (46.7)	0.9845
Number (%) of patients censored	2 (100.0)	1 (50.0)	97 (66.0)	80 (53.3)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.2 Treatment emergent adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	NC (NC to NC)	2.0370 (2.0370 to NC)	1.9384 (0.9528 to 4.6653)	0.8542 (0.7556 to 0.9856)	
Median (95% CI)	NC (NC to NC)	NC (2.0370 to NC)	NC (NC to NC)	NC (2.8912 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (2.0370 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.0273	
Hazard ratio (95% CI) vs Pd	-	NC		1.50 (1.04 to 2.16)	
P-value	-	0.9990		0.0283	
Hazard ratio inverted (95% CI) vs IPd			0.67 (0.46 to 0.96)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.7498 (0.6705 to 0.8126)	0.6105 (0.5273 to 0.6836)	
4 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.6986 (0.6158 to 0.7669)	0.5760 (0.4923 to 0.6508)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.2 Treatment emergent adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.6493 (0.5633 to 0.7226)	0.5688 (0.4851 to 0.6440)	
8 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.6400 (0.5533 to 0.7143)	0.5521 (0.4677 to 0.6285)	
10 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.6400 (0.5533 to 0.7143)	0.5333 (0.4480 to 0.6113)	
12 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.6400 (0.5533 to 0.7143)	0.5238 (0.4380 to 0.6026)	
14 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.6400 (0.5533 to 0.7143)	0.5100 (0.4223 to 0.5910)	
16 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.6400 (0.5533 to 0.7143)	0.5100 (0.4223 to 0.5910)	
Number of patients at risk[b]					
2 Months	2	2	107	90	
4 Months	2	1	92	80	
6 Months	2	1	76	69	
8 Months	2	1	67	64	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.2 Treatment emergent adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	1	1	66	56	
12 Months	1	1	58	50	
14 Months	1	0	37	34	
16 Months	0	0	23	14	
Oedema peripheral (days)					
Number (%) of events	0 (0.0)	0 (0.0)	16 (10.9)	20 (13.3)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	131 (89.1)	130 (86.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.7321	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.12 Treatment emergent severe adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	2	2	138	133	
4 Months	2	2	130	127	
6 Months	2	2	114	112	
8 Months	2	2	103	108	
10 Months	1	2	99	105	
12 Months	1	1	85	93	
14 Months	1	0	53	64	
16 Months	0	0	26	26	
Neutropenia (days)					
Number (%) of events	0 (0.0)	1 (50.0)	48 (32.7)	68 (45.3)	0.9848
Number (%) of patients censored	2 (100.0)	1 (50.0)	99 (67.3)	82 (54.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	2.0370 (2.0370 to NC)	1.9384 (0.9528 to 4.9938)	0.8542 (0.7556 to 1.0185)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.12 Treatment emergent severe adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (2.0370 to NC)	NC (NC to NC)	NC (3.0554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (2.0370 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.0258	
Hazard ratio (95% CI) vs Pd	-	NC		1.52 (1.05 to 2.20)	
P-value	-	0.9990		0.0268	
Hazard ratio inverted (95% CI) vs IPd			0.66 (0.46 to 0.95)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.7498 (0.6705 to 0.8126)	0.6170 (0.5338 to 0.6897)	
4 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.6986 (0.6158 to 0.7669)	0.5821 (0.4983 to 0.6567)	
6 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.6658 (0.5807 to 0.7375)	0.5821 (0.4983 to 0.6567)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.12 Treatment emergent severe adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.6565 (0.5706 to 0.7293)	0.5652 (0.4807 to 0.6412)	
10 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.6565 (0.5706 to 0.7293)	0.5460 (0.4604 to 0.6238)	
12 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.6565 (0.5706 to 0.7293)	0.5363 (0.4501 to 0.6149)	
14 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.6565 (0.5706 to 0.7293)	0.5222 (0.4338 to 0.6031)	
16 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.6565 (0.5706 to 0.7293)	0.5222 (0.4338 to 0.6031)	
Number of patients at risk[b]					
2 Months	2	2	107	90	
4 Months	2	1	92	80	
6 Months	2	1	78	70	
8 Months	2	1	69	65	
10 Months	1	1	68	56	
12 Months	1	1	59	50	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.12 Treatment emergent severe adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	1	0	37	34	
16 Months	0	0	23	14	
Pneumonia (days)					
Number (%) of events	0 (0.0)	0 (0.0)	22 (15.0)	25 (16.7)	1.0000
Number (%) of patients censored	2 (100.0)	2 (100.0)	125 (85.0)	125 (83.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.6304 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.7931	
Hazard ratio (95% CI) vs Pd	-	NC		1.08 (0.61 to 1.91)	
P-value	-			0.7934	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.3 Treatment emergent adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	88	90	37	28	
4 Months	82	84	32	26	
6 Months	66	76	31	25	
8 Months	60	70	28	25	
10 Months	57	64	27	24	
12 Months	48	55	23	23	
14 Months	30	35	12	16	
16 Months	15	14	7	6	
Neutropenia (days)					
Number (%) of events	32 (32.7)	47 (45.6)	14 (35.0)	20 (62.5)	0.2677
Number (%) of patients censored	66 (67.3)	56 (54.4)	26 (65.0)	12 (37.5)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.3 Treatment emergent adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	2.8255 (0.9856 to 7.6222)	0.8542 (0.7556 to 1.4456)	1.5441 (0.7556 to NC)	0.8049 (0.5257 to 0.8542)	
Median (95% CI)	NC (NC to NC)	NC (3.0554 to NC)	NC (4.9938 to NC)	1.6263 (0.8542 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.8912 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0645		0.0247	
Hazard ratio (95% CI) vs Pd	-	1.52 (0.97 to 2.39)		2.15 (1.08 to 4.27)	
P-value	-	0.0664		0.0283	
Hazard ratio inverted (95% CI) vs IPd			0.46 (0.23 to 0.92)		
Events probability (95% CI)[b]					
2 Months	0.7810 (0.6841 to 0.8513)	0.6374 (0.5361 to 0.7222)	0.7179 (0.5488 to 0.8328)	0.4375 (0.2646 to 0.5981)	
4 Months	0.7165 (0.6143 to 0.7960)	0.5978 (0.4960 to 0.6856)	0.6892 (0.5176 to 0.8103)	0.4063 (0.2383 to 0.5679)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.3 Treatment emergent adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.6684 (0.5624 to 0.7543)	0.5875 (0.4856 to 0.6760)	0.6266 (0.4501 to 0.7605)	0.4063 (0.2383 to 0.5679)	
8 Months	0.6553 (0.5482 to 0.7429)	0.5762 (0.4740 to 0.6657)	0.6266 (0.4501 to 0.7605)	0.3724 (0.2098 to 0.5353)	
10 Months	0.6553 (0.5482 to 0.7429)	0.5500 (0.4463 to 0.6422)	0.6266 (0.4501 to 0.7605)	0.3724 (0.2098 to 0.5353)	
12 Months	0.6553 (0.5482 to 0.7429)	0.5366 (0.4322 to 0.6301)	0.6266 (0.4501 to 0.7605)	0.3724 (0.2098 to 0.5353)	
14 Months	0.6553 (0.5482 to 0.7429)	0.5167 (0.4092 to 0.6140)	0.6266 (0.4501 to 0.7605)	0.3724 (0.2098 to 0.5353)	
16 Months	0.6553 (0.5482 to 0.7429)	0.5167 (0.4092 to 0.6140)	0.6266 (0.4501 to 0.7605)	0.3724 (0.2098 to 0.5353)	
Number of patients at risk[b]					
2 Months	74	65	28	14	
4 Months	65	58	23	13	
6 Months	53	52	20	12	
8 Months	48	48	16	11	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.3 Treatment emergent adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	46	41	16	10	
12 Months	40	36	15	10	
14 Months	26	25	8	5	
16 Months	15	9	6	2	
Oedema peripheral (days)					
Number (%) of events	10 (10.2)	16 (15.5)	4 (10.0)	3 (9.4)	0.4582
Number (%) of patients censored	88 (89.8)	87 (84.5)	36 (90.0)	29 (90.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (10.1191 to NC)	NC (2.6612 to NC)	NC (9.1992 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3985		0.7909	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.14 Treatment emergent severe adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	94	94	37	26	
4 Months	91	90	33	26	
6 Months	76	80	32	25	
8 Months	69	76	28	25	
10 Months	66	73	27	25	
12 Months	57	63	23	23	
14 Months	35	44	13	14	
16 Months	17	17	7	5	
Neutropenia (days)					
Number (%) of events	31 (31.6)	46 (44.7)	13 (32.5)	19 (59.4)	0.2653
Number (%) of patients censored	67 (68.4)	57 (55.3)	27 (67.5)	13 (40.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.8255 (0.9856 to NC)	0.8542 (0.7556 to 1.4456)	1.5441 (0.7556 to NC)	0.8049 (0.5257 to 0.8542)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.14 Treatment emergent severe adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (3.0554 to NC)	NC (4.9938 to NC)	1.8398 (0.8542 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.4908 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0614		0.0265	
Hazard ratio (95% CI) vs Pd	-	1.54 (0.98 to 2.43)		2.18 (1.08 to 4.43)	
P-value	-	0.0634		0.0305	
Hazard ratio inverted (95% CI) vs IPd			0.46 (0.23 to 0.93)		
Events probability (95% CI)[b]					
2 Months	0.7810 (0.6841 to 0.8513)	0.6374 (0.5361 to 0.7222)	0.7179 (0.5488 to 0.8328)	0.4648 (0.2868 to 0.6251)	
4 Months	0.7165 (0.6143 to 0.7960)	0.5978 (0.4960 to 0.6856)	0.6892 (0.5176 to 0.8103)	0.4316 (0.2579 to 0.5940)	
6 Months	0.6804 (0.5752 to 0.7648)	0.5978 (0.4960 to 0.6856)	0.6579 (0.4833 to 0.7858)	0.4316 (0.2579 to 0.5940)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.14 Treatment emergent severe adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.6673 (0.5609 to 0.7535)	0.5866 (0.4844 to 0.6753)	0.6579 (0.4833 to 0.7858)	0.3957 (0.2266 to 0.5604)	
10 Months	0.6673 (0.5609 to 0.7535)	0.5599 (0.4559 to 0.6516)	0.6579 (0.4833 to 0.7858)	0.3957 (0.2266 to 0.5604)	
12 Months	0.6673 (0.5609 to 0.7535)	0.5462 (0.4415 to 0.6394)	0.6579 (0.4833 to 0.7858)	0.3957 (0.2266 to 0.5604)	
14 Months	0.6673 (0.5609 to 0.7535)	0.5260 (0.4178 to 0.6232)	0.6579 (0.4833 to 0.7858)	0.3957 (0.2266 to 0.5604)	
16 Months	0.6673 (0.5609 to 0.7535)	0.5260 (0.4178 to 0.6232)	0.6579 (0.4833 to 0.7858)	0.3957 (0.2266 to 0.5604)	
Number of patients at risk[b]					
2 Months	74	65	28	14	
4 Months	65	58	23	13	
6 Months	54	53	21	12	
8 Months	49	49	17	11	
10 Months	47	41	17	10	
12 Months	41	36	15	10	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.14 Treatment emergent severe adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	26	25	8	5	
16 Months	15	9	6	2	
Pneumonia (days)					
Number (%) of events	18 (18.4)	19 (18.4)	4 (10.0)	5 (15.6)	0.8499
Number (%) of patients censored	80 (81.6)	84 (81.6)	36 (90.0)	27 (84.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (3.5154 to NC)	NC (6.2752 to NC)	NC (5.6838 to NC)	NC (2.8583 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9331		0.5845	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.51 to 1.85)		1.44 (0.39 to 5.37)	
P-value	-	0.9331		0.5865	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.3 Treatment emergent adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	87	89	47	42	
4 Months	81	83	41	38	
6 Months	65	75	39	35	
8 Months	59	69	36	35	
10 Months	56	63	34	34	
12 Months	47	54	29	32	
14 Months	29	35	18	23	
16 Months	14	14	9	11	
Neutropenia (days)					
Number (%) of events	32 (33.0)	45 (44.6)	18 (35.3)	25 (50.0)	0.8204
Number (%) of patients censored	65 (67.0)	56 (55.4)	33 (64.7)	25 (50.0)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_dghc_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.3 Treatment emergent adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	2.8255 (0.9856 to 7.6222)	0.8542 (0.7556 to 1.9384)	1.4127 (0.7885 to 5.0267)	0.8542 (0.5585 to 1.0185)	
Median (95% CI)	NC (NC to NC)	NC (4.4353 to NC)	NC (5.0267 to NC)	7.4908 (0.9856 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1021		0.1432	
Hazard ratio (95% CI) vs Pd	-	1.46 (0.93 to 2.29)		1.57 (0.85 to 2.87)	
P-value	-	0.1041		0.1466	
Events probability (95% CI)[b]					
2 Months	0.7787 (0.6810 to 0.8497)	0.6501 (0.5481 to 0.7347)	0.7000 (0.5525 to 0.8070)	0.5586 (0.4107 to 0.6832)	
4 Months	0.7135 (0.6105 to 0.7938)	0.6098 (0.5070 to 0.6975)	0.6774 (0.5281 to 0.7885)	0.5156 (0.3690 to 0.6440)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.3 Treatment emergent adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.6648 (0.5580 to 0.7515)	0.5993 (0.4963 to 0.6878)	0.6290 (0.4761 to 0.7486)	0.5156 (0.3690 to 0.6440)	
8 Months	0.6515 (0.5436 to 0.7399)	0.5878 (0.4844 to 0.6773)	0.6290 (0.4761 to 0.7486)	0.4870 (0.3392 to 0.6196)	
10 Months	0.6515 (0.5436 to 0.7399)	0.5610 (0.4560 to 0.6535)	0.6290 (0.4761 to 0.7486)	0.4870 (0.3392 to 0.6196)	
12 Months	0.6515 (0.5436 to 0.7399)	0.5474 (0.4416 to 0.6412)	0.6290 (0.4761 to 0.7486)	0.4870 (0.3392 to 0.6196)	
14 Months	0.6515 (0.5436 to 0.7399)	0.5271 (0.4180 to 0.6249)	0.6290 (0.4761 to 0.7486)	0.4870 (0.3392 to 0.6196)	
16 Months	0.6515 (0.5436 to 0.7399)	0.5271 (0.4180 to 0.6249)	0.6290 (0.4761 to 0.7486)	0.4870 (0.3392 to 0.6196)	
Number of patients at risk[b]					
2 Months	73	65	35	27	
4 Months	64	58	29	23	
6 Months	52	52	25	18	
8 Months	47	48	21	17	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.3 Treatment emergent adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	45	41	21	16	
12 Months	39	36	19	15	
14 Months	25	25	12	9	
16 Months	14	9	8	5	
Oedema peripheral (days)					
Number (%) of events	10 (10.3)	15 (14.9)	6 (11.8)	4 (8.0)	0.2997
Number (%) of patients censored	87 (89.7)	86 (85.1)	45 (88.2)	46 (92.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (10.1191 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4872		0.4531	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.15 Treatment emergent severe adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	93	92	46	42	
4 Months	90	88	41	40	
6 Months	75	78	40	35	
8 Months	68	74	36	35	
10 Months	65	71	34	35	
12 Months	56	61	29	32	
14 Months	34	43	19	21	
16 Months	16	17	9	9	
Neutropenia (days)					
Number (%) of events	31 (32.0)	44 (43.6)	17 (33.3)	24 (48.0)	0.8177
Number (%) of patients censored	66 (68.0)	57 (56.4)	34 (66.7)	26 (52.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.8255 (0.9856 to NC)	0.8542 (0.7556 to 1.9384)	1.4127 (0.7885 to NC)	0.8542 (0.5585 to 1.4127)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.15 Treatment emergent severe adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (6.0780 to NC)	NC (NC to NC)	NC (1.0185 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0976		0.1437	
Hazard ratio (95% CI) vs Pd	-	1.47 (0.93 to 2.33)		1.58 (0.85 to 2.95)	
P-value	-	0.0997		0.1472	
Events probability (95% CI)[b]					
2 Months	0.7787 (0.6810 to 0.8497)	0.6501 (0.5481 to 0.7347)	0.7000 (0.5525 to 0.8070)	0.5772 (0.4282 to 0.7005)	
4 Months	0.7135 (0.6105 to 0.7938)	0.6098 (0.5070 to 0.6975)	0.6774 (0.5281 to 0.7885)	0.5328 (0.3844 to 0.6607)	
6 Months	0.6769 (0.5709 to 0.7621)	0.6098 (0.5070 to 0.6975)	0.6532 (0.5018 to 0.7688)	0.5328 (0.3844 to 0.6607)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.15 Treatment emergent severe adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.6636 (0.5564 to 0.7507)	0.5983 (0.4950 to 0.6871)	0.6532 (0.5018 to 0.7688)	0.5032 (0.3530 to 0.6358)	
10 Months	0.6636 (0.5564 to 0.7507)	0.5711 (0.4659 to 0.6631)	0.6532 (0.5018 to 0.7688)	0.5032 (0.3530 to 0.6358)	
12 Months	0.6636 (0.5564 to 0.7507)	0.5572 (0.4511 to 0.6507)	0.6532 (0.5018 to 0.7688)	0.5032 (0.3530 to 0.6358)	
14 Months	0.6636 (0.5564 to 0.7507)	0.5365 (0.4268 to 0.6343)	0.6532 (0.5018 to 0.7688)	0.5032 (0.3530 to 0.6358)	
16 Months	0.6636 (0.5564 to 0.7507)	0.5365 (0.4268 to 0.6343)	0.6532 (0.5018 to 0.7688)	0.5032 (0.3530 to 0.6358)	
Number of patients at risk[b]					
2 Months	73	65	35	27	
4 Months	64	58	29	23	
6 Months	53	53	26	18	
8 Months	48	49	22	17	
10 Months	46	41	22	16	
12 Months	40	36	19	15	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.15 Treatment emergent severe adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	25	25	12	9	
16 Months	14	9	8	5	
Pneumonia (days)					
Number (%) of events	18 (18.6)	19 (18.8)	4 (7.8)	6 (12.0)	0.5626
Number (%) of patients censored	79 (81.4)	82 (81.2)	47 (92.2)	44 (88.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (3.5154 to NC)	NC (5.9795 to NC)	NC (NC to NC)	NC (11.6304 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9579		0.5503	
Hazard ratio (95% CI) vs Pd	-	0.98 (0.52 to 1.87)		1.47 (0.41 to 5.20)	
P-value	-	0.9579		0.5527	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.2 Treatment emergent adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	8	13	127	119	
4 Months	5	12	118	110	
6 Months	3	10	102	101	
8 Months	1	9	95	96	
10 Months	1	9	90	89	
12 Months	1	7	76	80	
14 Months	1	6	47	52	
16 Months	0	5	24	20	
Neutropenia (days)					
Number (%) of events	1 (10.0)	7 (50.0)	49 (35.3)	64 (46.4)	0.2436
Number (%) of patients censored	9 (90.0)	7 (50.0)	90 (64.7)	74 (53.6)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.2 Treatment emergent adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	NC (0.7556 to NC)	0.8542 (0.5257 to 2.0370)	1.9384 (0.9528 to 4.5010)	0.8542 (0.7556 to 1.0185)	
Median (95% CI)	NC (0.7556 to NC)	NC (0.7556 to NC)	NC (NC to NC)	NC (3.0554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (2.0370 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0749		0.0499	
Hazard ratio (95% CI) vs Pd	-	5.46 (0.67 to 44.45)		1.45 (1.00 to 2.10)	
P-value	-	0.1128		0.0512	
Events probability (95% CI)[b]					
2 Months	0.8889 (0.4330 to 0.9836)	0.5714 (0.2840 to 0.7797)	0.7441 (0.6622 to 0.8090)	0.6204 (0.5335 to 0.6957)	
4 Months	0.8889 (0.4330 to 0.9836)	0.5000 (0.2286 to 0.7221)	0.6911 (0.6059 to 0.7615)	0.5827 (0.4953 to 0.6602)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.2 Treatment emergent adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.8889 (0.4330 to 0.9836)	0.5000 (0.2286 to 0.7221)	0.6411 (0.5530 to 0.7163)	0.5748 (0.4873 to 0.6528)	
8 Months	0.8889 (0.4330 to 0.9836)	0.5000 (0.2286 to 0.7221)	0.6319 (0.5433 to 0.7080)	0.5567 (0.4685 to 0.6361)	
10 Months	0.8889 (0.4330 to 0.9836)	0.5000 (0.2286 to 0.7221)	0.6319 (0.5433 to 0.7080)	0.5365 (0.4472 to 0.6176)	
12 Months	0.8889 (0.4330 to 0.9836)	0.5000 (0.2286 to 0.7221)	0.6319 (0.5433 to 0.7080)	0.5262 (0.4364 to 0.6082)	
14 Months	0.8889 (0.4330 to 0.9836)	0.5000 (0.2286 to 0.7221)	0.6319 (0.5433 to 0.7080)	0.5111 (0.4192 to 0.5957)	
16 Months	0.8889 (0.4330 to 0.9836)	0.5000 (0.2286 to 0.7221)	0.6319 (0.5433 to 0.7080)	0.5111 (0.4192 to 0.5957)	
Number of patients at risk[b]					
2 Months	8	8	101	84	
4 Months	6	7	88	74	
6 Months	4	6	74	64	
8 Months	2	5	67	60	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.2 Treatment emergent adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	2	5	65	52	
12 Months	2	4	57	47	
14 Months	2	3	36	31	
16 Months	0	2	23	12	
Oedema peripheral (days)					
Number (%) of events	2 (20.0)	1 (7.1)	14 (10.1)	19 (13.8)	0.1518
Number (%) of patients censored	8 (80.0)	13 (92.9)	125 (89.9)	119 (86.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (0.3943 to NC)	NC (2.0370 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (0.3943 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2883		0.4785	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.10 Treatment emergent severe adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	9	13	131	122	
4 Months	7	13	125	116	
6 Months	5	11	111	103	
8 Months	2	10	103	100	
10 Months	2	10	98	97	
12 Months	2	8	84	86	
14 Months	2	7	52	57	
16 Months	0	5	26	21	
Neutropenia (days)					
Number (%) of events	1 (10.0)	7 (50.0)	47 (33.8)	62 (44.9)	0.2459
Number (%) of patients censored	9 (90.0)	7 (50.0)	92 (66.2)	76 (55.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (0.7556 to NC)	0.8542 (0.5257 to 2.0370)	1.9384 (0.9528 to 4.6653)	0.8542 (0.7556 to 1.0185)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.10 Treatment emergent severe adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (0.7556 to NC)	NC (0.7556 to NC)	NC (NC to NC)	NC (6.0780 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (2.0370 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0749		0.0488	
Hazard ratio (95% CI) vs Pd	-	5.46 (0.67 to 44.45)		1.46 (1.00 to 2.13)	
P-value	-	0.1128		0.0501	
Events probability (95% CI)[b]					
2 Months	0.8889 (0.4330 to 0.9836)	0.5714 (0.2840 to 0.7797)	0.7441 (0.6622 to 0.8090)	0.6275 (0.5408 to 0.7024)	
4 Months	0.8889 (0.4330 to 0.9836)	0.5000 (0.2286 to 0.7221)	0.6911 (0.6059 to 0.7615)	0.5894 (0.5019 to 0.6667)	
6 Months	0.8889 (0.4330 to 0.9836)	0.5000 (0.2286 to 0.7221)	0.6578 (0.5705 to 0.7315)	0.5894 (0.5019 to 0.6667)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.10 Treatment emergent severe adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.8889 (0.4330 to 0.9836)	0.5000 (0.2286 to 0.7221)	0.6486 (0.5607 to 0.7233)	0.5711 (0.4828 to 0.6499)	
10 Months	0.8889 (0.4330 to 0.9836)	0.5000 (0.2286 to 0.7221)	0.6486 (0.5607 to 0.7233)	0.5504 (0.4607 to 0.6312)	
12 Months	0.8889 (0.4330 to 0.9836)	0.5000 (0.2286 to 0.7221)	0.6486 (0.5607 to 0.7233)	0.5398 (0.4495 to 0.6216)	
14 Months	0.8889 (0.4330 to 0.9836)	0.5000 (0.2286 to 0.7221)	0.6486 (0.5607 to 0.7233)	0.5244 (0.4317 to 0.6089)	
16 Months	0.8889 (0.4330 to 0.9836)	0.5000 (0.2286 to 0.7221)	0.6486 (0.5607 to 0.7233)	0.5244 (0.4317 to 0.6089)	
Number of patients at risk[b]					
2 Months	8	8	101	84	
4 Months	6	7	88	74	
6 Months	4	6	76	65	
8 Months	2	5	69	61	
10 Months	2	5	67	52	
12 Months	2	4	58	47	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.10 Treatment emergent severe adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	2	3	36	31	
16 Months	0	2	23	12	
Pneumonia (days)					
Number (%) of events	0 (0.0)	3 (21.4)	22 (15.8)	22 (15.9)	0.9878
Number (%) of patients censored	10 (100.0)	11 (78.6)	117 (84.2)	116 (84.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.2300 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (1.0185 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1420		0.9319	
Hazard ratio (95% CI) vs Pd	-	NC		0.97 (0.54 to 1.76)	
P-value	-	0.9973		0.9319	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.2 Treatment emergent adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.9165 (0.8318 to 0.9596)	0.8067 (0.7033 to 0.8772)	0.8387 (0.6903 to 0.9198)	0.8877 (0.7668 to 0.9479)	
Number of patients at risk[b]					
2 Months	88	74	40	49	
4 Months	83	71	34	44	
6 Months	74	66	27	40	
8 Months	68	63	24	37	
10 Months	64	60	23	33	
12 Months	56	51	19	31	
14 Months	33	32	13	22	
16 Months	15	15	7	9	
Neutropenia (days)					
Number (%) of events	29 (30.9)	43 (50.0)	19 (40.4)	24 (44.4)	0.1716
Number (%) of patients censored	65 (69.1)	43 (50.0)	28 (59.6)	30 (55.6)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.2 Treatment emergent adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.8255 (0.9199 to NC)	0.8214 (0.6242 to 0.9856)	1.4456 (0.5914 to 3.3840)	0.8542 (0.7556 to 1.4784)	
Median (95% CI)	NC (NC to NC)	9.3306 (1.9384 to NC)	NC (2.9569 to NC)	NC (1.4784 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0072		0.7271	
Hazard ratio (95% CI) vs Pd	-	1.89 (1.18 to 3.03)		1.11 (0.61 to 2.03)	
P-value	-	0.0082		0.7273	
Hazard ratio inverted (95% CI) vs IPd	0.53 (0.33 to 0.85)				
Events probability (95% CI)[b]					
2 Months	0.7626 (0.6622 to 0.8368)	0.6040 (0.4925 to 0.6984)	0.7181 (0.5645 to 0.8255)	0.6111 (0.4683 to 0.7264)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.2 Treatment emergent adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	0.7293 (0.6261 to 0.8082)	0.5566 (0.4453 to 0.6543)	0.6238 (0.4655 to 0.7473)	0.5914 (0.4485 to 0.7089)	
6 Months	0.6908 (0.5838 to 0.7755)	0.5566 (0.4453 to 0.6543)	0.5758 (0.4175 to 0.7055)	0.5717 (0.4288 to 0.6912)	
8 Months	0.6770 (0.5686 to 0.7638)	0.5284 (0.4164 to 0.6285)	0.5758 (0.4175 to 0.7055)	0.5717 (0.4288 to 0.6912)	
10 Months	0.6770 (0.5686 to 0.7638)	0.4974 (0.3845 to 0.6003)	0.5758 (0.4175 to 0.7055)	0.5717 (0.4288 to 0.6912)	
12 Months	0.6770 (0.5686 to 0.7638)	0.4974 (0.3845 to 0.6003)	0.5758 (0.4175 to 0.7055)	0.5457 (0.4009 to 0.6694)	
14 Months	0.6770 (0.5686 to 0.7638)	0.4737 (0.3573 to 0.5812)	0.5758 (0.4175 to 0.7055)	0.5457 (0.4009 to 0.6694)	
16 Months	0.6770 (0.5686 to 0.7638)	0.4737 (0.3573 to 0.5812)	0.5758 (0.4175 to 0.7055)	0.5457 (0.4009 to 0.6694)	
Number of patients at risk[b]					
2 Months	70	51	33	33	
4 Months	63	45	26	30	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.2 Treatment emergent adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	52	40	23	27	
8 Months	47	37	19	25	
10 Months	45	32	19	22	
12 Months	40	28	17	20	
14 Months	23	18	13	13	
16 Months	15	9	6	4	
Oedema peripheral (days)					
Number (%) of events	10 (10.6)	15 (17.4)	6 (12.8)	5 (9.3)	0.2193
Number (%) of patients censored	84 (89.4)	71 (82.6)	41 (87.2)	49 (90.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (8.9035 to NC)	NC (8.1150 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.11 Treatment emergent severe adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	91	79	42	47	
4 Months	87	77	39	45	
6 Months	79	71	33	39	
8 Months	73	69	28	37	
10 Months	70	68	26	35	
12 Months	62	58	22	32	
14 Months	37	41	15	20	
16 Months	17	18	7	8	
Neutropenia (days)					
Number (%) of events	29 (30.9)	43 (50.0)	18 (38.3)	23 (42.6)	0.1891
Number (%) of patients censored	65 (69.1)	43 (50.0)	29 (61.7)	31 (57.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.8255 (0.9199 to NC)	0.8214 (0.6242 to 0.9856)	1.4456 (0.5914 to 3.3840)	0.8542 (0.7556 to 1.4784)	
Median (95% CI)	NC (NC to NC)	9.3306 (1.9384 to NC)	NC (2.9569 to NC)	NC (1.4784 to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.11 Treatment emergent severe adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0072		0.7027	
Hazard ratio (95% CI) vs Pd	-	1.89 (1.18 to 3.03)		1.13 (0.61 to 2.09)	
P-value	-	0.0082		0.7029	
Hazard ratio inverted (95% CI) vs IPd	0.53 (0.33 to 0.85)				
Events probability (95% CI)[b]					
2 Months	0.7626 (0.6622 to 0.8368)	0.6040 (0.4925 to 0.6984)	0.7181 (0.5645 to 0.8255)	0.6111 (0.4683 to 0.7264)	
4 Months	0.7293 (0.6261 to 0.8082)	0.5566 (0.4453 to 0.6543)	0.6238 (0.4655 to 0.7473)	0.5914 (0.4485 to 0.7089)	
6 Months	0.6908 (0.5838 to 0.7755)	0.5566 (0.4453 to 0.6543)	0.5998 (0.4413 to 0.7265)	0.5914 (0.4485 to 0.7089)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.11 Treatment emergent severe adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.6770 (0.5686 to 0.7638)	0.5284 (0.4164 to 0.6285)	0.5998 (0.4413 to 0.7265)	0.5914 (0.4485 to 0.7089)	
10 Months	0.6770 (0.5686 to 0.7638)	0.4974 (0.3845 to 0.6003)	0.5998 (0.4413 to 0.7265)	0.5914 (0.4485 to 0.7089)	
12 Months	0.6770 (0.5686 to 0.7638)	0.4974 (0.3845 to 0.6003)	0.5998 (0.4413 to 0.7265)	0.5645 (0.4188 to 0.6869)	
14 Months	0.6770 (0.5686 to 0.7638)	0.4737 (0.3573 to 0.5812)	0.5998 (0.4413 to 0.7265)	0.5645 (0.4188 to 0.6869)	
16 Months	0.6770 (0.5686 to 0.7638)	0.4737 (0.3573 to 0.5812)	0.5998 (0.4413 to 0.7265)	0.5645 (0.4188 to 0.6869)	
Number of patients at risk[b]					
2 Months	70	51	33	33	
4 Months	63	45	26	30	
6 Months	52	40	24	28	
8 Months	47	37	20	26	
10 Months	45	32	20	22	
12 Months	40	28	18	20	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.11 Treatment emergent severe adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	23	18	13	13	
16 Months	15	9	6	4	
Pneumonia (days)					
Number (%) of events	12 (12.8)	11 (12.8)	10 (21.3)	14 (25.9)	0.7873
Number (%) of patients censored	82 (87.2)	75 (87.2)	37 (78.7)	40 (74.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.6756 to NC)	6.2752 (2.0698 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9476		0.7454	
Hazard ratio (95% CI) vs Pd	-	0.97 (0.43 to 2.21)		1.14 (0.51 to 2.58)	
P-value	-	0.9477		0.7456	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.2 Treatment emergent adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0	0	24	25	
Neutropenia (days)					
Number (%) of events	1 (50.0)	0 (0.0)	49 (33.3)	71 (47.3)	0.9823
Number (%) of patients censored	1 (50.0)	2 (100.0)	98 (66.7)	79 (52.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.1643 (0.1643 to NC)	NC (NC to NC)	2.0370 (0.9856 to 4.9938)	0.8542 (0.7556 to 0.9856)	
Median (95% CI)	NC (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.7926 to NC)	
75% quantile (95% CI)	NC (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.0135	
Hazard ratio (95% CI) vs Pd	-	NC		1.58 (1.10 to 2.27)	
P-value	-	0.9990		0.0143	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.2 Treatment emergent adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.63 (0.44 to 0.91)		
Events probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.7566 (0.6778 to 0.8187)	0.6105 (0.5273 to 0.6836)	
4 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.7054 (0.6230 to 0.7731)	0.5692 (0.4855 to 0.6443)	
6 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.6568 (0.5711 to 0.7295)	0.5620 (0.4783 to 0.6375)	
8 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.6477 (0.5613 to 0.7213)	0.5452 (0.4609 to 0.6219)	
10 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.6477 (0.5613 to 0.7213)	0.5264 (0.4411 to 0.6047)	
12 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.6477 (0.5613 to 0.7213)	0.5168 (0.4311 to 0.5958)	
14 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.6477 (0.5613 to 0.7213)	0.5025 (0.4147 to 0.5839)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.2 Treatment emergent adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.6477 (0.5613 to 0.7213)	0.5025 (0.4147 to 0.5839)	
Number of patients at risk[b]					
2 Months	1	2	108	90	
4 Months	1	2	93	79	
6 Months	0	2	78	68	
8 Months	0	2	69	63	
10 Months	0	2	67	55	
12 Months	0	2	59	49	
14 Months	0	2	38	32	
16 Months	0	0	23	14	
Oedema peripheral (days)					
Number (%) of events	0 (0.0)	0 (0.0)	16 (10.9)	20 (13.3)	1.0000
Number (%) of patients censored	2 (100.0)	2 (100.0)	131 (89.1)	130 (86.7)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.10 Treatment emergent severe adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	2	2	138	133	
4 Months	2	2	130	127	
6 Months	1	2	115	112	
8 Months	0	2	105	108	
10 Months	0	2	100	105	
12 Months	0	2	86	92	
14 Months	0	2	54	62	
16 Months	0	0	26	26	
Neutropenia (days)					
Number (%) of events	1 (50.0)	0 (0.0)	47 (32.0)	69 (46.0)	0.9827
Number (%) of patients censored	1 (50.0)	2 (100.0)	100 (68.0)	81 (54.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.1643 (0.1643 to NC)	NC (NC to NC)	2.0370 (0.9856 to 4.9938)	0.8542 (0.7556 to 1.0185)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.10 Treatment emergent severe adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.8912 to NC)	
75% quantile (95% CI)	NC (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.0127	
Hazard ratio (95% CI) vs Pd	-	NC		1.60 (1.10 to 2.31)	
P-value	-	0.9990		0.0135	
Hazard ratio inverted (95% CI) vs IPd			0.63 (0.43 to 0.91)		
Events probability (95% CI)[b]					
2 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.7566 (0.6778 to 0.8187)	0.6170 (0.5338 to 0.6897)	
4 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.7054 (0.6230 to 0.7731)	0.5752 (0.4914 to 0.6502)	
6 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.6731 (0.5883 to 0.7442)	0.5752 (0.4914 to 0.6502)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.10 Treatment emergent severe adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.6640 (0.5784 to 0.7361)	0.5583 (0.4738 to 0.6345)	
10 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.6640 (0.5784 to 0.7361)	0.5390 (0.4534 to 0.6170)	
12 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.6640 (0.5784 to 0.7361)	0.5292 (0.4430 to 0.6081)	
14 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.6640 (0.5784 to 0.7361)	0.5145 (0.4260 to 0.5960)	
16 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.6640 (0.5784 to 0.7361)	0.5145 (0.4260 to 0.5960)	
Number of patients at risk[b]					
2 Months	1	2	108	90	
4 Months	1	2	93	79	
6 Months	0	2	80	69	
8 Months	0	2	71	64	
10 Months	0	2	69	55	
12 Months	0	2	60	49	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.10 Treatment emergent severe adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0	2	38	32	
16 Months	0	0	23	14	
Pneumonia (days)					
Number (%) of events	0 (0.0)	0 (0.0)	22 (15.0)	25 (16.7)	1.0000
Number (%) of patients censored	2 (100.0)	2 (100.0)	125 (85.0)	125 (83.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.6304 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.7858	
Hazard ratio (95% CI) vs Pd	-	NC		1.08 (0.61 to 1.92)	
P-value	-			0.7862	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.3 Treatment emergent adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.8787 (0.7948 to 0.9298)	0.8394 (0.7566 to 0.8960)	0.9426 (0.7887 to 0.9854)	0.8472 (0.6679 to 0.9341)	
Number of patients at risk[b]					
2 Months	99	102	36	30	
4 Months	89	95	34	27	
6 Months	76	86	29	25	
8 Months	69	81	27	24	
10 Months	64	74	27	24	
12 Months	53	67	24	20	
14 Months	34	46	14	12	
16 Months	16	22	8	3	
Neutropenia (days)					
Number (%) of events	40 (36.0)	55 (47.0)	10 (26.3)	16 (45.7)	0.3043
Number (%) of patients censored	71 (64.0)	62 (53.0)	28 (73.7)	19 (54.3)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.3 Treatment emergent adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.4127 (0.7885 to 3.3840)	0.8542 (0.7556 to 1.0185)	4.9938 (1.4456 to NC)	0.7556 (0.5257 to 1.9384)	
Median (95% CI)	NC (NC to NC)	NC (2.7926 to NC)	NC (NC to NC)	NC (0.9856 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1294		0.0497	
Hazard ratio (95% CI) vs Pd	-	1.37 (0.91 to 2.06)		2.17 (0.98 to 4.79)	
P-value	-	0.1310		0.0555	
Events probability (95% CI)[b]					
2 Months	0.7150 (0.6200 to 0.7902)	0.6205 (0.5256 to 0.7018)	0.8655 (0.7065 to 0.9417)	0.6000 (0.4200 to 0.7402)	
4 Months	0.6666 (0.5690 to 0.7470)	0.5855 (0.4903 to 0.6690)	0.8087 (0.6398 to 0.9040)	0.5397 (0.3619 to 0.6878)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.3 Treatment emergent adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.6232 (0.5230 to 0.7082)	0.5765 (0.4812 to 0.6606)	0.7465 (0.5679 to 0.8598)	0.5397 (0.3619 to 0.6878)	
8 Months	0.6232 (0.5230 to 0.7082)	0.5554 (0.4592 to 0.6411)	0.7126 (0.5293 to 0.8348)	0.5397 (0.3619 to 0.6878)	
10 Months	0.6232 (0.5230 to 0.7082)	0.5312 (0.4337 to 0.6193)	0.7126 (0.5293 to 0.8348)	0.5397 (0.3619 to 0.6878)	
12 Months	0.6232 (0.5230 to 0.7082)	0.5189 (0.4208 to 0.6081)	0.7126 (0.5293 to 0.8348)	0.5397 (0.3619 to 0.6878)	
14 Months	0.6232 (0.5230 to 0.7082)	0.5003 (0.3993 to 0.5931)	0.7126 (0.5293 to 0.8348)	0.5397 (0.3619 to 0.6878)	
16 Months	0.6232 (0.5230 to 0.7082)	0.5003 (0.3993 to 0.5931)	0.7126 (0.5293 to 0.8348)	0.5397 (0.3619 to 0.6878)	
Number of patients at risk[b]					
2 Months	77	71	32	21	
4 Months	66	65	28	16	
6 Months	54	55	24	15	
8 Months	49	51	20	14	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.3 Treatment emergent adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	47	43	20	14	
12 Months	42	38	17	13	
14 Months	27	25	11	9	
16 Months	15	12	8	2	
Oedema peripheral (days)					
Number (%) of events	12 (10.8)	15 (12.8)	4 (10.5)	5 (14.3)	0.8183
Number (%) of patients censored	99 (89.2)	102 (87.2)	34 (89.5)	30 (85.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.2710 to NC)	NC (7.2279 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8563		0.6907	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.12 Treatment emergent severe adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	103	107	37	28	
4 Months	97	103	35	26	
6 Months	85	90	31	24	
8 Months	77	87	28	23	
10 Months	72	84	28	23	
12 Months	61	75	25	19	
14 Months	39	52	15	12	
16 Months	17	23	9	3	
Neutropenia (days)					
Number (%) of events	38 (34.2)	54 (46.2)	10 (26.3)	15 (42.9)	0.4372
Number (%) of patients censored	73 (65.8)	63 (53.8)	28 (73.7)	20 (57.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.4127 (0.7885 to 3.3840)	0.8542 (0.7556 to 1.0185)	4.9938 (1.4456 to NC)	0.7556 (0.5257 to 2.1027)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.12 Treatment emergent severe adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (2.7926 to NC)	NC (NC to NC)	NC (1.4127 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0971		0.0794	
Hazard ratio (95% CI) vs Pd	-	1.42 (0.94 to 2.15)		2.02 (0.91 to 4.51)	
P-value	-	0.0988		0.0856	
Events probability (95% CI)[b]					
2 Months	0.7150 (0.6200 to 0.7902)	0.6205 (0.5256 to 0.7018)	0.8655 (0.7065 to 0.9417)	0.6273 (0.4459 to 0.7639)	
4 Months	0.6666 (0.5690 to 0.7470)	0.5855 (0.4903 to 0.6690)	0.8087 (0.6398 to 0.9040)	0.5642 (0.3833 to 0.7107)	
6 Months	0.6451 (0.5461 to 0.7279)	0.5855 (0.4903 to 0.6690)	0.7465 (0.5679 to 0.8598)	0.5642 (0.3833 to 0.7107)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.12 Treatment emergent severe adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.6451 (0.5461 to 0.7279)	0.5644 (0.4683 to 0.6497)	0.7126 (0.5293 to 0.8348)	0.5642 (0.3833 to 0.7107)	
10 Months	0.6451 (0.5461 to 0.7279)	0.5399 (0.4422 to 0.6277)	0.7126 (0.5293 to 0.8348)	0.5642 (0.3833 to 0.7107)	
12 Months	0.6451 (0.5461 to 0.7279)	0.5273 (0.4289 to 0.6164)	0.7126 (0.5293 to 0.8348)	0.5642 (0.3833 to 0.7107)	
14 Months	0.6451 (0.5461 to 0.7279)	0.5085 (0.4069 to 0.6013)	0.7126 (0.5293 to 0.8348)	0.5642 (0.3833 to 0.7107)	
16 Months	0.6451 (0.5461 to 0.7279)	0.5085 (0.4069 to 0.6013)	0.7126 (0.5293 to 0.8348)	0.5642 (0.3833 to 0.7107)	
Number of patients at risk[b]					
2 Months	77	71	32	21	
4 Months	66	65	28	16	
6 Months	56	56	24	15	
8 Months	51	52	20	14	
10 Months	49	43	20	14	
12 Months	43	38	17	13	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.12 Treatment emergent severe adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	27	25	11	9	
16 Months	15	12	8	2	
Pneumonia (days)					
Number (%) of events	16 (14.4)	20 (17.1)	6 (15.8)	5 (14.3)	0.7185
Number (%) of patients censored	95 (85.6)	97 (82.9)	32 (84.2)	30 (85.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (6.7351 to NC)	NC (2.6283 to NC)	NC (2.0698 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6866		0.8543	
Hazard ratio (95% CI) vs Pd	-	1.14 (0.59 to 2.21)		0.90 (0.27 to 2.93)	
P-value	-	0.6869		0.8548	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.2 Treatment emergent adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	126	125	9	7	
4 Months	116	115	7	7	
6 Months	98	104	7	7	
8 Months	89	100	7	5	
10 Months	84	93	7	5	
12 Months	70	82	7	5	
14 Months	43	55	5	3	
16 Months	22	25	2	0	
Neutropenia (days)					
Number (%) of events	45 (32.1)	67 (46.2)	5 (55.6)	4 (57.1)	0.5826
Number (%) of patients censored	95 (67.9)	78 (53.8)	4 (44.4)	3 (42.9)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.2 Treatment emergent adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	2.8255 (0.9856 to 5.0267)	0.8542 (0.7556 to 1.0185)	0.9856 (0.5914 to 4.6653)	0.7228 (0.5585 to 9.3306)	
Median (95% CI)	NC (NC to NC)	NC (2.8912 to NC)	4.6653 (0.5914 to NC)	9.3306 (0.5585 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.8255 to NC)	NC (1.4456 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0172		0.8898	
Hazard ratio (95% CI) vs Pd	-	1.58 (1.08 to 2.30)		1.10 (0.29 to 4.09)	
P-value	-	0.0182		0.8898	
Hazard ratio inverted (95% CI) vs IPd	0.63 (0.43 to 0.93)				
Events probability (95% CI)[b]					
2 Months	0.7589 (0.6781 to 0.8221)	0.6178 (0.5332 to 0.6916)	0.6667 (0.2817 to 0.8783)	0.5714 (0.1719 to 0.8371)	
4 Months	0.7127 (0.6284 to 0.7812)	0.5750 (0.4899 to 0.6512)	0.5556 (0.2042 to 0.8045)	0.5714 (0.1719 to 0.8371)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.2 Treatment emergent adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.6693 (0.5816 to 0.7426)	0.5676 (0.4823 to 0.6441)	0.4444 (0.1359 to 0.7193)	0.5714 (0.1719 to 0.8371)	
8 Months	0.6594 (0.5709 to 0.7340)	0.5501 (0.4642 to 0.6279)	0.4444 (0.1359 to 0.7193)	0.5714 (0.1719 to 0.8371)	
10 Months	0.6594 (0.5709 to 0.7340)	0.5405 (0.4540 to 0.6191)	0.4444 (0.1359 to 0.7193)	0.3810 (0.0612 to 0.7164)	
12 Months	0.6594 (0.5709 to 0.7340)	0.5306 (0.4437 to 0.6101)	0.4444 (0.1359 to 0.7193)	0.3810 (0.0612 to 0.7164)	
14 Months	0.6594 (0.5709 to 0.7340)	0.5159 (0.4266 to 0.5980)	0.4444 (0.1359 to 0.7193)	0.3810 (0.0612 to 0.7164)	
16 Months	0.6594 (0.5709 to 0.7340)	0.5159 (0.4266 to 0.5980)	0.4444 (0.1359 to 0.7193)	0.3810 (0.0612 to 0.7164)	
Number of patients at risk[b]					
2 Months	103	88	6	4	
4 Months	89	77	5	4	
6 Months	74	66	4	4	
8 Months	65	62	4	3	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.2 Treatment emergent adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	63	55	4	2	
12 Months	55	49	4	2	
14 Months	35	32	3	2	
16 Months	21	14	2	0	
Oedema peripheral (days)					
Number (%) of events	13 (9.3)	19 (13.1)	3 (33.3)	1 (14.3)	0.3439
Number (%) of patients censored	127 (90.7)	126 (86.9)	6 (66.7)	6 (85.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	8.1150 (1.7741 to NC)	NC (7.2279 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.7741 to NC)	NC (7.2279 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4767		0.4601	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.10 Treatment emergent severe adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	131	128	9	7	
4 Months	123	122	9	7	
6 Months	107	108	9	6	
8 Months	96	105	9	5	
10 Months	91	102	9	5	
12 Months	78	89	8	5	
14 Months	49	61	5	3	
16 Months	24	26	2	0	
Neutropenia (days)					
Number (%) of events	43 (30.7)	65 (44.8)	5 (55.6)	4 (57.1)	0.5738
Number (%) of patients censored	97 (69.3)	80 (55.2)	4 (44.4)	3 (42.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.8255 (0.9856 to 7.6222)	0.8542 (0.7556 to 1.0185)	0.9856 (0.5914 to 4.6653)	0.7228 (0.5585 to 9.3306)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.10 Treatment emergent severe adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (3.0554 to NC)	4.6653 (0.5914 to NC)	9.3306 (0.5585 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.8255 to NC)	NC (1.4456 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0160		0.8898	
Hazard ratio (95% CI) vs Pd	-	1.60 (1.09 to 2.35)		1.10 (0.29 to 4.09)	
P-value	-	0.0170		0.8898	
Hazard ratio inverted (95% CI) vs IPd	0.63 (0.43 to 0.92)				
Events probability (95% CI)[b]					
2 Months	0.7589 (0.6781 to 0.8221)	0.6245 (0.5399 to 0.6979)	0.6667 (0.2817 to 0.8783)	0.5714 (0.1719 to 0.8371)	
4 Months	0.7127 (0.6284 to 0.7812)	0.5812 (0.4959 to 0.6572)	0.5556 (0.2042 to 0.8045)	0.5714 (0.1719 to 0.8371)	
6 Months	0.6867 (0.6002 to 0.7582)	0.5812 (0.4959 to 0.6572)	0.4444 (0.1359 to 0.7193)	0.5714 (0.1719 to 0.8371)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_refr1_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.10 Treatment emergent severe adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.6769 (0.5894 to 0.7497)	0.5636 (0.4775 to 0.6410)	0.4444 (0.1359 to 0.7193)	0.5714 (0.1719 to 0.8371)	
10 Months	0.6769 (0.5894 to 0.7497)	0.5537 (0.4670 to 0.6320)	0.4444 (0.1359 to 0.7193)	0.3810 (0.0612 to 0.7164)	
12 Months	0.6769 (0.5894 to 0.7497)	0.5437 (0.4563 to 0.6229)	0.4444 (0.1359 to 0.7193)	0.3810 (0.0612 to 0.7164)	
14 Months	0.6769 (0.5894 to 0.7497)	0.5286 (0.4387 to 0.6106)	0.4444 (0.1359 to 0.7193)	0.3810 (0.0612 to 0.7164)	
16 Months	0.6769 (0.5894 to 0.7497)	0.5286 (0.4387 to 0.6106)	0.4444 (0.1359 to 0.7193)	0.3810 (0.0612 to 0.7164)	
Number of patients at risk[b]					
2 Months	103	88	6	4	
4 Months	89	77	5	4	
6 Months	76	67	4	4	
8 Months	67	63	4	3	
10 Months	65	55	4	2	
12 Months	56	49	4	2	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.10 Treatment emergent severe adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	35	32	3	2	
16 Months	21	14	2	0	
Pneumonia (days)					
Number (%) of events	20 (14.3)	24 (16.6)	2 (22.2)	1 (14.3)	0.6604
Number (%) of patients censored	120 (85.7)	121 (83.4)	7 (77.8)	6 (85.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.6304 to NC)	NC (0.1971 to NC)	NC (0.2628 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.1971 to NC)	NC (0.2628 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7035		0.6989	
Hazard ratio (95% CI) vs Pd	-	1.12 (0.62 to 2.03)		0.63 (0.06 to 6.90)	
P-value	-	0.7045		0.7015	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.3 Treatment emergent adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	77	78	58	54	
4 Months	72	71	51	51	
6 Months	62	64	43	47	
8 Months	56	62	40	43	
10 Months	56	59	35	39	
12 Months	47	53	30	34	
14 Months	28	33	20	25	
16 Months	13	13	11	12	
Neutropenia (days)					
Number (%) of events	28 (32.2)	42 (46.2)	22 (35.5)	29 (47.5)	0.7205
Number (%) of patients censored	59 (67.8)	49 (53.8)	40 (64.5)	32 (52.5)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.3 Treatment emergent adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	1.9055 (0.7885 to NC)	0.8214 (0.6899 to 1.3799)	2.0370 (0.9856 to 4.6653)	0.9199 (0.7556 to 1.4784)	
Median (95% CI)	NC (NC to NC)	NC (2.1027 to NC)	NC (4.6653 to NC)	13.8645 (1.9384 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0554		0.2047	
Hazard ratio (95% CI) vs Pd	-	1.59 (0.99 to 2.57)		1.43 (0.82 to 2.49)	
P-value	-	0.0576		0.2071	
Events probability (95% CI)[b]					
2 Months	0.7445 (0.6384 to 0.8237)	0.6113 (0.5027 to 0.7032)	0.7648 (0.6353 to 0.8535)	0.6225 (0.4887 to 0.7307)	
4 Months	0.7203 (0.6123 to 0.8030)	0.5541 (0.4453 to 0.6499)	0.6754 (0.5389 to 0.7794)	0.6057 (0.4717 to 0.7157)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.3 Treatment emergent adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.6805 (0.5691 to 0.7688)	0.5541 (0.4453 to 0.6499)	0.6138 (0.4732 to 0.7274)	0.5884 (0.4543 to 0.7001)	
8 Months	0.6660 (0.5533 to 0.7565)	0.5253 (0.4154 to 0.6239)	0.6138 (0.4732 to 0.7274)	0.5884 (0.4543 to 0.7001)	
10 Months	0.6660 (0.5533 to 0.7565)	0.5253 (0.4154 to 0.6239)	0.6138 (0.4732 to 0.7274)	0.5448 (0.4082 to 0.6625)	
12 Months	0.6660 (0.5533 to 0.7565)	0.5253 (0.4154 to 0.6239)	0.6138 (0.4732 to 0.7274)	0.5221 (0.3847 to 0.6427)	
14 Months	0.6660 (0.5533 to 0.7565)	0.5253 (0.4154 to 0.6239)	0.6138 (0.4732 to 0.7274)	0.4914 (0.3501 to 0.6182)	
16 Months	0.6660 (0.5533 to 0.7565)	0.5253 (0.4154 to 0.6239)	0.6138 (0.4732 to 0.7274)	0.4914 (0.3501 to 0.6182)	
Number of patients at risk[b]					
2 Months	64	55	45	37	
4 Months	58	46	36	35	
6 Months	50	39	28	31	
8 Months	44	36	25	29	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.3 Treatment emergent adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	44	33	23	24	
12 Months	38	31	21	20	
14 Months	24	19	14	15	
16 Months	14	6	9	8	
Oedema peripheral (days)					
Number (%) of events	8 (9.2)	12 (13.2)	8 (12.9)	8 (13.1)	0.4913
Number (%) of patients censored	79 (90.8)	79 (86.8)	54 (87.1)	53 (86.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (10.7762 to NC)	NC (8.1150 to NC)	NC (9.1992 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4744		0.7682	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.16 Treatment emergent severe adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	81	77	59	58	
4 Months	77	73	55	56	
6 Months	69	65	47	49	
8 Months	61	63	44	47	
10 Months	60	62	40	45	
12 Months	52	56	34	38	
14 Months	33	37	21	27	
16 Months	15	14	11	12	
Neutropenia (days)					
Number (%) of events	27 (31.0)	41 (45.1)	21 (33.9)	28 (45.9)	0.7359
Number (%) of patients censored	60 (69.0)	50 (54.9)	41 (66.1)	33 (54.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.9055 (0.7885 to NC)	0.8214 (0.6899 to 1.4127)	2.0370 (0.9856 to 4.6653)	0.9199 (0.7556 to 1.4784)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.16 Treatment emergent severe adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (2.7926 to NC)	NC (4.6653 to NC)	NC (1.9384 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0536		0.1896	
Hazard ratio (95% CI) vs Pd	-	1.61 (0.99 to 2.61)		1.46 (0.83 to 2.57)	
P-value	-	0.0559		0.1922	
Events probability (95% CI)[b]					
2 Months	0.7445 (0.6384 to 0.8237)	0.6219 (0.5132 to 0.7130)	0.7648 (0.6353 to 0.8535)	0.6225 (0.4887 to 0.7307)	
4 Months	0.7203 (0.6123 to 0.8030)	0.5636 (0.4544 to 0.6592)	0.6754 (0.5389 to 0.7794)	0.6057 (0.4717 to 0.7157)	
6 Months	0.6936 (0.5832 to 0.7802)	0.5636 (0.4544 to 0.6592)	0.6350 (0.4956 to 0.7454)	0.6057 (0.4717 to 0.7157)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.16 Treatment emergent severe adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.6792 (0.5672 to 0.7679)	0.5343 (0.4237 to 0.6329)	0.6350 (0.4956 to 0.7454)	0.6057 (0.4717 to 0.7157)	
10 Months	0.6792 (0.5672 to 0.7679)	0.5343 (0.4237 to 0.6329)	0.6350 (0.4956 to 0.7454)	0.5608 (0.4233 to 0.6777)	
12 Months	0.6792 (0.5672 to 0.7679)	0.5343 (0.4237 to 0.6329)	0.6350 (0.4956 to 0.7454)	0.5375 (0.3987 to 0.6576)	
14 Months	0.6792 (0.5672 to 0.7679)	0.5343 (0.4237 to 0.6329)	0.6350 (0.4956 to 0.7454)	0.5058 (0.3625 to 0.6327)	
16 Months	0.6792 (0.5672 to 0.7679)	0.5343 (0.4237 to 0.6329)	0.6350 (0.4956 to 0.7454)	0.5058 (0.3625 to 0.6327)	
Number of patients at risk[b]					
2 Months	64	55	45	37	
4 Months	58	46	36	35	
6 Months	51	39	29	32	
8 Months	45	36	26	30	
10 Months	45	33	24	24	
12 Months	39	31	21	20	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.16 Treatment emergent severe adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	24	19	14	15	
16 Months	14	6	9	8	
Pneumonia (days)					
Number (%) of events	12 (13.8)	14 (15.4)	10 (16.1)	11 (18.0)	0.9510
Number (%) of patients censored	75 (86.2)	77 (84.6)	52 (83.9)	50 (82.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (6.2752 to NC)	NC (5.4209 to NC)	NC (4.2710 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7987		0.9072	
Hazard ratio (95% CI) vs Pd	-	1.11 (0.51 to 2.39)		1.05 (0.45 to 2.48)	
P-value	-	0.7992		0.9073	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_llen_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Nausea (days)							
Number (%) of events	6 (8.8)	6 (11.1)	6 (11.3)	12 (18.2)	2 (7.1)	5 (15.6)	0.8552
Number (%) of patients censored	62 (91.2)	48 (88.9)	47 (88.7)	54 (81.8)	26 (92.9)	27 (84.4)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.3080 to NC)	NC (9.5934 to NC)	NC (0.2957 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.6622		0.3459		0.3220	
Hazard ratio (95% CI) vs Pd	-	1.29 (0.41 to 3.99)		1.60 (0.60 to 4.25)		2.24 (0.43 to 11.56)	
P-value	-	0.6630		0.3503		0.3350	
Events probability (95% CI)[b]							

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9552 (0.8676 to 0.9853)	0.9074 (0.7917 to 0.9604)	0.9426 (0.8325 to 0.9811)	0.8932 (0.7889 to 0.9476)	0.9630 (0.7649 to 0.9947)	0.8438 (0.6646 to 0.9318)	
4 Months	0.9396 (0.8469 to 0.9769)	0.9074 (0.7917 to 0.9604)	0.8811 (0.7539 to 0.9448)	0.8619 (0.7512 to 0.9256)	0.9630 (0.7649 to 0.9947)	0.8438 (0.6646 to 0.9318)	
6 Months	0.9218 (0.8218 to 0.9668)	0.8868 (0.7649 to 0.9476)	0.8811 (0.7539 to 0.9448)	0.8619 (0.7512 to 0.9256)	0.9630 (0.7649 to 0.9947)	0.8438 (0.6646 to 0.9318)	
8 Months	0.9018 (0.7929 to 0.9550)	0.8868 (0.7649 to 0.9476)	0.8811 (0.7539 to 0.9448)	0.8446 (0.7301 to 0.9133)	0.9630 (0.7649 to 0.9947)	0.8438 (0.6646 to 0.9318)	
10 Months	0.9018 (0.7929 to 0.9550)	0.8868 (0.7649 to 0.9476)	0.8811 (0.7539 to 0.9448)	0.8446 (0.7301 to 0.9133)	0.8988 (0.6361 to 0.9751)	0.8438 (0.6646 to 0.9318)	
12 Months	0.9018 (0.7929 to 0.9550)	0.8868 (0.7649 to 0.9476)	0.8811 (0.7539 to 0.9448)	0.8053 (0.6811 to 0.8851)	0.8988 (0.6361 to 0.9751)	0.8438 (0.6646 to 0.9318)	
14 Months	0.9018 (0.7929 to 0.9550)	0.8868 (0.7649 to 0.9476)	0.8811 (0.7539 to 0.9448)	0.8053 (0.6811 to 0.8851)	0.8988 (0.6361 to 0.9751)	0.8438 (0.6646 to 0.9318)	
16 Months	0.9018 (0.7929 to 0.9550)	0.8868 (0.7649 to 0.9476)	0.8811 (0.7539 to 0.9448)	0.8053 (0.6811 to 0.8851)	0.8988 (0.6361 to 0.9751)	0.8438 (0.6646 to 0.9318)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	63	48	47	57	25	27	
4 Months	58	45	42	55	23	22	
6 Months	49	40	39	50	17	21	
8 Months	44	36	36	48	16	21	
10 Months	42	34	35	44	14	20	
12 Months	37	31	30	38	10	18	
14 Months	22	19	19	25	7	14	
16 Months	12	10	8	11	4	4	
Neutropenia (days)							
Number (%) of events	19 (27.9)	24 (44.4)	18 (34.0)	30 (45.5)	13 (46.4)	17 (53.1)	0.5666
Number (%) of patients censored	49 (72.1)	30 (55.6)	35 (66.0)	36 (54.5)	15 (53.6)	15 (46.9)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	4.9938 (1.1499 to NC)	0.8214 (0.5914 to 1.9384)	1.8398 (0.7556 to NC)	0.9856 (0.7885 to 1.9055)	0.7721 (0.2300 to 4.3039)	0.7885 (0.5257 to 0.9199)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.2 Treatment emergent adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	33	44	16	20	
16 Months	13	21	10	7	
Nausea (days)					
Number (%) of events	9 (9.0)	13 (12.9)	5 (10.2)	10 (19.6)	0.6579
Number (%) of patients censored	91 (91.0)	88 (87.1)	44 (89.8)	41 (80.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.5934 to NC)	NC (1.1499 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3897		0.2164	
Hazard ratio (95% CI) vs Pd	-	1.45 (0.62 to 3.39)		1.94 (0.66 to 5.69)	
P-value	-	0.3924		0.2249	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.2 Treatment emergent adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9488 (0.8812 to 0.9783)	0.9008 (0.8234 to 0.9453)	0.9587 (0.8449 to 0.9895)	0.8627 (0.7335 to 0.9321)	
4 Months	0.9158 (0.8384 to 0.9570)	0.8899 (0.8100 to 0.9375)	0.9370 (0.8170 to 0.9792)	0.8427 (0.7099 to 0.9180)	
6 Months	0.9034 (0.8222 to 0.9486)	0.8899 (0.8100 to 0.9375)	0.9370 (0.8170 to 0.9792)	0.8211 (0.6840 to 0.9027)	
8 Months	0.9034 (0.8222 to 0.9486)	0.8779 (0.7946 to 0.9289)	0.9077 (0.7693 to 0.9649)	0.8211 (0.6840 to 0.9027)	
10 Months	0.9034 (0.8222 to 0.9486)	0.8779 (0.7946 to 0.9289)	0.8741 (0.7174 to 0.9469)	0.8211 (0.6840 to 0.9027)	
12 Months	0.9034 (0.8222 to 0.9486)	0.8644 (0.7770 to 0.9193)	0.8741 (0.7174 to 0.9469)	0.7946 (0.6500 to 0.8845)	
14 Months	0.9034 (0.8222 to 0.9486)	0.8644 (0.7770 to 0.9193)	0.8741 (0.7174 to 0.9469)	0.7946 (0.6500 to 0.8845)	
16 Months	0.9034 (0.8222 to 0.9486)	0.8644 (0.7770 to 0.9193)	0.8741 (0.7174 to 0.9469)	0.7946 (0.6500 to 0.8845)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_plne_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.2 Treatment emergent adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	89	89	46	43	
4 Months	81	80	42	42	
6 Months	70	74	35	37	
8 Months	66	71	30	34	
10 Months	65	66	26	32	
12 Months	53	60	24	27	
14 Months	33	41	15	17	
16 Months	14	18	10	7	
Neutropenia (days)					
Number (%) of events	35 (35.0)	46 (45.5)	15 (30.6)	25 (49.0)	0.4629
Number (%) of patients censored	65 (65.0)	55 (54.5)	34 (69.4)	26 (51.0)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.9 Treatment emergent not severe adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	91	96	48	49	
4 Months	84	88	45	46	
6 Months	74	79	38	40	
8 Months	68	76	32	38	
10 Months	67	71	29	34	
12 Months	54	65	26	28	
14 Months	33	44	16	20	
16 Months	13	21	10	7	
Nausea (days)					
Number (%) of events	9 (9.0)	13 (12.9)	5 (10.2)	10 (19.6)	0.6579
Number (%) of patients censored	91 (91.0)	88 (87.1)	44 (89.8)	41 (80.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.5934 to NC)	NC (1.1499 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.9 Treatment emergent not severe adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3897		0.2164	
Hazard ratio (95% CI) vs Pd	-	1.45 (0.62 to 3.39)		1.94 (0.66 to 5.69)	
P-value	-	0.3924		0.2249	
Events probability (95% CI)[b]					
2 Months	0.9488 (0.8812 to 0.9783)	0.9008 (0.8234 to 0.9453)	0.9587 (0.8449 to 0.9895)	0.8627 (0.7335 to 0.9321)	
4 Months	0.9158 (0.8384 to 0.9570)	0.8899 (0.8100 to 0.9375)	0.9370 (0.8170 to 0.9792)	0.8427 (0.7099 to 0.9180)	
6 Months	0.9034 (0.8222 to 0.9486)	0.8899 (0.8100 to 0.9375)	0.9370 (0.8170 to 0.9792)	0.8211 (0.6840 to 0.9027)	
8 Months	0.9034 (0.8222 to 0.9486)	0.8779 (0.7946 to 0.9289)	0.9077 (0.7693 to 0.9649)	0.8211 (0.6840 to 0.9027)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.9 Treatment emergent not severe adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.9034 (0.8222 to 0.9486)	0.8779 (0.7946 to 0.9289)	0.8741 (0.7174 to 0.9469)	0.8211 (0.6840 to 0.9027)	
12 Months	0.9034 (0.8222 to 0.9486)	0.8644 (0.7770 to 0.9193)	0.8741 (0.7174 to 0.9469)	0.7946 (0.6500 to 0.8845)	
14 Months	0.9034 (0.8222 to 0.9486)	0.8644 (0.7770 to 0.9193)	0.8741 (0.7174 to 0.9469)	0.7946 (0.6500 to 0.8845)	
16 Months	0.9034 (0.8222 to 0.9486)	0.8644 (0.7770 to 0.9193)	0.8741 (0.7174 to 0.9469)	0.7946 (0.6500 to 0.8845)	
Number of patients at risk[b]					
2 Months	89	89	46	43	
4 Months	81	80	42	42	
6 Months	70	74	35	37	
8 Months	66	71	30	34	
10 Months	65	66	26	32	
12 Months	53	60	24	27	
14 Months	33	41	15	17	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.9 Treatment emergent not severe adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	14	18	10	7	
Oedema peripheral (days)					
Number (%) of events	11 (11.0)	12 (11.9)	5 (10.2)	8 (15.7)	0.6683
Number (%) of patients censored	89 (89.0)	89 (88.1)	44 (89.8)	43 (84.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.1992 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9918		0.6204	
Hazard ratio (95% CI) vs Pd	-	1.00 (0.44 to 2.28)		1.33 (0.43 to 4.05)	
P-value	-	0.9918		0.6215	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_plne_s_t_x.rtf (16FEB2021 22:50)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.3 Treatment emergent adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	47	58	49	47	
12 Months	37	51	43	42	
14 Months	24	33	25	31	
16 Months	13	16	10	12	
Nausea (days)					
Number (%) of events	5 (7.4)	11 (12.5)	9 (11.1)	12 (18.8)	0.9850
Number (%) of patients censored	63 (92.6)	77 (87.5)	72 (88.9)	52 (81.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.1499 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3207		0.2092	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_sex_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.3 Treatment emergent adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	1.70 (0.59 to 4.89)		1.73 (0.73 to 4.10)	
P-value	-	0.3265		0.2149	
Events probability (95% CI)[b]					
2 Months	0.9396 (0.8469 to 0.9769)	0.9087 (0.8257 to 0.9533)	0.9623 (0.8877 to 0.9877)	0.8594 (0.7472 to 0.9242)	
4 Months	0.9242 (0.8273 to 0.9677)	0.9087 (0.8257 to 0.9533)	0.9211 (0.8325 to 0.9638)	0.8269 (0.7092 to 0.9002)	
6 Months	0.9242 (0.8273 to 0.9677)	0.8961 (0.8096 to 0.9446)	0.9060 (0.8124 to 0.9542)	0.8269 (0.7092 to 0.9002)	
8 Months	0.9242 (0.8273 to 0.9677)	0.8961 (0.8096 to 0.9446)	0.8879 (0.7867 to 0.9427)	0.8085 (0.6871 to 0.8866)	
10 Months	0.9242 (0.8273 to 0.9677)	0.8961 (0.8096 to 0.9446)	0.8685 (0.7600 to 0.9302)	0.8085 (0.6871 to 0.8866)	
12 Months	0.9242 (0.8273 to 0.9677)	0.8652 (0.7683 to 0.9235)	0.8685 (0.7600 to 0.9302)	0.8085 (0.6871 to 0.8866)	
14 Months	0.9242 (0.8273 to 0.9677)	0.8652 (0.7683 to 0.9235)	0.8685 (0.7600 to 0.9302)	0.8085 (0.6871 to 0.8866)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_sex_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.3 Treatment emergent adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.9242 (0.8273 to 0.9677)	0.8652 (0.7683 to 0.9235)	0.8685 (0.7600 to 0.9302)	0.8085 (0.6871 to 0.8866)	
Number of patients at risk[b]					
2 Months	61	78	74	54	
4 Months	57	73	66	49	
6 Months	50	66	55	45	
8 Months	49	63	47	42	
10 Months	46	58	45	40	
12 Months	37	50	40	37	
14 Months	23	31	25	27	
16 Months	14	16	10	9	
Neutropenia (days)					
Number (%) of events	19 (27.9)	36 (40.9)	31 (38.3)	35 (54.7)	0.8255
Number (%) of patients censored	49 (72.1)	52 (59.1)	50 (61.7)	29 (45.3)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_sex_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.2 Treatment emergent adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	44	50	3	10	
16 Months	20	24	1	3	
Nausea (days)					
Number (%) of events	12 (9.8)	21 (18.1)	2 (10.5)	1 (4.2)	0.2183
Number (%) of patients censored	110 (90.2)	95 (81.9)	17 (89.5)	23 (95.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (6.3080 to NC)	NC (0.5257 to NC)	NC (11.2033 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0791		0.4054	
Hazard ratio (95% CI) vs Pd	-	1.87 (0.92 to 3.80)		0.38 (0.03 to 4.14)	
P-value	-	0.0840		0.4239	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_race_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.2 Treatment emergent adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9584 (0.9029 to 0.9825)	0.8621 (0.7848 to 0.9131)	0.8947 (0.6408 to 0.9726)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9224 (0.8560 to 0.9589)	0.8444 (0.7644 to 0.8990)	0.8947 (0.6408 to 0.9726)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9121 (0.8425 to 0.9518)	0.8350 (0.7535 to 0.8915)	0.8947 (0.6408 to 0.9726)	1.0000 (1.0000 to 1.0000)	
8 Months	0.9004 (0.8265 to 0.9439)	0.8251 (0.7419 to 0.8835)	0.8947 (0.6408 to 0.9726)	1.0000 (1.0000 to 1.0000)	
10 Months	0.8879 (0.8096 to 0.9353)	0.8251 (0.7419 to 0.8835)	0.8947 (0.6408 to 0.9726)	1.0000 (1.0000 to 1.0000)	
12 Months	0.8879 (0.8096 to 0.9353)	0.8138 (0.7283 to 0.8746)	0.8947 (0.6408 to 0.9726)	0.9474 (0.6812 to 0.9924)	
14 Months	0.8879 (0.8096 to 0.9353)	0.8138 (0.7283 to 0.8746)	0.8947 (0.6408 to 0.9726)	0.9474 (0.6812 to 0.9924)	
16 Months	0.8879 (0.8096 to 0.9353)	0.8138 (0.7283 to 0.8746)	0.8947 (0.6408 to 0.9726)	0.9474 (0.6812 to 0.9924)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_race_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.2 Treatment emergent adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	111	100	17	23	
4 Months	100	93	17	22	
6 Months	84	84	17	22	
8 Months	75	80	17	20	
10 Months	71	74	16	19	
12 Months	63	66	12	16	
14 Months	44	42	2	12	
16 Months	21	19	1	5	
Neutropenia (days)					
Number (%) of events	42 (34.4)	49 (42.2)	6 (31.6)	18 (75.0)	0.0330
Number (%) of patients censored	80 (65.6)	67 (57.8)	13 (68.4)	6 (25.0)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_race_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.3 Treatment emergent adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0	4	43	52	
16 Months	0	1	20	24	
Nausea (days)					
Number (%) of events	0 (0.0)	1 (25.0)	12 (9.2)	19 (14.8)	0.9876
Number (%) of patients censored	3 (100.0)	3 (75.0)	118 (90.8)	109 (85.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (10.4148 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (10.4148 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.4148 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6171		0.1762	
Hazard ratio (95% CI) vs Pd	-	NC		1.64 (0.80 to 3.38)	
P-value	-	0.9988		0.1806	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_ethn_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.3 Treatment emergent adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9454 (0.8889 to 0.9736)	0.8828 (0.8132 to 0.9276)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9290 (0.8679 to 0.9624)	0.8666 (0.7942 to 0.9149)	
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9198 (0.8558 to 0.9561)	0.8666 (0.7942 to 0.9149)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9094 (0.8419 to 0.9490)	0.8575 (0.7832 to 0.9078)	
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8983 (0.8269 to 0.9413)	0.8575 (0.7832 to 0.9078)	
12 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.8983 (0.8269 to 0.9413)	0.8469 (0.7700 to 0.8997)	
14 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.8983 (0.8269 to 0.9413)	0.8469 (0.7700 to 0.8997)	
16 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.8983 (0.8269 to 0.9413)	0.8469 (0.7700 to 0.8997)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_ethn_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.3 Treatment emergent adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	2	4	118	112	
4 Months	2	4	110	104	
6 Months	1	4	95	96	
8 Months	1	4	86	90	
10 Months	1	4	81	83	
12 Months	0	3	69	73	
14 Months	0	3	42	49	
16 Months	0	1	21	22	
Neutropenia (days)					
Number (%) of events	1 (33.3)	2 (50.0)	45 (34.6)	59 (46.1)	0.8143
Number (%) of patients censored	2 (66.7)	2 (50.0)	85 (65.4)	69 (53.9)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_ethn_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
4 Months	59	45	19	26	5	7	15	17	31	39	
6 Months	55	39	15	23	5	6	15	16	22	35	
8 Months	46	37	14	21	5	6	15	15	20	35	
10 Months	46	35	13	19	5	5	14	14	18	32	
12 Months	39	31	12	16	3	5	11	12	15	29	
14 Months	28	19	8	12	1	2	2	9	10	22	
16 Months	12	7	3	4	0	1	1	3	7	13	
Nausea (days)											
Number (%) of events	7 (9.5)	5 (9.1)	4 (20.0)	5 (17.9)	1 (20.0)	4 (57.1)	1 (6.7)	1 (4.8)	1 (2.9)	8 (19.5)	0.4432
Number (%) of patients censored	67 (90.5)	50 (90.9)	16 (80.0)	23 (82.1)	4 (80.0)	3 (42.9)	14 (93.3)	20 (95.2)	34 (97.1)	33 (80.5)	
Kaplan-Meier estimates of event in months											

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_greg_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	9.5934 (0.7228 to NC)	NC (0.1971 to NC)	NC (0.0657 to NC)	1.0513 (0.1971 to 10.4148)	NC (1.6756 to NC)	NC (11.2033 to NC)	NC (NC to NC)	NC (0.7885 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.5934 to NC)	NC (NC to NC)	NC (0.0657 to NC)	10.4148 (0.1971 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.0657 to NC)	NC (3.4497 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.9469		0.9172		0.2761		0.7557		0.0315	
Hazard ratio (95% CI) vs Pd	-	0.96 (0.31 to 3.03)		0.93 (0.25 to 3.47)		3.20 (0.35 to 29.14)		0.65 (0.04 to 10.40)		7.07 (0.88 to 56.50)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_greg_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
P-value	-	0.9470		0.9169		0.3016		0.7576		0.0653	
Events probability (95% CI)[b]											
2 Months	0.9577 (0.8747 to 0.9862)	0.9269 (0.8169 to 0.9719)	0.9474 (0.6812 to 0.9924)	0.8214 (0.6230 to 0.9215)	0.8000 (0.2038 to 0.9692)	0.7143 (0.2582 to 0.9198)	0.9333 (0.6126 to 0.9903)	1.0000 (1.0000 to 1.0000)	0.9714 (0.8140 to 0.9959)	0.8537 (0.7029 to 0.9314)	
4 Months	0.8966 (0.7949 to 0.9494)	0.9269 (0.8169 to 0.9719)	0.9474 (0.6812 to 0.9924)	0.8214 (0.6230 to 0.9215)	0.8000 (0.2038 to 0.9692)	0.5714 (0.1719 to 0.8371)	0.9333 (0.6126 to 0.9903)	1.0000 (1.0000 to 1.0000)	0.9714 (0.8140 to 0.9959)	0.8286 (0.6736 to 0.9144)	
6 Months	0.8966 (0.7949 to 0.9494)	0.9269 (0.8169 to 0.9719)	0.8842 (0.6082 to 0.9700)	0.8214 (0.6230 to 0.9215)	0.8000 (0.2038 to 0.9692)	0.5714 (0.1719 to 0.8371)	0.9333 (0.6126 to 0.9903)	1.0000 (1.0000 to 1.0000)	0.9714 (0.8140 to 0.9959)	0.8027 (0.6437 to 0.8961)	
8 Months	0.8966 (0.7949 to 0.9494)	0.9031 (0.7813 to 0.9588)	0.8162 (0.5280 to 0.9375)	0.8214 (0.6230 to 0.9215)	0.8000 (0.2038 to 0.9692)	0.5714 (0.1719 to 0.8371)	0.9333 (0.6126 to 0.9903)	1.0000 (1.0000 to 1.0000)	0.9714 (0.8140 to 0.9959)	0.8027 (0.6437 to 0.8961)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_greg_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
10 Months	0.8966 (0.7949 to 0.9494)	0.9031 (0.7813 to 0.9588)	0.7420 (0.4443 to 0.8960)	0.8214 (0.6230 to 0.9215)	0.8000 (0.2038 to 0.9692)	0.5714 (0.1719 to 0.8371)	0.9333 (0.6126 to 0.9903)	1.0000 (1.0000 to 1.0000)	0.9714 (0.8140 to 0.9959)	0.8027 (0.6437 to 0.8961)	
12 Months	0.8966 (0.7949 to 0.9494)	0.9031 (0.7813 to 0.9588)	0.7420 (0.4443 to 0.8960)	0.8214 (0.6230 to 0.9215)	0.8000 (0.2038 to 0.9692)	0.3810 (0.0612 to 0.7164)	0.9333 (0.6126 to 0.9903)	0.9444 (0.6664 to 0.9920)	0.9714 (0.8140 to 0.9959)	0.8027 (0.6437 to 0.8961)	
14 Months	0.8966 (0.7949 to 0.9494)	0.9031 (0.7813 to 0.9588)	0.7420 (0.4443 to 0.8960)	0.8214 (0.6230 to 0.9215)	0.8000 (0.2038 to 0.9692)	0.3810 (0.0612 to 0.7164)	0.9333 (0.6126 to 0.9903)	0.9444 (0.6664 to 0.9920)	0.9714 (0.8140 to 0.9959)	0.8027 (0.6437 to 0.8961)	
16 Months	0.8966 (0.7949 to 0.9494)	0.9031 (0.7813 to 0.9588)	0.7420 (0.4443 to 0.8960)	0.8214 (0.6230 to 0.9215)	0.8000 (0.2038 to 0.9692)	0.3810 (0.0612 to 0.7164)	0.9333 (0.6126 to 0.9903)	0.9444 (0.6664 to 0.9920)	0.9714 (0.8140 to 0.9959)	0.8027 (0.6437 to 0.8961)	
Number of patients at risk[b]											
2 Months	66	49	18	23	4	5	14	20	33	35	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
4 Months	56	44	18	22	4	4	14	19	31	33	
6 Months	52	39	13	19	4	4	14	19	22	30	
8 Months	45	37	12	17	4	4	14	18	21	29	
10 Months	45	35	10	16	4	3	13	18	19	26	
12 Months	40	32	9	14	2	2	10	15	16	24	
14 Months	29	19	6	8	1	0	1	11	11	20	
16 Months	13	6	2	3	0	0	1	5	8	11	
Neutropenia (days)											
Number (%) of events	19 (25.7)	23 (41.8)	10 (50.0)	14 (50.0)	3 (60.0)	4 (57.1)	6 (40.0)	15 (71.4)	12 (34.3)	15 (36.6)	0.4254
Number (%) of patients censored	55 (74.3)	32 (58.2)	10 (50.0)	14 (50.0)	2 (40.0)	3 (42.9)	9 (60.0)	6 (28.6)	23 (65.7)	26 (63.4)	
Kaplan-Meier estimates of event in months											

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.3 Treatment emergent adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	33	29	16	35	
16 Months	14	12	9	16	
Nausea (days)					
Number (%) of events	9 (9.6)	15 (19.5)	5 (9.1)	8 (10.7)	0.4335
Number (%) of patients censored	85 (90.4)	62 (80.5)	50 (90.9)	67 (89.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (3.4497 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0763		0.7831	
Hazard ratio (95% CI) vs Pd	-	2.08 (0.91 to 4.75)		1.17 (0.38 to 3.58)	
P-value	-	0.0830		0.7833	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.3 Treatment emergent adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9457 (0.8745 to 0.9771)	0.8692 (0.7705 to 0.9274)	0.9630 (0.8599 to 0.9906)	0.9067 (0.8142 to 0.9544)	
4 Months	0.8984 (0.8135 to 0.9459)	0.8416 (0.7378 to 0.9068)	0.9630 (0.8599 to 0.9906)	0.9067 (0.8142 to 0.9544)	
6 Months	0.8984 (0.8135 to 0.9459)	0.8268 (0.7202 to 0.8957)	0.9411 (0.8275 to 0.9807)	0.9067 (0.8142 to 0.9544)	
8 Months	0.8984 (0.8135 to 0.9459)	0.8109 (0.7011 to 0.8837)	0.9169 (0.7920 to 0.9683)	0.9067 (0.8142 to 0.9544)	
10 Months	0.8984 (0.8135 to 0.9459)	0.8109 (0.7011 to 0.8837)	0.8915 (0.7564 to 0.9538)	0.9067 (0.8142 to 0.9544)	
12 Months	0.8984 (0.8135 to 0.9459)	0.7933 (0.6794 to 0.8705)	0.8915 (0.7564 to 0.9538)	0.8889 (0.7890 to 0.9431)	
14 Months	0.8984 (0.8135 to 0.9459)	0.7933 (0.6794 to 0.8705)	0.8915 (0.7564 to 0.9538)	0.8889 (0.7890 to 0.9431)	
16 Months	0.8984 (0.8135 to 0.9459)	0.7933 (0.6794 to 0.8705)	0.8915 (0.7564 to 0.9538)	0.8889 (0.7890 to 0.9431)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.3 Treatment emergent adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	84	65	51	67	
4 Months	73	58	50	64	
6 Months	66	52	39	59	
8 Months	58	49	38	56	
10 Months	56	46	35	52	
12 Months	49	41	28	46	
14 Months	34	25	14	33	
16 Months	15	9	9	16	
Neutropenia (days)					
Number (%) of events	25 (26.6)	33 (42.9)	25 (45.5)	38 (50.7)	0.3315
Number (%) of patients censored	69 (73.4)	44 (57.1)	30 (54.5)	37 (49.3)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.2 Treatment emergent adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	45	59	4	5	
16 Months	20	25	3	3	
Nausea (days)					
Number (%) of events	13 (9.6)	19 (14.0)	1 (7.1)	4 (25.0)	0.3660
Number (%) of patients censored	122 (90.4)	117 (86.0)	13 (92.9)	12 (75.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.8542 to NC)	10.4148 (0.0000 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.4148 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3028		0.1838	
Hazard ratio (95% CI) vs Pd	-	1.45 (0.71 to 2.93)		3.96 (0.44 to 35.44)	
P-value	-	0.3056		0.2187	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.2 Treatment emergent adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9545 (0.9015 to 0.9793)	0.8971 (0.8324 to 0.9377)	0.9286 (0.5908 to 0.9896)	0.8036 (0.5060 to 0.9322)	
4 Months	0.9221 (0.8599 to 0.9573)	0.8819 (0.8144 to 0.9259)	0.9286 (0.5908 to 0.9896)	0.8036 (0.5060 to 0.9322)	
6 Months	0.9130 (0.8482 to 0.9510)	0.8740 (0.8051 to 0.9197)	0.9286 (0.5908 to 0.9896)	0.8036 (0.5060 to 0.9322)	
8 Months	0.9030 (0.8349 to 0.9439)	0.8655 (0.7949 to 0.9131)	0.9286 (0.5908 to 0.9896)	0.8036 (0.5060 to 0.9322)	
10 Months	0.8924 (0.8209 to 0.9364)	0.8655 (0.7949 to 0.9131)	0.9286 (0.5908 to 0.9896)	0.8036 (0.5060 to 0.9322)	
12 Months	0.8924 (0.8209 to 0.9364)	0.8558 (0.7828 to 0.9057)	0.9286 (0.5908 to 0.9896)	0.6888 (0.3446 to 0.8777)	
14 Months	0.8924 (0.8209 to 0.9364)	0.8558 (0.7828 to 0.9057)	0.9286 (0.5908 to 0.9896)	0.6888 (0.3446 to 0.8777)	
16 Months	0.8924 (0.8209 to 0.9364)	0.8558 (0.7828 to 0.9057)	0.9286 (0.5908 to 0.9896)	0.6888 (0.3446 to 0.8777)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.2 Treatment emergent adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	122	121	13	11	
4 Months	111	114	12	8	
6 Months	96	104	9	7	
8 Months	88	98	8	7	
10 Months	84	91	7	7	
12 Months	72	81	5	6	
14 Months	45	55	3	3	
16 Months	22	23	2	2	
Neutropenia (days)					
Number (%) of events	45 (33.3)	63 (46.3)	5 (35.7)	8 (50.0)	0.8565
Number (%) of patients censored	90 (66.7)	73 (53.7)	9 (64.3)	8 (50.0)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0.9193 (0.7987 to 0.9690)	0.9031 (0.7967 to 0.9553)	0.9394 (0.8226 to 0.9802)	0.9329 (0.8048 to 0.9780)	1.0000 (1.0000 to 1.0000)	0.8261 (0.5836 to 0.9345)	
16 Months	0.9193 (0.7987 to 0.9690)	0.9031 (0.7967 to 0.9553)	0.9394 (0.8226 to 0.9802)	0.9329 (0.8048 to 0.9780)	1.0000 (1.0000 to 1.0000)	0.8261 (0.5836 to 0.9345)	
Number of patients at risk[b]							
2 Months	50	60	51	51	35	31	
4 Months	47	57	51	47	29	28	
6 Months	47	50	43	44	20	23	
8 Months	44	49	37	42	17	21	
10 Months	43	47	35	37	16	19	
12 Months	38	42	26	32	14	17	
14 Months	22	30	17	22	10	10	
16 Months	12	15	7	8	4	5	
Nausea (days)							
Number (%) of events	5 (9.8)	11 (17.5)	6 (10.9)	7 (13.2)	3 (7.5)	3 (9.1)	0.7937

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_seiss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of patients censored	46 (90.2)	52 (82.5)	49 (89.1)	46 (86.8)	37 (92.5)	30 (90.9)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (1.1499 to NC)	NC (9.5934 to NC)	NC (11.2033 to NC)	NC (3.9754 to NC)	NC (0.6242 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2350		0.7557		0.8457	
Hazard ratio (95% CI) vs Pd	-	1.88 (0.65 to 5.41)		1.19 (0.40 to 3.54)		1.17 (0.24 to 5.81)	
P-value	-	0.2428		0.7564		0.8458	
Events probability (95% CI)[b]							
2 Months	0.9216 (0.8044 to 0.9698)	0.8571 (0.7434 to 0.9230)	0.9815 (0.8757 to 0.9974)	0.9245 (0.8113 to 0.9710)	0.9471 (0.8043 to 0.9866)	0.9081 (0.7414 to 0.9694)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
4 Months	0.9216 (0.8044 to 0.9698)	0.8410 (0.7246 to 0.9111)	0.9249 (0.8120 to 0.9711)	0.9040 (0.7843 to 0.9589)	0.9121 (0.7482 to 0.9712)	0.9081 (0.7414 to 0.9694)	
6 Months	0.9015 (0.7794 to 0.9578)	0.8410 (0.7246 to 0.9111)	0.9249 (0.8120 to 0.9711)	0.9040 (0.7843 to 0.9589)	0.9121 (0.7482 to 0.9712)	0.9081 (0.7414 to 0.9694)	
8 Months	0.9015 (0.7794 to 0.9578)	0.8410 (0.7246 to 0.9111)	0.8999 (0.7741 to 0.9574)	0.8819 (0.7553 to 0.9453)	0.9121 (0.7482 to 0.9712)	0.9081 (0.7414 to 0.9694)	
10 Months	0.9015 (0.7794 to 0.9578)	0.8410 (0.7246 to 0.9111)	0.8726 (0.7346 to 0.9416)	0.8819 (0.7553 to 0.9453)	0.9121 (0.7482 to 0.9712)	0.9081 (0.7414 to 0.9694)	
12 Months	0.9015 (0.7794 to 0.9578)	0.8219 (0.7009 to 0.8974)	0.8726 (0.7346 to 0.9416)	0.8567 (0.7210 to 0.9295)	0.9121 (0.7482 to 0.9712)	0.9081 (0.7414 to 0.9694)	
14 Months	0.9015 (0.7794 to 0.9578)	0.8219 (0.7009 to 0.8974)	0.8726 (0.7346 to 0.9416)	0.8567 (0.7210 to 0.9295)	0.9121 (0.7482 to 0.9712)	0.9081 (0.7414 to 0.9694)	
16 Months	0.9015 (0.7794 to 0.9578)	0.8219 (0.7009 to 0.8974)	0.8726 (0.7346 to 0.9416)	0.8567 (0.7210 to 0.9295)	0.9121 (0.7482 to 0.9712)	0.9081 (0.7414 to 0.9694)	
Number of patients at risk[b]							
2 Months	47	54	52	47	33	29	
4 Months	46	52	49	43	26	25	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	45	47	41	41	17	22	
8 Months	44	46	35	39	15	19	
10 Months	43	44	32	35	14	18	
12 Months	39	39	24	31	12	16	
14 Months	24	25	15	21	9	11	
16 Months	13	13	7	7	4	5	
Neutropenia (days)							
Number (%) of events	16 (31.4)	31 (49.2)	17 (30.9)	25 (47.2)	17 (42.5)	15 (45.5)	0.4136
Number (%) of patients censored	35 (68.6)	32 (50.8)	38 (69.1)	28 (52.8)	23 (57.5)	18 (54.5)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	3.0883 (0.7556 to NC)	0.8542 (0.7556 to 1.9384)	2.8255 (0.9199 to NC)	0.8542 (0.5914 to 0.9856)	0.9856 (0.5257 to 2.9569)	0.7721 (0.5257 to 1.4784)	
Median (95% CI)	NC (NC to NC)	13.8645 (2.1027 to NC)	NC (NC to NC)	NC (0.9856 to NC)	NC (1.4456 to NC)	NC (0.8214 to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.2 Treatment emergent adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	28	32	77	79	7	8	
8 Months	27	32	67	75	6	7	
10 Months	27	32	63	67	6	6	
12 Months	24	29	51	58	5	6	
14 Months	12	18	33	41	4	5	
16 Months	7	10	15	16	1	2	
Nausea (days)							
Number (%) of events	3 (9.7)	4 (10.3)	9 (9.3)	18 (18.4)	2 (9.5)	1 (6.7)	0.5185
Number (%) of patients censored	28 (90.3)	35 (89.7)	88 (90.7)	80 (81.6)	19 (90.5)	14 (93.3)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (0.8542 to NC)	NC (10.4148 to NC)	NC (NC to NC)	NC (4.5339 to NC)	NC (1.6756 to NC)	NC (0.6242 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.2 Treatment emergent adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.9417		0.0670		0.7096	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.24 to 4.72)		2.08 (0.93 to 4.63)		0.64 (0.06 to 7.03)	
P-value	-	0.9419		0.0733		0.7119	
Events probability (95% CI)[b]							
2 Months	0.9032 (0.7293 to 0.9677)	0.9487 (0.8102 to 0.9869)	0.9686 (0.9059 to 0.9898)	0.8571 (0.7707 to 0.9128)	0.9444 (0.6664 to 0.9920)	0.9286 (0.5908 to 0.9896)	
4 Months	0.9032 (0.7293 to 0.9677)	0.9224 (0.7782 to 0.9743)	0.9362 (0.8635 to 0.9708)	0.8463 (0.7580 to 0.9044)	0.8586 (0.5291 to 0.9641)	0.9286 (0.5908 to 0.9896)	
6 Months	0.9032 (0.7293 to 0.9677)	0.9224 (0.7782 to 0.9743)	0.9241 (0.8470 to 0.9631)	0.8352 (0.7450 to 0.8956)	0.8586 (0.5291 to 0.9641)	0.9286 (0.5908 to 0.9896)	
8 Months	0.9032 (0.7293 to 0.9677)	0.9224 (0.7782 to 0.9743)	0.9103 (0.8278 to 0.9543)	0.8229 (0.7303 to 0.8861)	0.8586 (0.5291 to 0.9641)	0.9286 (0.5908 to 0.9896)	
10 Months	0.9032 (0.7293 to 0.9677)	0.9224 (0.7782 to 0.9743)	0.8951 (0.8065 to 0.9445)	0.8229 (0.7303 to 0.8861)	0.8586 (0.5291 to 0.9641)	0.9286 (0.5908 to 0.9896)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.2 Treatment emergent adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
12 Months	0.9032 (0.7293 to 0.9677)	0.8944 (0.7423 to 0.9591)	0.8951 (0.8065 to 0.9445)	0.8087 (0.7127 to 0.8754)	0.8586 (0.5291 to 0.9641)	0.9286 (0.5908 to 0.9896)	
14 Months	0.9032 (0.7293 to 0.9677)	0.8944 (0.7423 to 0.9591)	0.8951 (0.8065 to 0.9445)	0.8087 (0.7127 to 0.8754)	0.8586 (0.5291 to 0.9641)	0.9286 (0.5908 to 0.9896)	
16 Months	0.9032 (0.7293 to 0.9677)	0.8944 (0.7423 to 0.9591)	0.8951 (0.8065 to 0.9445)	0.8087 (0.7127 to 0.8754)	0.8586 (0.5291 to 0.9641)	0.9286 (0.5908 to 0.9896)	
Number of patients at risk[b]							
2 Months	28	37	91	82	16	13	
4 Months	28	35	85	77	10	10	
6 Months	28	33	72	69	5	9	
8 Months	28	33	64	65	4	7	
10 Months	28	33	59	59	4	6	
12 Months	26	30	48	51	3	6	
14 Months	15	18	30	34	3	6	
16 Months	9	10	14	13	1	2	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.2 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	9	3	35	53	
16 Months	4	1	16	23	
Nausea (days)					
Number (%) of events	0 (0.0)	3 (21.4)	11 (11.8)	16 (13.8)	0.9897
Number (%) of patients censored	21 (100.0)	11 (78.6)	82 (88.2)	100 (86.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.1971 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (0.6899 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0257		0.7007	
Hazard ratio (95% CI) vs Pd	-	NC		1.16 (0.54 to 2.51)	
P-value	-	0.9973		0.7010	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.2 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.7738 (0.4493 to 0.9211)	0.9348 (0.8605 to 0.9702)	0.8966 (0.8250 to 0.9399)	
4 Months	1.0000 (1.0000 to 1.0000)	0.7738 (0.4493 to 0.9211)	0.8895 (0.8043 to 0.9390)	0.8966 (0.8250 to 0.9399)	
6 Months	1.0000 (1.0000 to 1.0000)	0.7738 (0.4493 to 0.9211)	0.8772 (0.7890 to 0.9301)	0.8873 (0.8138 to 0.9330)	
8 Months	1.0000 (1.0000 to 1.0000)	0.7738 (0.4493 to 0.9211)	0.8772 (0.7890 to 0.9301)	0.8777 (0.8021 to 0.9257)	
10 Months	1.0000 (1.0000 to 1.0000)	0.7738 (0.4493 to 0.9211)	0.8772 (0.7890 to 0.9301)	0.8777 (0.8021 to 0.9257)	
12 Months	1.0000 (1.0000 to 1.0000)	0.7738 (0.4493 to 0.9211)	0.8772 (0.7890 to 0.9301)	0.8561 (0.7753 to 0.9095)	
14 Months	1.0000 (1.0000 to 1.0000)	0.7738 (0.4493 to 0.9211)	0.8772 (0.7890 to 0.9301)	0.8561 (0.7753 to 0.9095)	
16 Months	1.0000 (1.0000 to 1.0000)	0.7738 (0.4493 to 0.9211)	0.8772 (0.7890 to 0.9301)	0.8561 (0.7753 to 0.9095)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.2 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	18	9	85	104	
4 Months	15	6	77	99	
6 Months	10	5	65	92	
8 Months	10	4	61	89	
10 Months	10	3	58	83	
12 Months	10	3	48	72	
14 Months	9	2	32	49	
16 Months	4	0	16	22	
Neutropenia (days)					
Number (%) of events	7 (33.3)	6 (42.9)	28 (30.1)	57 (49.1)	0.7209
Number (%) of patients censored	14 (66.7)	8 (57.1)	65 (69.9)	59 (50.9)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_cyto_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.13.3 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	13	7	30	47	
16 Months	7	2	13	21	
Nausea (days)					
Number (%) of events	1 (2.9)	5 (21.7)	9 (11.8)	13 (12.6)	0.0775
Number (%) of patients censored	33 (97.1)	18 (78.3)	67 (88.2)	90 (87.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (5.0267 to NC)	NC (0.1971 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0198		0.9033	
Hazard ratio (95% CI) vs Pd	-	8.41 (0.98 to 72.05)		1.05 (0.45 to 2.47)	
P-value	-	0.0520		0.9038	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.3 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.7743 (0.5398 to 0.8993)	0.9200 (0.8305 to 0.9632)	0.9126 (0.8388 to 0.9535)	
4 Months	1.0000 (1.0000 to 1.0000)	0.7743 (0.5398 to 0.8993)	0.8788 (0.7799 to 0.9350)	0.9126 (0.8388 to 0.9535)	
6 Months	0.9545 (0.7187 to 0.9935)	0.7743 (0.5398 to 0.8993)	0.8788 (0.7799 to 0.9350)	0.9021 (0.8257 to 0.9461)	
8 Months	0.9545 (0.7187 to 0.9935)	0.7743 (0.5398 to 0.8993)	0.8788 (0.7799 to 0.9350)	0.8911 (0.8119 to 0.9382)	
10 Months	0.9545 (0.7187 to 0.9935)	0.7743 (0.5398 to 0.8993)	0.8788 (0.7799 to 0.9350)	0.8911 (0.8119 to 0.9382)	
12 Months	0.9545 (0.7187 to 0.9935)	0.7743 (0.5398 to 0.8993)	0.8788 (0.7799 to 0.9350)	0.8665 (0.7805 to 0.9205)	
14 Months	0.9545 (0.7187 to 0.9935)	0.7743 (0.5398 to 0.8993)	0.8788 (0.7799 to 0.9350)	0.8665 (0.7805 to 0.9205)	
16 Months	0.9545 (0.7187 to 0.9935)	0.7743 (0.5398 to 0.8993)	0.8788 (0.7799 to 0.9350)	0.8665 (0.7805 to 0.9205)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.3 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	31	16	68	94	
4 Months	27	13	64	89	
6 Months	19	12	55	82	
8 Months	19	10	51	80	
10 Months	19	9	48	74	
12 Months	16	8	41	64	
14 Months	12	6	29	42	
16 Months	6	1	14	20	
Neutropenia (days)					
Number (%) of events	13 (38.2)	13 (56.5)	22 (28.9)	49 (47.6)	0.8732
Number (%) of patients censored	21 (61.8)	10 (43.5)	54 (71.1)	54 (52.4)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.3 Treatment emergent adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	30	32	19	32	
16 Months	14	15	9	13	
Nausea (days)					
Number (%) of events	11 (12.5)	12 (14.8)	3 (4.9)	11 (15.5)	0.2245
Number (%) of patients censored	77 (87.5)	69 (85.2)	58 (95.1)	60 (84.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.2033 to NC)	NC (NC to NC)	NC (10.4148 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6344		0.0635	
Hazard ratio (95% CI) vs Pd	-	1.22 (0.54 to 2.76)		3.14 (0.88 to 11.27)	
P-value	-	0.6342		0.0788	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.3 Treatment emergent adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9544 (0.8831 to 0.9826)	0.9006 (0.8110 to 0.9490)	0.9485 (0.8486 to 0.9831)	0.8732 (0.7706 to 0.9319)	
4 Months	0.9063 (0.8213 to 0.9521)	0.8877 (0.7953 to 0.9400)	0.9485 (0.8486 to 0.9831)	0.8582 (0.7524 to 0.9211)	
6 Months	0.8926 (0.8034 to 0.9428)	0.8741 (0.7784 to 0.9302)	0.9485 (0.8486 to 0.9831)	0.8582 (0.7524 to 0.9211)	
8 Months	0.8777 (0.7838 to 0.9326)	0.8592 (0.7598 to 0.9196)	0.9485 (0.8486 to 0.9831)	0.8582 (0.7524 to 0.9211)	
10 Months	0.8621 (0.7634 to 0.9216)	0.8592 (0.7598 to 0.9196)	0.9485 (0.8486 to 0.9831)	0.8582 (0.7524 to 0.9211)	
12 Months	0.8621 (0.7634 to 0.9216)	0.8413 (0.7360 to 0.9072)	0.9485 (0.8486 to 0.9831)	0.8403 (0.7295 to 0.9085)	
14 Months	0.8621 (0.7634 to 0.9216)	0.8413 (0.7360 to 0.9072)	0.9485 (0.8486 to 0.9831)	0.8403 (0.7295 to 0.9085)	
16 Months	0.8621 (0.7634 to 0.9216)	0.8413 (0.7360 to 0.9072)	0.9485 (0.8486 to 0.9831)	0.8403 (0.7295 to 0.9085)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.3 Treatment emergent adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	82	71	53	61	
4 Months	73	66	50	56	
6 Months	62	60	43	51	
8 Months	58	54	38	51	
10 Months	55	50	36	48	
12 Months	48	44	29	43	
14 Months	30	27	18	31	
16 Months	15	12	9	13	
Neutropenia (days)					
Number (%) of events	28 (31.8)	34 (42.0)	22 (36.1)	37 (52.1)	0.9366
Number (%) of patients censored	60 (68.2)	47 (58.0)	39 (63.9)	34 (47.9)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.2 Treatment emergent adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	1	0	48	64	
16 Months	0	0	23	28	
Nausea (days)					
Number (%) of events	0 (0.0)	0 (0.0)	14 (9.5)	23 (15.3)	0.9998
Number (%) of patients censored	2 (100.0)	2 (100.0)	133 (90.5)	127 (84.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.1438	
Hazard ratio (95% CI) vs Pd	-	NC		1.63 (0.84 to 3.17)	
P-value	-			0.1478	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.2 Treatment emergent adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9513 (0.9006 to 0.9765)	0.8863 (0.8235 to 0.9278)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9216 (0.8627 to 0.9558)	0.8722 (0.8069 to 0.9165)	
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9132 (0.8520 to 0.9498)	0.8647 (0.7981 to 0.9106)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9038 (0.8395 to 0.9432)	0.8567 (0.7886 to 0.9042)	
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8938 (0.8264 to 0.9361)	0.8567 (0.7886 to 0.9042)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8938 (0.8264 to 0.9361)	0.8386 (0.7664 to 0.8901)	
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8938 (0.8264 to 0.9361)	0.8386 (0.7664 to 0.8901)	
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8938 (0.8264 to 0.9361)	0.8386 (0.7664 to 0.8901)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.2 Treatment emergent adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	2	2	133	130	
4 Months	2	2	121	120	
6 Months	2	2	103	109	
8 Months	2	2	94	103	
10 Months	1	2	90	96	
12 Months	1	1	76	86	
14 Months	1	0	47	58	
16 Months	0	0	24	25	
Neutropenia (days)					
Number (%) of events	0 (0.0)	1 (50.0)	50 (34.0)	70 (46.7)	0.9845
Number (%) of patients censored	2 (100.0)	1 (50.0)	97 (66.0)	80 (53.3)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.3 Treatment emergent adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	32	43	12	15	
16 Months	15	18	6	6	
Nausea (days)					
Number (%) of events	12 (12.2)	17 (16.5)	2 (5.0)	4 (12.5)	0.8298
Number (%) of patients censored	86 (87.8)	86 (83.5)	38 (95.0)	28 (87.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (10.4148 to NC)	NC (NC to NC)	NC (1.1499 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4057		0.2760	
Hazard ratio (95% CI) vs Pd	-	1.37 (0.65 to 2.86)		2.49 (0.46 to 13.59)	
P-value	-	0.4076		0.2926	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.3 Treatment emergent adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9375 (0.8661 to 0.9714)	0.8832 (0.8035 to 0.9319)	0.9750 (0.8355 to 0.9964)	0.9063 (0.7369 to 0.9688)	
4 Months	0.9048 (0.8249 to 0.9493)	0.8731 (0.7916 to 0.9243)	0.9486 (0.8098 to 0.9869)	0.8727 (0.6951 to 0.9503)	
6 Months	0.8922 (0.8085 to 0.9406)	0.8624 (0.7786 to 0.9161)	0.9486 (0.8098 to 0.9869)	0.8727 (0.6951 to 0.9503)	
8 Months	0.8780 (0.7896 to 0.9309)	0.8509 (0.7646 to 0.9074)	0.9486 (0.8098 to 0.9869)	0.8727 (0.6951 to 0.9503)	
10 Months	0.8629 (0.7695 to 0.9204)	0.8509 (0.7646 to 0.9074)	0.9486 (0.8098 to 0.9869)	0.8727 (0.6951 to 0.9503)	
12 Months	0.8629 (0.7695 to 0.9204)	0.8241 (0.7310 to 0.8874)	0.9486 (0.8098 to 0.9869)	0.8727 (0.6951 to 0.9503)	
14 Months	0.8629 (0.7695 to 0.9204)	0.8241 (0.7310 to 0.8874)	0.9486 (0.8098 to 0.9869)	0.8727 (0.6951 to 0.9503)	
16 Months	0.8629 (0.7695 to 0.9204)	0.8241 (0.7310 to 0.8874)	0.9486 (0.8098 to 0.9869)	0.8727 (0.6951 to 0.9503)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_semm_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.3 Treatment emergent adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	88	90	37	28	
4 Months	82	84	32	26	
6 Months	66	76	31	25	
8 Months	60	70	28	25	
10 Months	57	64	27	24	
12 Months	48	55	23	23	
14 Months	30	35	12	16	
16 Months	15	14	7	6	
Neutropenia (days)					
Number (%) of events	32 (32.7)	47 (45.6)	14 (35.0)	20 (62.5)	0.2677
Number (%) of patients censored	66 (67.3)	56 (54.4)	26 (65.0)	12 (37.5)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.3 Treatment emergent adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	31	42	17	22	
16 Months	14	18	8	10	
Nausea (days)					
Number (%) of events	12 (12.4)	16 (15.8)	2 (3.9)	7 (14.0)	0.2474
Number (%) of patients censored	85 (87.6)	85 (84.2)	49 (96.1)	43 (86.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.2033 to NC)	NC (NC to NC)	NC (3.4497 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.5071		0.0857	
Hazard ratio (95% CI) vs Pd	-	1.29 (0.61 to 2.72)		3.62 (0.75 to 17.44)	
P-value	-	0.5083		0.1084	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.3 Treatment emergent adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9368 (0.8647 to 0.9711)	0.8908 (0.8114 to 0.9380)	0.9804 (0.8689 to 0.9972)	0.8800 (0.7522 to 0.9442)	
4 Months	0.9037 (0.8231 to 0.9487)	0.8805 (0.7992 to 0.9303)	0.9591 (0.8459 to 0.9896)	0.8574 (0.7237 to 0.9295)	
6 Months	0.8910 (0.8065 to 0.9399)	0.8695 (0.7858 to 0.9221)	0.9591 (0.8459 to 0.9896)	0.8574 (0.7237 to 0.9295)	
8 Months	0.8766 (0.7873 to 0.9301)	0.8578 (0.7714 to 0.9133)	0.9591 (0.8459 to 0.9896)	0.8574 (0.7237 to 0.9295)	
10 Months	0.8613 (0.7669 to 0.9194)	0.8578 (0.7714 to 0.9133)	0.9591 (0.8459 to 0.9896)	0.8574 (0.7237 to 0.9295)	
12 Months	0.8613 (0.7669 to 0.9194)	0.8303 (0.7366 to 0.8931)	0.9591 (0.8459 to 0.9896)	0.8574 (0.7237 to 0.9295)	
14 Months	0.8613 (0.7669 to 0.9194)	0.8303 (0.7366 to 0.8931)	0.9591 (0.8459 to 0.9896)	0.8574 (0.7237 to 0.9295)	
16 Months	0.8613 (0.7669 to 0.9194)	0.8303 (0.7366 to 0.8931)	0.9591 (0.8459 to 0.9896)	0.8574 (0.7237 to 0.9295)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.3 Treatment emergent adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	87	89	47	42	
4 Months	81	83	41	38	
6 Months	65	75	39	35	
8 Months	59	69	36	35	
10 Months	56	63	34	34	
12 Months	47	54	29	32	
14 Months	29	35	18	23	
16 Months	14	14	9	11	
Neutropenia (days)					
Number (%) of events	32 (33.0)	45 (44.6)	18 (35.3)	25 (50.0)	0.8204
Number (%) of patients censored	65 (67.0)	56 (55.4)	33 (64.7)	25 (50.0)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.2 Treatment emergent adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	2	7	47	57	
16 Months	0	5	23	23	
Nausea (days)					
Number (%) of events	2 (20.0)	1 (7.1)	12 (8.6)	22 (15.9)	0.1147
Number (%) of patients censored	8 (80.0)	13 (92.9)	127 (91.4)	116 (84.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (0.0657 to NC)	NC (0.6899 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (0.0657 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2993		0.0658	
Hazard ratio (95% CI) vs Pd	-	0.30 (0.03 to 3.33)		1.91 (0.95 to 3.87)	
P-value	-	0.3278		0.0706	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.2 Treatment emergent adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9000 (0.4730 to 0.9853)	0.9286 (0.5908 to 0.9896)	0.9559 (0.9045 to 0.9800)	0.8837 (0.8172 to 0.9271)	
4 Months	0.7714 (0.3449 to 0.9387)	0.9286 (0.5908 to 0.9896)	0.9326 (0.8744 to 0.9644)	0.8683 (0.7991 to 0.9150)	
6 Months	0.7714 (0.3449 to 0.9387)	0.9286 (0.5908 to 0.9896)	0.9240 (0.8632 to 0.9585)	0.8602 (0.7896 to 0.9085)	
8 Months	0.7714 (0.3449 to 0.9387)	0.9286 (0.5908 to 0.9896)	0.9145 (0.8505 to 0.9519)	0.8516 (0.7793 to 0.9017)	
10 Months	0.7714 (0.3449 to 0.9387)	0.9286 (0.5908 to 0.9896)	0.9045 (0.8371 to 0.9449)	0.8516 (0.7793 to 0.9017)	
12 Months	0.7714 (0.3449 to 0.9387)	0.9286 (0.5908 to 0.9896)	0.9045 (0.8371 to 0.9449)	0.8322 (0.7556 to 0.8865)	
14 Months	0.7714 (0.3449 to 0.9387)	0.9286 (0.5908 to 0.9896)	0.9045 (0.8371 to 0.9449)	0.8322 (0.7556 to 0.8865)	
16 Months	0.7714 (0.3449 to 0.9387)	0.9286 (0.5908 to 0.9896)	0.9045 (0.8371 to 0.9449)	0.8322 (0.7556 to 0.8865)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.2 Treatment emergent adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	8	13	127	119	
4 Months	5	12	118	110	
6 Months	3	10	102	101	
8 Months	1	9	95	96	
10 Months	1	9	90	89	
12 Months	1	7	76	80	
14 Months	1	6	47	52	
16 Months	0	5	24	20	
Neutropenia (days)					
Number (%) of events	1 (10.0)	7 (50.0)	49 (35.3)	64 (46.4)	0.2436
Number (%) of patients censored	9 (90.0)	7 (50.0)	90 (64.7)	74 (53.6)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.2 Treatment emergent adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	33	39	14	21	
16 Months	15	19	6	8	
Nausea (days)					
Number (%) of events	7 (7.4)	16 (18.6)	7 (14.9)	6 (11.1)	0.0655
Number (%) of patients censored	87 (92.6)	70 (81.4)	40 (85.1)	48 (88.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (6.3080 to NC)	NC (2.9897 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0297		0.5399	
Hazard ratio (95% CI) vs Pd	-	2.58 (1.06 to 6.28)		0.71 (0.24 to 2.12)	
P-value	-	0.0363		0.5418	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.2 Treatment emergent adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.39 (0.16 to 0.94)				
Events probability (95% CI)[b]					
2 Months	0.9679 (0.9036 to 0.9895)	0.8721 (0.7810 to 0.9270)	0.9120 (0.7822 to 0.9660)	0.9074 (0.7917 to 0.9604)	
4 Months	0.9567 (0.8888 to 0.9835)	0.8603 (0.7671 to 0.9181)	0.8387 (0.6903 to 0.9198)	0.8877 (0.7668 to 0.9479)	
6 Months	0.9441 (0.8707 to 0.9764)	0.8478 (0.7523 to 0.9087)	0.8387 (0.6903 to 0.9198)	0.8877 (0.7668 to 0.9479)	
8 Months	0.9308 (0.8519 to 0.9685)	0.8348 (0.7368 to 0.8987)	0.8387 (0.6903 to 0.9198)	0.8877 (0.7668 to 0.9479)	
10 Months	0.9165 (0.8318 to 0.9596)	0.8348 (0.7368 to 0.8987)	0.8387 (0.6903 to 0.9198)	0.8877 (0.7668 to 0.9479)	
12 Months	0.9165 (0.8318 to 0.9596)	0.8067 (0.7033 to 0.8772)	0.8387 (0.6903 to 0.9198)	0.8877 (0.7668 to 0.9479)	
14 Months	0.9165 (0.8318 to 0.9596)	0.8067 (0.7033 to 0.8772)	0.8387 (0.6903 to 0.9198)	0.8877 (0.7668 to 0.9479)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.2 Treatment emergent adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.9165 (0.8318 to 0.9596)	0.8067 (0.7033 to 0.8772)	0.8387 (0.6903 to 0.9198)	0.8877 (0.7668 to 0.9479)	
Number of patients at risk[b]					
2 Months	88	74	40	49	
4 Months	83	71	34	44	
6 Months	74	66	27	40	
8 Months	68	63	24	37	
10 Months	64	60	23	33	
12 Months	56	51	19	31	
14 Months	33	32	13	22	
16 Months	15	15	7	9	
Neutropenia (days)					
Number (%) of events	29 (30.9)	43 (50.0)	19 (40.4)	24 (44.4)	0.1716
Number (%) of patients censored	65 (69.1)	43 (50.0)	28 (59.6)	30 (55.6)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.2 Treatment emergent adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	2	2	137	143	
4 Months	2	2	127	132	
6 Months	1	2	111	117	
8 Months	0	2	100	112	
10 Months	0	2	96	103	
12 Months	0	2	80	91	
14 Months	0	2	49	62	
16 Months	0	0	23	28	
Nausea (days)					
Number (%) of events	0 (0.0)	0 (0.0)	14 (9.5)	23 (15.3)	0.9998
Number (%) of patients censored	2 (100.0)	2 (100.0)	133 (90.5)	127 (84.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.2 Treatment emergent adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.1420	
Hazard ratio (95% CI) vs Pd	-	NC		1.64 (0.84 to 3.18)	
P-value	-			0.1460	
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9513 (0.9006 to 0.9765)	0.8863 (0.8235 to 0.9278)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9216 (0.8627 to 0.9558)	0.8722 (0.8069 to 0.9165)	
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9133 (0.8521 to 0.9499)	0.8647 (0.7981 to 0.9106)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9040 (0.8400 to 0.9433)	0.8567 (0.7886 to 0.9042)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.2 Treatment emergent adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8942 (0.8270 to 0.9363)	0.8567 (0.7886 to 0.9042)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8942 (0.8270 to 0.9363)	0.8386 (0.7664 to 0.8901)	
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8942 (0.8270 to 0.9363)	0.8386 (0.7664 to 0.8901)	
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8942 (0.8270 to 0.9363)	0.8386 (0.7664 to 0.8901)	
Number of patients at risk[b]					
2 Months	2	2	133	130	
4 Months	2	2	121	120	
6 Months	1	2	104	109	
8 Months	0	2	96	103	
10 Months	0	2	91	96	
12 Months	0	2	77	85	
14 Months	0	2	48	56	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.2 Treatment emergent adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0	0	24	25	
Neutropenia (days)					
Number (%) of events	1 (50.0)	0 (0.0)	49 (33.3)	71 (47.3)	0.9823
Number (%) of patients censored	1 (50.0)	2 (100.0)	98 (66.7)	79 (52.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.1643 (0.1643 to NC)	NC (NC to NC)	2.0370 (0.9856 to 4.9938)	0.8542 (0.7556 to 0.9856)	
Median (95% CI)	NC (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.7926 to NC)	
75% quantile (95% CI)	NC (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.0135	
Hazard ratio (95% CI) vs Pd	-	NC		1.58 (1.10 to 2.27)	
P-value	-	0.9990		0.0143	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.3 Treatment emergent adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	69	81	27	24	
12 Months	56	73	24	20	
14 Months	35	52	14	12	
16 Months	15	24	8	4	
Nausea (days)					
Number (%) of events	12 (10.8)	18 (15.4)	2 (5.3)	5 (14.3)	0.4350
Number (%) of patients censored	99 (89.2)	99 (84.6)	36 (94.7)	30 (85.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.4600 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3458		0.1882	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.3 Treatment emergent adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Pd	-	1.42 (0.68 to 2.95)		2.86 (0.56 to 14.76)	
P-value	-	0.3483		0.2087	
Events probability (95% CI)[b]					
2 Months	0.9447 (0.8811 to 0.9748)	0.8884 (0.8156 to 0.9336)	0.9730 (0.8232 to 0.9961)	0.8857 (0.7236 to 0.9555)	
4 Months	0.9050 (0.8305 to 0.9478)	0.8706 (0.7946 to 0.9199)	0.9730 (0.8232 to 0.9961)	0.8857 (0.7236 to 0.9555)	
6 Months	0.9050 (0.8305 to 0.9478)	0.8612 (0.7833 to 0.9126)	0.9426 (0.7887 to 0.9854)	0.8857 (0.7236 to 0.9555)	
8 Months	0.8925 (0.8135 to 0.9392)	0.8511 (0.7711 to 0.9048)	0.9426 (0.7887 to 0.9854)	0.8857 (0.7236 to 0.9555)	
10 Months	0.8787 (0.7948 to 0.9298)	0.8511 (0.7711 to 0.9048)	0.9426 (0.7887 to 0.9854)	0.8857 (0.7236 to 0.9555)	
12 Months	0.8787 (0.7948 to 0.9298)	0.8394 (0.7566 to 0.8960)	0.9426 (0.7887 to 0.9854)	0.8472 (0.6679 to 0.9341)	
14 Months	0.8787 (0.7948 to 0.9298)	0.8394 (0.7566 to 0.8960)	0.9426 (0.7887 to 0.9854)	0.8472 (0.6679 to 0.9341)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.3 Treatment emergent adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.8787 (0.7948 to 0.9298)	0.8394 (0.7566 to 0.8960)	0.9426 (0.7887 to 0.9854)	0.8472 (0.6679 to 0.9341)	
Number of patients at risk[b]					
2 Months	99	102	36	30	
4 Months	89	95	34	27	
6 Months	76	86	29	25	
8 Months	69	81	27	24	
10 Months	64	74	27	24	
12 Months	53	67	24	20	
14 Months	34	46	14	12	
16 Months	16	22	8	3	
Neutropenia (days)					
Number (%) of events	40 (36.0)	55 (47.0)	10 (26.3)	16 (45.7)	0.3043
Number (%) of patients censored	71 (64.0)	62 (53.0)	28 (73.7)	19 (54.3)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.2 Treatment emergent adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	45	63	4	1	
16 Months	22	28	1	0	
Nausea (days)					
Number (%) of events	12 (8.6)	23 (15.9)	2 (22.2)	0 (0.0)	0.9895
Number (%) of patients censored	128 (91.4)	122 (84.1)	7 (77.8)	7 (100.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.9897 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.9897 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0727		0.1987	
Hazard ratio (95% CI) vs Pd	-	1.88 (0.93 to 3.77)		NC	
P-value	-	0.0775		0.9977	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.2 Treatment emergent adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9488 (0.8956 to 0.9753)	0.8824 (0.8176 to 0.9252)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9334 (0.8758 to 0.9648)	0.8677 (0.8005 to 0.9135)	0.7778 (0.3648 to 0.9393)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9245 (0.8640 to 0.9587)	0.8600 (0.7913 to 0.9074)	0.7778 (0.3648 to 0.9393)	1.0000 (1.0000 to 1.0000)	
8 Months	0.9145 (0.8502 to 0.9519)	0.8517 (0.7814 to 0.9008)	0.7778 (0.3648 to 0.9393)	1.0000 (1.0000 to 1.0000)	
10 Months	0.9037 (0.8354 to 0.9446)	0.8517 (0.7814 to 0.9008)	0.7778 (0.3648 to 0.9393)	1.0000 (1.0000 to 1.0000)	
12 Months	0.9037 (0.8354 to 0.9446)	0.8330 (0.7587 to 0.8862)	0.7778 (0.3648 to 0.9393)	1.0000 (1.0000 to 1.0000)	
14 Months	0.9037 (0.8354 to 0.9446)	0.8330 (0.7587 to 0.8862)	0.7778 (0.3648 to 0.9393)	1.0000 (1.0000 to 1.0000)	
16 Months	0.9037 (0.8354 to 0.9446)	0.8330 (0.7587 to 0.8862)	0.7778 (0.3648 to 0.9393)	1.0000 (1.0000 to 1.0000)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.2 Treatment emergent adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	126	125	9	7	
4 Months	116	115	7	7	
6 Months	98	104	7	7	
8 Months	89	100	7	5	
10 Months	84	93	7	5	
12 Months	70	82	7	5	
14 Months	43	55	5	3	
16 Months	22	25	2	0	
Neutropenia (days)					
Number (%) of events	45 (32.1)	67 (46.2)	5 (55.6)	4 (57.1)	0.5826
Number (%) of patients censored	95 (67.9)	78 (53.8)	4 (44.4)	3 (42.9)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.3 Treatment emergent adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	30	38	19	26	
16 Months	13	15	10	13	
Nausea (days)					
Number (%) of events	8 (9.2)	14 (15.4)	6 (9.7)	9 (14.8)	0.8415
Number (%) of patients censored	79 (90.8)	77 (84.6)	56 (90.3)	52 (85.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.2033 to NC)	NC (NC to NC)	NC (6.3080 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.2106		0.4410	
Hazard ratio (95% CI) vs Pd	-	1.73 (0.73 to 4.12)		1.50 (0.53 to 4.21)	
P-value	-	0.2163		0.4441	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.3 Treatment emergent adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	0.9295 (0.8498 to 0.9677)	0.8786 (0.7915 to 0.9309)	0.9839 (0.8910 to 0.9977)	0.9016 (0.7941 to 0.9546)	
4 Months	0.9173 (0.8343 to 0.9597)	0.8786 (0.7915 to 0.9309)	0.9302 (0.8243 to 0.9733)	0.8679 (0.7531 to 0.9317)	
6 Months	0.9034 (0.8157 to 0.9506)	0.8660 (0.7760 to 0.9217)	0.9302 (0.8243 to 0.9733)	0.8679 (0.7531 to 0.9317)	
8 Months	0.9034 (0.8157 to 0.9506)	0.8660 (0.7760 to 0.9217)	0.9075 (0.7902 to 0.9608)	0.8495 (0.7303 to 0.9188)	
10 Months	0.9034 (0.8157 to 0.9506)	0.8660 (0.7760 to 0.9217)	0.8823 (0.7533 to 0.9461)	0.8495 (0.7303 to 0.9188)	
12 Months	0.9034 (0.8157 to 0.9506)	0.8359 (0.7372 to 0.9000)	0.8823 (0.7533 to 0.9461)	0.8495 (0.7303 to 0.9188)	
14 Months	0.9034 (0.8157 to 0.9506)	0.8359 (0.7372 to 0.9000)	0.8823 (0.7533 to 0.9461)	0.8495 (0.7303 to 0.9188)	
16 Months	0.9034 (0.8157 to 0.9506)	0.8359 (0.7372 to 0.9000)	0.8823 (0.7533 to 0.9461)	0.8495 (0.7303 to 0.9188)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.3 Treatment emergent adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	77	78	58	54	
4 Months	72	71	51	51	
6 Months	62	64	43	47	
8 Months	56	62	40	43	
10 Months	56	59	35	39	
12 Months	47	53	30	34	
14 Months	28	33	20	25	
16 Months	13	13	11	12	
Neutropenia (days)					
Number (%) of events	28 (32.2)	42 (46.2)	22 (35.5)	29 (47.5)	0.7205
Number (%) of patients censored	59 (67.8)	49 (53.8)	40 (64.5)	32 (52.5)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0.9172 (0.8116 to 0.9648)	0.8719 (0.7352 to 0.9407)	0.9796 (0.8638 to 0.9971)	0.9017 (0.7937 to 0.9547)	0.9630 (0.7649 to 0.9947)	0.8820 (0.6720 to 0.9611)	
16 Months	0.9172 (0.8116 to 0.9648)	0.8719 (0.7352 to 0.9407)	0.9796 (0.8638 to 0.9971)	0.9017 (0.7937 to 0.9547)	0.9630 (0.7649 to 0.9947)	0.8820 (0.6720 to 0.9611)	
Number of patients at risk[b]							
2 Months	64	52	48	62	25	31	
4 Months	60	49	46	62	23	27	
6 Months	50	43	43	53	18	25	
8 Months	45	38	40	52	16	25	
10 Months	43	36	39	48	15	23	
12 Months	38	31	34	43	11	20	
14 Months	24	20	20	31	8	14	
16 Months	13	10	7	14	4	4	
Infusion related reaction (days)							
Number (%) of events	1 (1.5)	23 (42.6)	1 (1.9)	24 (36.4)	0 (0.0)	9 (28.1)	0.9555

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of patients censored	67 (98.5)	31 (57.4)	52 (98.1)	42 (63.6)	28 (100.0)	23 (71.9)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1643)	NC (NC to NC)	0.1314 (0.0657 to 0.1971)	NC (NC to NC)	0.1807 (0.0657 to NC)	
Median (95% CI)	NC (NC to NC)	NC (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001		0.0030	
Hazard ratio (95% CI) vs Pd	-	36.45 (4.92 to 270.22)		23.16 (3.13 to 171.35)		NC	
P-value	-	0.0004		0.0021		0.9952	
Hazard ratio inverted (95% CI) vs IPd	0.03 (0.00 to 0.20)		0.04 (0.01 to 0.32)				

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]							
2 Months	0.9851 (0.8987 to 0.9979)	0.5741 (0.4319 to 0.6929)	1.0000 (1.0000 to 1.0000)	0.6364 (0.5083 to 0.7394)	1.0000 (1.0000 to 1.0000)	0.7188 (0.5291 to 0.8426)	
4 Months	0.9851 (0.8987 to 0.9979)	0.5741 (0.4319 to 0.6929)	1.0000 (1.0000 to 1.0000)	0.6364 (0.5083 to 0.7394)	1.0000 (1.0000 to 1.0000)	0.7188 (0.5291 to 0.8426)	
6 Months	0.9851 (0.8987 to 0.9979)	0.5741 (0.4319 to 0.6929)	1.0000 (1.0000 to 1.0000)	0.6364 (0.5083 to 0.7394)	1.0000 (1.0000 to 1.0000)	0.7188 (0.5291 to 0.8426)	
8 Months	0.9851 (0.8987 to 0.9979)	0.5741 (0.4319 to 0.6929)	0.9773 (0.8494 to 0.9968)	0.6364 (0.5083 to 0.7394)	1.0000 (1.0000 to 1.0000)	0.7188 (0.5291 to 0.8426)	
10 Months	0.9851 (0.8987 to 0.9979)	0.5741 (0.4319 to 0.6929)	0.9773 (0.8494 to 0.9968)	0.6364 (0.5083 to 0.7394)	1.0000 (1.0000 to 1.0000)	0.7188 (0.5291 to 0.8426)	
12 Months	0.9851 (0.8987 to 0.9979)	0.5741 (0.4319 to 0.6929)	0.9773 (0.8494 to 0.9968)	0.6364 (0.5083 to 0.7394)	1.0000 (1.0000 to 1.0000)	0.7188 (0.5291 to 0.8426)	
14 Months	0.9851 (0.8987 to 0.9979)	0.5741 (0.4319 to 0.6929)	0.9773 (0.8494 to 0.9968)	0.6364 (0.5083 to 0.7394)	1.0000 (1.0000 to 1.0000)	0.7188 (0.5291 to 0.8426)	
16 Months	0.9851 (0.8987 to 0.9979)	0.5741 (0.4319 to 0.6929)	0.9773 (0.8494 to 0.9968)	0.6364 (0.5083 to 0.7394)	1.0000 (1.0000 to 1.0000)	0.7188 (0.5291 to 0.8426)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
2 Months	65	31	50	41	26	23	
4 Months	62	29	48	41	24	20	
6 Months	54	25	45	37	18	19	
8 Months	49	22	40	36	16	19	
10 Months	47	21	39	32	15	18	
12 Months	41	18	34	29	11	16	
14 Months	25	9	20	20	8	11	
16 Months	14	3	8	9	4	3	
Insomnia (days)							
Number (%) of events	6 (8.8)	4 (7.4)	5 (9.4)	4 (6.1)	1 (3.6)	5 (15.6)	0.3203
Number (%) of patients censored	62 (91.2)	50 (92.6)	48 (90.6)	62 (93.9)	27 (96.4)	27 (84.4)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.5996 to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.2 Treatment emergent adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	90	96	47	49	
4 Months	85	89	44	49	
6 Months	75	79	36	42	
8 Months	70	77	31	38	
10 Months	69	70	28	37	
12 Months	57	63	26	31	
14 Months	35	42	17	23	
16 Months	14	19	10	9	
Infusion related reaction (days)					
Number (%) of events	2 (2.0)	38 (37.6)	0 (0.0)	18 (35.3)	0.9859
Number (%) of patients censored	98 (98.0)	63 (62.4)	49 (100.0)	33 (64.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1643)	NC (NC to NC)	0.1643 (0.1314 to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.2 Treatment emergent adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.2300 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Pd	-	22.70 (5.47 to 94.16)		NC	
P-value	-	<.0001		0.9893	
Hazard ratio inverted (95% CI) vs IPd	0.04 (0.01 to 0.18)				
Events probability (95% CI)[b]					
2 Months	0.9896 (0.9284 to 0.9985)	0.6238 (0.5217 to 0.7100)	1.0000 (1.0000 to 1.0000)	0.6471 (0.4998 to 0.7609)	
4 Months	0.9896 (0.9284 to 0.9985)	0.6238 (0.5217 to 0.7100)	1.0000 (1.0000 to 1.0000)	0.6471 (0.4998 to 0.7609)	
6 Months	0.9896 (0.9284 to 0.9985)	0.6238 (0.5217 to 0.7100)	1.0000 (1.0000 to 1.0000)	0.6471 (0.4998 to 0.7609)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.2 Treatment emergent adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.9771 (0.9108 to 0.9942)	0.6238 (0.5217 to 0.7100)	1.0000 (1.0000 to 1.0000)	0.6471 (0.4998 to 0.7609)	
10 Months	0.9771 (0.9108 to 0.9942)	0.6238 (0.5217 to 0.7100)	1.0000 (1.0000 to 1.0000)	0.6471 (0.4998 to 0.7609)	
12 Months	0.9771 (0.9108 to 0.9942)	0.6238 (0.5217 to 0.7100)	1.0000 (1.0000 to 1.0000)	0.6471 (0.4998 to 0.7609)	
14 Months	0.9771 (0.9108 to 0.9942)	0.6238 (0.5217 to 0.7100)	1.0000 (1.0000 to 1.0000)	0.6471 (0.4998 to 0.7609)	
16 Months	0.9771 (0.9108 to 0.9942)	0.6238 (0.5217 to 0.7100)	1.0000 (1.0000 to 1.0000)	0.6471 (0.4998 to 0.7609)	
Number of patients at risk[b]					
2 Months	93	62	48	33	
4 Months	89	57	45	33	
6 Months	79	51	38	30	
8 Months	72	49	33	28	
10 Months	71	45	30	26	
12 Months	59	41	27	22	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.2 Treatment emergent adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	36	25	17	15	
16 Months	16	10	10	5	
Insomnia (days)					
Number (%) of events	7 (7.0)	7 (6.9)	5 (10.2)	6 (11.8)	0.9027
Number (%) of patients censored	93 (93.0)	94 (93.1)	44 (89.8)	45 (88.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.7906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9164		0.9515	
Hazard ratio (95% CI) vs Pd	-	0.95 (0.33 to 2.70)		1.04 (0.32 to 3.40)	
P-value	-	0.9164		0.9515	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.3 Treatment emergent adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	64	83	73	62	
4 Months	61	79	68	59	
6 Months	54	69	57	52	
8 Months	52	65	49	50	
10 Months	49	59	48	48	
12 Months	40	51	43	43	
14 Months	26	33	26	32	
16 Months	14	16	10	12	
Infusion related reaction (days)					
Number (%) of events	1 (1.5)	27 (30.7)	1 (1.2)	29 (45.3)	0.6577
Number (%) of patients censored	67 (98.5)	61 (69.3)	80 (98.8)	35 (54.7)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_sex_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.3 Treatment emergent adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0986 to NC)	NC (NC to NC)	0.0986 (0.0657 to 0.1643)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.1643 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Pd	-	24.25 (3.29 to 178.57)		46.83 (6.37 to 344.19)	
P-value	-	0.0017		0.0002	
Hazard ratio inverted (95% CI) vs IPd	0.04 (0.01 to 0.30)		0.02 (0.00 to 0.16)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.6932 (0.5854 to 0.7782)	0.9872 (0.9125 to 0.9982)	0.5469 (0.4176 to 0.6590)	
4 Months	1.0000 (1.0000 to 1.0000)	0.6932 (0.5854 to 0.7782)	0.9872 (0.9125 to 0.9982)	0.5469 (0.4176 to 0.6590)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.3 Treatment emergent adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	1.0000 (1.0000 to 1.0000)	0.6932 (0.5854 to 0.7782)	0.9872 (0.9125 to 0.9982)	0.5469 (0.4176 to 0.6590)	
8 Months	0.9818 (0.8779 to 0.9974)	0.6932 (0.5854 to 0.7782)	0.9872 (0.9125 to 0.9982)	0.5469 (0.4176 to 0.6590)	
10 Months	0.9818 (0.8779 to 0.9974)	0.6932 (0.5854 to 0.7782)	0.9872 (0.9125 to 0.9982)	0.5469 (0.4176 to 0.6590)	
12 Months	0.9818 (0.8779 to 0.9974)	0.6932 (0.5854 to 0.7782)	0.9872 (0.9125 to 0.9982)	0.5469 (0.4176 to 0.6590)	
14 Months	0.9818 (0.8779 to 0.9974)	0.6932 (0.5854 to 0.7782)	0.9872 (0.9125 to 0.9982)	0.5469 (0.4176 to 0.6590)	
16 Months	0.9818 (0.8779 to 0.9974)	0.6932 (0.5854 to 0.7782)	0.9872 (0.9125 to 0.9982)	0.5469 (0.4176 to 0.6590)	
Number of patients at risk[b]					
2 Months	65	60	76	35	
4 Months	62	56	72	34	
6 Months	55	49	62	32	
8 Months	52	47	53	30	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.3 Treatment emergent adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	49	42	52	29	
12 Months	40	37	46	26	
14 Months	26	21	27	19	
16 Months	15	8	11	7	
Insomnia (days)					
Number (%) of events	4 (5.9)	9 (10.2)	8 (9.9)	4 (6.3)	0.2189
Number (%) of patients censored	64 (94.1)	79 (89.8)	73 (90.1)	60 (93.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3835		0.3842	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.2 Treatment emergent adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	111	113	19	22	
4 Months	104	109	19	21	
6 Months	89	96	18	20	
8 Months	80	92	17	18	
10 Months	77	85	16	17	
12 Months	69	74	12	15	
14 Months	47	50	3	11	
16 Months	21	23	1	4	
Infusion related reaction (days)					
Number (%) of events	2 (1.6)	40 (34.5)	0 (0.0)	12 (50.0)	0.9867
Number (%) of patients censored	120 (98.4)	76 (65.5)	19 (100.0)	12 (50.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1150 (0.0657 to 0.1971)	NC (NC to NC)	0.1314 (0.0657 to 0.1643)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.2 Treatment emergent adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.1314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		0.0005	
Hazard ratio (95% CI) vs Pd	-	24.96 (6.03 to 103.32)		NC	
P-value	-	<.0001		0.9944	
Hazard ratio inverted (95% CI) vs IPd	0.04 (0.01 to 0.17)				
Events probability (95% CI)[b]					
2 Months	0.9915 (0.9414 to 0.9988)	0.6552 (0.5611 to 0.7338)	1.0000 (1.0000 to 1.0000)	0.5000 (0.2910 to 0.6776)	
4 Months	0.9915 (0.9414 to 0.9988)	0.6552 (0.5611 to 0.7338)	1.0000 (1.0000 to 1.0000)	0.5000 (0.2910 to 0.6776)	
6 Months	0.9915 (0.9414 to 0.9988)	0.6552 (0.5611 to 0.7338)	1.0000 (1.0000 to 1.0000)	0.5000 (0.2910 to 0.6776)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.2 Treatment emergent adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.9809 (0.9249 to 0.9952)	0.6552 (0.5611 to 0.7338)	1.0000 (1.0000 to 1.0000)	0.5000 (0.2910 to 0.6776)	
10 Months	0.9809 (0.9249 to 0.9952)	0.6552 (0.5611 to 0.7338)	1.0000 (1.0000 to 1.0000)	0.5000 (0.2910 to 0.6776)	
12 Months	0.9809 (0.9249 to 0.9952)	0.6552 (0.5611 to 0.7338)	1.0000 (1.0000 to 1.0000)	0.5000 (0.2910 to 0.6776)	
14 Months	0.9809 (0.9249 to 0.9952)	0.6552 (0.5611 to 0.7338)	1.0000 (1.0000 to 1.0000)	0.5000 (0.2910 to 0.6776)	
16 Months	0.9809 (0.9249 to 0.9952)	0.6552 (0.5611 to 0.7338)	1.0000 (1.0000 to 1.0000)	0.5000 (0.2910 to 0.6776)	
Number of patients at risk[b]					
2 Months	115	76	19	12	
4 Months	109	74	19	11	
6 Months	94	66	19	11	
8 Months	83	63	18	10	
10 Months	80	58	17	9	
12 Months	71	51	13	8	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.2 Treatment emergent adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	48	32	3	5	
16 Months	23	12	1	2	
Insomnia (days)					
Number (%) of events	11 (9.0)	12 (10.3)	1 (5.3)	1 (4.2)	0.8434
Number (%) of patients censored	111 (91.0)	104 (89.7)	18 (94.7)	23 (95.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.2300 to NC)	NC (5.7166 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8887		0.8777	
Hazard ratio (95% CI) vs Pd	-	1.06 (0.47 to 2.40)		0.80 (0.05 to 12.87)	
P-value	-	0.8887		0.8780	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.3 Treatment emergent adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	1	4	121	123	
4 Months	1	4	115	118	
6 Months	1	3	99	105	
8 Months	1	3	89	99	
10 Months	1	3	85	92	
12 Months	0	3	73	79	
14 Months	0	3	46	54	
16 Months	0	1	21	24	
Infusion related reaction (days)					
Number (%) of events	0 (0.0)	2 (50.0)	2 (1.5)	47 (36.7)	0.9918
Number (%) of patients censored	3 (100.0)	2 (50.0)	128 (98.5)	81 (63.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.0821 (0.0657 to NC)	NC (NC to NC)	0.1314 (0.0986 to 0.1643)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.3 Treatment emergent adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (0.0657 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.0657 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1869		<.0001	
Hazard ratio (95% CI) vs Pd	-	NC		28.83 (7.00 to 118.74)	
P-value	-	0.9977		<.0001	
Hazard ratio inverted (95% CI) vs IPd			0.03 (0.01 to 0.14)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.9921 (0.9454 to 0.9989)	0.6328 (0.5431 to 0.7097)	
4 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.9921 (0.9454 to 0.9989)	0.6328 (0.5431 to 0.7097)	
6 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.9921 (0.9454 to 0.9989)	0.6328 (0.5431 to 0.7097)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.3 Treatment emergent adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.9826 (0.9317 to 0.9956)	0.6328 (0.5431 to 0.7097)	
10 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.9826 (0.9317 to 0.9956)	0.6328 (0.5431 to 0.7097)	
12 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.9826 (0.9317 to 0.9956)	0.6328 (0.5431 to 0.7097)	
14 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.9826 (0.9317 to 0.9956)	0.6328 (0.5431 to 0.7097)	
16 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0578 to 0.8449)	0.9826 (0.9317 to 0.9956)	0.6328 (0.5431 to 0.7097)	
Number of patients at risk[b]					
2 Months	2	2	124	81	
4 Months	2	2	119	78	
6 Months	1	2	105	70	
8 Months	1	2	93	66	
10 Months	1	2	89	60	
12 Months	0	2	76	52	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.3 Treatment emergent adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0	2	47	34	
16 Months	0	1	23	13	
Insomnia (days)					
Number (%) of events	0 (0.0)	0 (0.0)	9 (6.9)	11 (8.6)	1.0000
Number (%) of patients censored	3 (100.0)	4 (100.0)	121 (93.1)	117 (91.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			0.7146	
Hazard ratio (95% CI) vs Pd	-	NC		1.18 (0.49 to 2.84)	
P-value	-			0.7149	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_ethn_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
14 Months	30	20	8	12	1	0	2	10	11	23	
16 Months	13	7	2	4	0	0	1	4	8	13	
Infusion related reaction (days)											
Number (%) of events	2 (2.7)	21 (38.2)	0 (0.0)	5 (17.9)	0 (0.0)	3 (42.9)	0 (0.0)	12 (57.1)	0 (0.0)	15 (36.6)	1.0000
Number (%) of patients censored	72 (97.3)	34 (61.8)	20 (100.0)	23 (82.1)	5 (100.0)	4 (57.1)	15 (100.0)	9 (42.9)	35 (100.0)	26 (63.4)	
Kaplan-Meier estimates of event in months											
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1643)	NC (NC to NC)	NC (0.0329 to NC)	NC (NC to NC)	0.0986 (0.0986 to NC)	NC (NC to NC)	0.1314 (0.0657 to 0.1643)	NC (NC to NC)	0.1314 (0.0657 to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Median (95% CI)	NC (NC to NC)	NC (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.0986 to NC)	NC (NC to NC)	0.1643 (0.1314 to NC)	NC (NC to NC)	NC (0.1971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.1971 to NC)	NC (NC to NC)	NC (0.2300 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	<.0001		0.0504		0.1202		0.0008		0.0001	
Hazard ratio (95% CI) vs Pd	-	17.27 (4.04 to 73.76)		NC		NC		NC		NC	
P-value	-	0.0001		0.9965		0.9973		0.9944		0.9902	
Hazard ratio inverted (95% CI) vs IPd	0.06 (0.01 to 0.25)										

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Events probability (95% CI)[b]											
2 Months	0.9857 (0.9029 to 0.9980)	0.6182 (0.4768 to 0.7318)	1.0000 (1.0000 to 1.0000)	0.8214 (0.6230 to 0.9215)	1.0000 (1.0000 to 1.0000)	0.5714 (0.1719 to 0.8371)	1.0000 (1.0000 to 1.0000)	0.4286 (0.2192 to 0.6231)	1.0000 (1.0000 to 1.0000)	0.6341 (0.4682 to 0.7608)	
4 Months	0.9857 (0.9029 to 0.9980)	0.6182 (0.4768 to 0.7318)	1.0000 (1.0000 to 1.0000)	0.8214 (0.6230 to 0.9215)	1.0000 (1.0000 to 1.0000)	0.5714 (0.1719 to 0.8371)	1.0000 (1.0000 to 1.0000)	0.4286 (0.2192 to 0.6231)	1.0000 (1.0000 to 1.0000)	0.6341 (0.4682 to 0.7608)	
6 Months	0.9857 (0.9029 to 0.9980)	0.6182 (0.4768 to 0.7318)	1.0000 (1.0000 to 1.0000)	0.8214 (0.6230 to 0.9215)	1.0000 (1.0000 to 1.0000)	0.5714 (0.1719 to 0.8371)	1.0000 (1.0000 to 1.0000)	0.4286 (0.2192 to 0.6231)	1.0000 (1.0000 to 1.0000)	0.6341 (0.4682 to 0.7608)	
8 Months	0.9687 (0.8800 to 0.9921)	0.6182 (0.4768 to 0.7318)	1.0000 (1.0000 to 1.0000)	0.8214 (0.6230 to 0.9215)	1.0000 (1.0000 to 1.0000)	0.5714 (0.1719 to 0.8371)	1.0000 (1.0000 to 1.0000)	0.4286 (0.2192 to 0.6231)	1.0000 (1.0000 to 1.0000)	0.6341 (0.4682 to 0.7608)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
10 Months	0.9687 (0.8800 to 0.9921)	0.6182 (0.4768 to 0.7318)	1.0000 (1.0000 to 1.0000)	0.8214 (0.6230 to 0.9215)	1.0000 (1.0000 to 1.0000)	0.5714 (0.1719 to 0.8371)	1.0000 (1.0000 to 1.0000)	0.4286 (0.2192 to 0.6231)	1.0000 (1.0000 to 1.0000)	0.6341 (0.4682 to 0.7608)	
12 Months	0.9687 (0.8800 to 0.9921)	0.6182 (0.4768 to 0.7318)	1.0000 (1.0000 to 1.0000)	0.8214 (0.6230 to 0.9215)	1.0000 (1.0000 to 1.0000)	0.5714 (0.1719 to 0.8371)	1.0000 (1.0000 to 1.0000)	0.4286 (0.2192 to 0.6231)	1.0000 (1.0000 to 1.0000)	0.6341 (0.4682 to 0.7608)	
14 Months	0.9687 (0.8800 to 0.9921)	0.6182 (0.4768 to 0.7318)	1.0000 (1.0000 to 1.0000)	0.8214 (0.6230 to 0.9215)	1.0000 (1.0000 to 1.0000)	0.5714 (0.1719 to 0.8371)	1.0000 (1.0000 to 1.0000)	0.4286 (0.2192 to 0.6231)	1.0000 (1.0000 to 1.0000)	0.6341 (0.4682 to 0.7608)	
16 Months	0.9687 (0.8800 to 0.9921)	0.6182 (0.4768 to 0.7318)	1.0000 (1.0000 to 1.0000)	0.8214 (0.6230 to 0.9215)	1.0000 (1.0000 to 1.0000)	0.5714 (0.1719 to 0.8371)	1.0000 (1.0000 to 1.0000)	0.4286 (0.2192 to 0.6231)	1.0000 (1.0000 to 1.0000)	0.6341 (0.4682 to 0.7608)	
Number of patients at risk[b]											
2 Months	68	33	19	23	5	4	15	9	34	26	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
4 Months	63	31	19	22	5	4	15	8	32	25	
6 Months	59	27	15	19	5	3	15	8	23	24	
8 Months	49	26	15	17	5	3	15	8	21	23	
10 Months	49	25	14	16	5	2	14	8	19	20	
12 Months	43	23	13	14	3	2	11	7	16	17	
14 Months	30	14	9	8	1	0	2	4	11	14	
16 Months	14	4	3	4	0	0	1	2	8	5	
Insomnia (days)											
Number (%) of events	7 (9.5)	3 (5.5)	0 (0.0)	2 (7.1)	1 (20.0)	3 (42.9)	1 (6.7)	1 (4.8)	3 (8.6)	4 (9.8)	0.8645
Number (%) of patients censored	67 (90.5)	52 (94.5)	20 (100.0)	26 (92.9)	4 (80.0)	4 (57.1)	14 (93.3)	20 (95.2)	32 (91.4)	37 (90.2)	
Kaplan-Meier estimates of event in months											

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.3 Treatment emergent adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	85	74	52	71	
4 Months	78	69	51	69	
6 Months	72	59	39	62	
8 Months	62	56	39	59	
10 Months	60	51	37	56	
12 Months	53	44	30	50	
14 Months	35	28	17	37	
16 Months	15	11	9	17	
Infusion related reaction (days)					
Number (%) of events	2 (2.1)	28 (36.4)	0 (0.0)	28 (37.3)	0.9900
Number (%) of patients censored	92 (97.9)	49 (63.6)	55 (100.0)	47 (62.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1971)	NC (NC to NC)	0.1314 (0.0657 to 0.1971)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.3 Treatment emergent adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Pd	-	20.72 (4.93 to 87.05)		NC	
P-value	-	<.0001		0.9868	
Hazard ratio inverted (95% CI) vs IPd	0.05 (0.01 to 0.20)				
Events probability (95% CI)[b]					
2 Months	0.9889 (0.9237 to 0.9984)	0.6364 (0.5186 to 0.7326)	1.0000 (1.0000 to 1.0000)	0.6267 (0.5070 to 0.7250)	
4 Months	0.9889 (0.9237 to 0.9984)	0.6364 (0.5186 to 0.7326)	1.0000 (1.0000 to 1.0000)	0.6267 (0.5070 to 0.7250)	
6 Months	0.9889 (0.9237 to 0.9984)	0.6364 (0.5186 to 0.7326)	1.0000 (1.0000 to 1.0000)	0.6267 (0.5070 to 0.7250)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.3 Treatment emergent adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.9755 (0.9051 to 0.9939)	0.6364 (0.5186 to 0.7326)	1.0000 (1.0000 to 1.0000)	0.6267 (0.5070 to 0.7250)	
10 Months	0.9755 (0.9051 to 0.9939)	0.6364 (0.5186 to 0.7326)	1.0000 (1.0000 to 1.0000)	0.6267 (0.5070 to 0.7250)	
12 Months	0.9755 (0.9051 to 0.9939)	0.6364 (0.5186 to 0.7326)	1.0000 (1.0000 to 1.0000)	0.6267 (0.5070 to 0.7250)	
14 Months	0.9755 (0.9051 to 0.9939)	0.6364 (0.5186 to 0.7326)	1.0000 (1.0000 to 1.0000)	0.6267 (0.5070 to 0.7250)	
16 Months	0.9755 (0.9051 to 0.9939)	0.6364 (0.5186 to 0.7326)	1.0000 (1.0000 to 1.0000)	0.6267 (0.5070 to 0.7250)	
Number of patients at risk[b]					
2 Months	88	48	53	47	
4 Months	82	46	52	44	
6 Months	75	41	42	40	
8 Months	63	39	42	38	
10 Months	61	37	40	34	
12 Months	53	33	33	30	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.3 Treatment emergent adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	35	21	18	19	
16 Months	16	7	10	8	
Insomnia (days)					
Number (%) of events	11 (11.7)	9 (11.7)	1 (1.8)	4 (5.3)	0.3588
Number (%) of patients censored	83 (88.3)	68 (88.3)	54 (98.2)	71 (94.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8739		0.3364	
Hazard ratio (95% CI) vs Pd	-	0.93 (0.39 to 2.25)		2.80 (0.31 to 25.04)	
P-value	-	0.8743		0.3575	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.2 Treatment emergent adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	124	132	13	13	
4 Months	117	128	12	10	
6 Months	101	114	10	7	
8 Months	92	108	9	7	
10 Months	89	100	8	7	
12 Months	77	87	6	7	
14 Months	48	61	4	4	
16 Months	21	25	3	3	
Infusion related reaction (days)					
Number (%) of events	2 (1.5)	48 (35.3)	0 (0.0)	8 (50.0)	0.9887
Number (%) of patients censored	133 (98.5)	88 (64.7)	14 (100.0)	8 (50.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0986 to 0.1971)	NC (NC to NC)	0.0657 (0.0329 to 0.1643)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_ecog_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.2 Treatment emergent adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.0657 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.1643 to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		0.0034	
Hazard ratio (95% CI) vs Pd	-	28.54 (6.93 to 117.49)		NC	
P-value	-	<.0001		0.9954	
Hazard ratio inverted (95% CI) vs IPd	0.04 (0.01 to 0.14)				
Events probability (95% CI)[b]					
2 Months	0.9923 (0.9467 to 0.9989)	0.6471 (0.5605 to 0.7209)	1.0000 (1.0000 to 1.0000)	0.5000 (0.2452 to 0.7105)	
4 Months	0.9923 (0.9467 to 0.9989)	0.6471 (0.5605 to 0.7209)	1.0000 (1.0000 to 1.0000)	0.5000 (0.2452 to 0.7105)	
6 Months	0.9923 (0.9467 to 0.9989)	0.6471 (0.5605 to 0.7209)	1.0000 (1.0000 to 1.0000)	0.5000 (0.2452 to 0.7105)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_ecog_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.2 Treatment emergent adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.9829 (0.9331 to 0.9957)	0.6471 (0.5605 to 0.7209)	1.0000 (1.0000 to 1.0000)	0.5000 (0.2452 to 0.7105)	
10 Months	0.9829 (0.9331 to 0.9957)	0.6471 (0.5605 to 0.7209)	1.0000 (1.0000 to 1.0000)	0.5000 (0.2452 to 0.7105)	
12 Months	0.9829 (0.9331 to 0.9957)	0.6471 (0.5605 to 0.7209)	1.0000 (1.0000 to 1.0000)	0.5000 (0.2452 to 0.7105)	
14 Months	0.9829 (0.9331 to 0.9957)	0.6471 (0.5605 to 0.7209)	1.0000 (1.0000 to 1.0000)	0.5000 (0.2452 to 0.7105)	
16 Months	0.9829 (0.9331 to 0.9957)	0.6471 (0.5605 to 0.7209)	1.0000 (1.0000 to 1.0000)	0.5000 (0.2452 to 0.7105)	
Number of patients at risk[b]					
2 Months	127	88	14	7	
4 Months	121	85	13	5	
6 Months	107	78	10	3	
8 Months	96	74	9	3	
10 Months	93	68	8	3	
12 Months	80	60	6	3	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_ecog_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.2 Treatment emergent adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	49	39	4	1	
16 Months	23	14	3	1	
Insomnia (days)					
Number (%) of events	12 (8.9)	13 (9.6)	0 (0.0)	0 (0.0)	1.0000
Number (%) of patients censored	123 (91.1)	123 (90.4)	14 (100.0)	16 (100.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9903			
Hazard ratio (95% CI) vs Pd	-	1.00 (0.45 to 2.18)		NC	
P-value	-	0.9903			

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_ecog_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	0.9408 (0.8275 to 0.9805)	0.8425 (0.7175 to 0.9153)	0.9577 (0.8410 to 0.9893)	0.9378 (0.8191 to 0.9795)	0.9452 (0.7980 to 0.9860)	0.9226 (0.7174 to 0.9807)	
Number of patients at risk[b]							
2 Months	49	60	52	50	33	32	
4 Months	48	60	52	47	27	28	
6 Months	47	53	42	42	20	24	
8 Months	44	51	38	41	17	21	
10 Months	43	48	36	38	16	19	
12 Months	39	42	28	33	14	17	
14 Months	24	28	18	23	10	12	
16 Months	13	14	7	8	4	6	
Infusion related reaction (days)							
Number (%) of events	1 (2.0)	27 (42.9)	0 (0.0)	21 (39.6)	1 (2.5)	8 (24.2)	0.8347
Number (%) of patients censored	50 (98.0)	36 (57.1)	55 (100.0)	32 (60.4)	39 (97.5)	25 (75.8)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_seiss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1643)	NC (NC to NC)	0.0986 (0.0657 to 0.1971)	NC (6.0780 to NC)	NC (0.0657 to NC)	
Median (95% CI)	NC (NC to NC)	NC (0.1971 to NC)	NC (NC to NC)	NC (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001		0.0067	
Hazard ratio (95% CI) vs Pd	-	27.60 (3.75 to 203.30)		NC		10.19 (1.27 to 81.56)	
P-value	-	0.0011		0.9884		0.0287	
Hazard ratio inverted (95% CI) vs IPd	0.04 (0.00 to 0.27)				0.10 (0.01 to 0.79)		
Events probability (95% CI)[b]							

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_seiss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9804 (0.8689 to 0.9972)	0.5714 (0.4404 to 0.6826)	1.0000 (1.0000 to 1.0000)	0.6038 (0.4596 to 0.7207)	1.0000 (1.0000 to 1.0000)	0.7576 (0.5733 to 0.8706)	
4 Months	0.9804 (0.8689 to 0.9972)	0.5714 (0.4404 to 0.6826)	1.0000 (1.0000 to 1.0000)	0.6038 (0.4596 to 0.7207)	1.0000 (1.0000 to 1.0000)	0.7576 (0.5733 to 0.8706)	
6 Months	0.9804 (0.8689 to 0.9972)	0.5714 (0.4404 to 0.6826)	1.0000 (1.0000 to 1.0000)	0.6038 (0.4596 to 0.7207)	1.0000 (1.0000 to 1.0000)	0.7576 (0.5733 to 0.8706)	
8 Months	0.9804 (0.8689 to 0.9972)	0.5714 (0.4404 to 0.6826)	1.0000 (1.0000 to 1.0000)	0.6038 (0.4596 to 0.7207)	0.9500 (0.6947 to 0.9928)	0.7576 (0.5733 to 0.8706)	
10 Months	0.9804 (0.8689 to 0.9972)	0.5714 (0.4404 to 0.6826)	1.0000 (1.0000 to 1.0000)	0.6038 (0.4596 to 0.7207)	0.9500 (0.6947 to 0.9928)	0.7576 (0.5733 to 0.8706)	
12 Months	0.9804 (0.8689 to 0.9972)	0.5714 (0.4404 to 0.6826)	1.0000 (1.0000 to 1.0000)	0.6038 (0.4596 to 0.7207)	0.9500 (0.6947 to 0.9928)	0.7576 (0.5733 to 0.8706)	
14 Months	0.9804 (0.8689 to 0.9972)	0.5714 (0.4404 to 0.6826)	1.0000 (1.0000 to 1.0000)	0.6038 (0.4596 to 0.7207)	0.9500 (0.6947 to 0.9928)	0.7576 (0.5733 to 0.8706)	
16 Months	0.9804 (0.8689 to 0.9972)	0.5714 (0.4404 to 0.6826)	1.0000 (1.0000 to 1.0000)	0.6038 (0.4596 to 0.7207)	0.9500 (0.6947 to 0.9928)	0.7576 (0.5733 to 0.8706)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_seiss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	50	36	53	32	35	24	
4 Months	50	35	53	30	29	22	
6 Months	50	31	45	28	20	19	
8 Months	47	31	40	27	16	16	
10 Months	46	29	38	24	15	15	
12 Months	42	26	29	21	13	13	
14 Months	26	15	18	14	9	8	
16 Months	15	8	7	4	4	3	
Insomnia (days)							
Number (%) of events	5 (9.8)	4 (6.3)	4 (7.3)	6 (11.3)	3 (7.5)	3 (9.1)	0.6253
Number (%) of patients censored	46 (90.2)	59 (93.7)	51 (92.7)	47 (88.7)	37 (92.5)	30 (90.9)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.8008 to NC)	NC (10.7433 to NC)	NC (4.5996 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.2 Treatment emergent adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Infusion related reaction (days)							
Number (%) of events	0 (0.0)	17 (43.6)	1 (1.0)	33 (33.7)	1 (4.8)	6 (40.0)	0.7065
Number (%) of patients censored	31 (100.0)	22 (56.4)	96 (99.0)	65 (66.3)	20 (95.2)	9 (60.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1643)	NC (NC to NC)	0.1643 (0.0657 to 0.2300)	NC (6.0780 to NC)	0.0657 (0.0329 to NC)	
Median (95% CI)	NC (NC to NC)	NC (0.1314 to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.0780 to NC)	NC (0.0657 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001		0.0133	
Hazard ratio (95% CI) vs Pd	-	NC		38.68 (5.29 to 282.92)		9.10 (1.09 to 75.87)	
P-value	-	0.9896		0.0003		0.0412	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_seriss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.2 Treatment emergent adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.03 (0.00 to 0.19)		0.11 (0.01 to 0.92)		
Events probability (95% CI)[b]							
2 Months	1.0000 (1.0000 to 1.0000)	0.5641 (0.3957 to 0.7022)	0.9894 (0.9269 to 0.9985)	0.6633 (0.5605 to 0.7474)	1.0000 (1.0000 to 1.0000)	0.6000 (0.3176 to 0.7965)	
4 Months	1.0000 (1.0000 to 1.0000)	0.5641 (0.3957 to 0.7022)	0.9894 (0.9269 to 0.9985)	0.6633 (0.5605 to 0.7474)	1.0000 (1.0000 to 1.0000)	0.6000 (0.3176 to 0.7965)	
6 Months	1.0000 (1.0000 to 1.0000)	0.5641 (0.3957 to 0.7022)	0.9894 (0.9269 to 0.9985)	0.6633 (0.5605 to 0.7474)	1.0000 (1.0000 to 1.0000)	0.6000 (0.3176 to 0.7965)	
8 Months	1.0000 (1.0000 to 1.0000)	0.5641 (0.3957 to 0.7022)	0.9894 (0.9269 to 0.9985)	0.6633 (0.5605 to 0.7474)	0.8571 (0.3341 to 0.9786)	0.6000 (0.3176 to 0.7965)	
10 Months	1.0000 (1.0000 to 1.0000)	0.5641 (0.3957 to 0.7022)	0.9894 (0.9269 to 0.9985)	0.6633 (0.5605 to 0.7474)	0.8571 (0.3341 to 0.9786)	0.6000 (0.3176 to 0.7965)	
12 Months	1.0000 (1.0000 to 1.0000)	0.5641 (0.3957 to 0.7022)	0.9894 (0.9269 to 0.9985)	0.6633 (0.5605 to 0.7474)	0.8571 (0.3341 to 0.9786)	0.6000 (0.3176 to 0.7965)	
14 Months	1.0000 (1.0000 to 1.0000)	0.5641 (0.3957 to 0.7022)	0.9894 (0.9269 to 0.9985)	0.6633 (0.5605 to 0.7474)	0.8571 (0.3341 to 0.9786)	0.6000 (0.3176 to 0.7965)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_seriss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.2 Treatment emergent adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.5641 (0.3957 to 0.7022)	0.9894 (0.9269 to 0.9985)	0.6633 (0.5605 to 0.7474)	0.8571 (0.3341 to 0.9786)	0.6000 (0.3176 to 0.7965)	
Number of patients at risk[b]							
2 Months	31	22	93	65	17	8	
4 Months	31	21	91	62	12	7	
6 Months	31	20	79	55	7	6	
8 Months	30	20	70	53	5	4	
10 Months	30	20	66	48	5	3	
12 Months	28	18	54	42	4	3	
14 Months	16	9	34	28	3	3	
16 Months	10	6	15	9	1	0	
Insomnia (days)							
Number (%) of events	3 (9.7)	1 (2.6)	7 (7.2)	10 (10.2)	2 (9.5)	2 (13.3)	0.4100
Number (%) of patients censored	28 (90.3)	38 (97.4)	90 (92.8)	88 (89.8)	19 (90.5)	13 (86.7)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_seriss_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.2 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	17	12	87	112	
4 Months	14	9	83	108	
6 Months	10	6	71	97	
8 Months	10	5	65	94	
10 Months	10	4	62	87	
12 Months	10	3	52	76	
14 Months	9	2	35	55	
16 Months	4	0	16	24	
Infusion related reaction (days)					
Number (%) of events	0 (0.0)	6 (42.9)	2 (2.2)	39 (33.6)	0.9901
Number (%) of patients censored	21 (100.0)	8 (57.1)	91 (97.8)	77 (66.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0657 to NC)	NC (NC to NC)	0.1314 (0.0657 to 0.1971)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.2 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (0.0986 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0010		<.0001	
Hazard ratio (95% CI) vs Pd	-	NC		18.48 (4.46 to 76.58)	
P-value	-	0.9962		<.0001	
Hazard ratio inverted (95% CI) vs IPd			0.05 (0.01 to 0.22)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.5714 (0.2840 to 0.7797)	0.9890 (0.9246 to 0.9984)	0.6638 (0.5700 to 0.7417)	
4 Months	1.0000 (1.0000 to 1.0000)	0.5714 (0.2840 to 0.7797)	0.9890 (0.9246 to 0.9984)	0.6638 (0.5700 to 0.7417)	
6 Months	1.0000 (1.0000 to 1.0000)	0.5714 (0.2840 to 0.7797)	0.9890 (0.9246 to 0.9984)	0.6638 (0.5700 to 0.7417)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.2 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	1.0000 (1.0000 to 1.0000)	0.5714 (0.2840 to 0.7797)	0.9758 (0.9062 to 0.9939)	0.6638 (0.5700 to 0.7417)	
10 Months	1.0000 (1.0000 to 1.0000)	0.5714 (0.2840 to 0.7797)	0.9758 (0.9062 to 0.9939)	0.6638 (0.5700 to 0.7417)	
12 Months	1.0000 (1.0000 to 1.0000)	0.5714 (0.2840 to 0.7797)	0.9758 (0.9062 to 0.9939)	0.6638 (0.5700 to 0.7417)	
14 Months	1.0000 (1.0000 to 1.0000)	0.5714 (0.2840 to 0.7797)	0.9758 (0.9062 to 0.9939)	0.6638 (0.5700 to 0.7417)	
16 Months	1.0000 (1.0000 to 1.0000)	0.5714 (0.2840 to 0.7797)	0.9758 (0.9062 to 0.9939)	0.6638 (0.5700 to 0.7417)	
Number of patients at risk[b]					
2 Months	18	7	90	77	
4 Months	15	6	87	73	
6 Months	10	5	76	67	
8 Months	10	4	68	65	
10 Months	10	3	65	60	
12 Months	10	3	54	52	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.2 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	9	2	36	33	
16 Months	4	0	18	13	
Insomnia (days)					
Number (%) of events	1 (4.8)	1 (7.1)	7 (7.5)	11 (9.5)	0.8450
Number (%) of patients censored	20 (95.2)	13 (92.9)	86 (92.5)	105 (90.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (10.7433 to NC)	NC (4.6653 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (10.7433 to NC)	NC (4.6653 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.6613		0.7192	
Hazard ratio (95% CI) vs Pd	-	1.85 (0.11 to 30.58)		1.19 (0.46 to 3.07)	
P-value	-	0.6660		0.7195	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.3 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	29	21	71	99	
4 Months	25	18	70	95	
6 Months	19	15	60	84	
8 Months	19	13	54	82	
10 Months	19	12	51	75	
12 Months	16	9	44	66	
14 Months	12	6	31	48	
16 Months	6	1	14	22	
Infusion related reaction (days)					
Number (%) of events	1 (2.9)	8 (34.8)	1 (1.3)	36 (35.0)	0.5504
Number (%) of patients censored	33 (97.1)	15 (65.2)	75 (98.7)	67 (65.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1643 (0.0657 to NC)	NC (NC to NC)	0.0986 (0.0657 to 0.1971)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.3 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0009		<.0001	
Hazard ratio (95% CI) vs Pd	-	14.34 (1.79 to 114.99)		31.56 (4.33 to 230.26)	
P-value	-	0.0121		0.0007	
Hazard ratio inverted (95% CI) vs IPd	0.07 (0.01 to 0.56)		0.03 (0.00 to 0.23)		
Events probability (95% CI)[b]					
2 Months	0.9697 (0.8037 to 0.9957)	0.6522 (0.4235 to 0.8084)	1.0000 (1.0000 to 1.0000)	0.6505 (0.5501 to 0.7339)	
4 Months	0.9697 (0.8037 to 0.9957)	0.6522 (0.4235 to 0.8084)	1.0000 (1.0000 to 1.0000)	0.6505 (0.5501 to 0.7339)	
6 Months	0.9697 (0.8037 to 0.9957)	0.6522 (0.4235 to 0.8084)	1.0000 (1.0000 to 1.0000)	0.6505 (0.5501 to 0.7339)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.3 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.9697 (0.8037 to 0.9957)	0.6522 (0.4235 to 0.8084)	0.9841 (0.8926 to 0.9977)	0.6505 (0.5501 to 0.7339)	
10 Months	0.9697 (0.8037 to 0.9957)	0.6522 (0.4235 to 0.8084)	0.9841 (0.8926 to 0.9977)	0.6505 (0.5501 to 0.7339)	
12 Months	0.9697 (0.8037 to 0.9957)	0.6522 (0.4235 to 0.8084)	0.9841 (0.8926 to 0.9977)	0.6505 (0.5501 to 0.7339)	
14 Months	0.9697 (0.8037 to 0.9957)	0.6522 (0.4235 to 0.8084)	0.9841 (0.8926 to 0.9977)	0.6505 (0.5501 to 0.7339)	
16 Months	0.9697 (0.8037 to 0.9957)	0.6522 (0.4235 to 0.8084)	0.9841 (0.8926 to 0.9977)	0.6505 (0.5501 to 0.7339)	
Number of patients at risk[b]					
2 Months	30	14	74	67	
4 Months	27	13	73	63	
6 Months	20	12	64	57	
8 Months	20	10	56	56	
10 Months	20	9	53	51	
12 Months	17	7	45	45	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.3 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	13	5	31	28	
16 Months	7	1	15	11	
Insomnia (days)					
Number (%) of events	2 (5.9)	2 (8.7)	6 (7.9)	9 (8.7)	0.7822
Number (%) of patients censored	32 (94.1)	21 (91.3)	70 (92.1)	94 (91.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (10.7433 to NC)	NC (4.6653 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7282		0.9194	
Hazard ratio (95% CI) vs Pd	-	1.41 (0.20 to 10.07)		1.05 (0.38 to 2.96)	
P-value	-	0.7295		0.9198	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.3 Treatment emergent adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	83	79	54	66	
4 Months	78	75	51	63	
6 Months	66	66	45	55	
8 Months	61	60	40	55	
10 Months	59	55	38	52	
12 Months	52	47	31	47	
14 Months	33	32	19	33	
16 Months	15	14	9	14	
Infusion related reaction (days)					
Number (%) of events	2 (2.3)	29 (35.8)	0 (0.0)	27 (38.0)	0.9894
Number (%) of patients censored	86 (97.7)	52 (64.2)	61 (100.0)	44 (62.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0657 to 0.2300)	NC (NC to NC)	0.1314 (0.0657 to 0.1971)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.3 Treatment emergent adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.1971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Pd	-	19.05 (4.54 to 79.91)		NC	
P-value	-	<.0001		0.9869	
Hazard ratio inverted (95% CI) vs IPd	0.05 (0.01 to 0.22)				
Events probability (95% CI)[b]					
2 Months	0.9885 (0.9212 to 0.9984)	0.6420 (0.5275 to 0.7356)	1.0000 (1.0000 to 1.0000)	0.6197 (0.4965 to 0.7211)	
4 Months	0.9885 (0.9212 to 0.9984)	0.6420 (0.5275 to 0.7356)	1.0000 (1.0000 to 1.0000)	0.6197 (0.4965 to 0.7211)	
6 Months	0.9885 (0.9212 to 0.9984)	0.6420 (0.5275 to 0.7356)	1.0000 (1.0000 to 1.0000)	0.6197 (0.4965 to 0.7211)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.3 Treatment emergent adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.9746 (0.9015 to 0.9936)	0.6420 (0.5275 to 0.7356)	1.0000 (1.0000 to 1.0000)	0.6197 (0.4965 to 0.7211)	
10 Months	0.9746 (0.9015 to 0.9936)	0.6420 (0.5275 to 0.7356)	1.0000 (1.0000 to 1.0000)	0.6197 (0.4965 to 0.7211)	
12 Months	0.9746 (0.9015 to 0.9936)	0.6420 (0.5275 to 0.7356)	1.0000 (1.0000 to 1.0000)	0.6197 (0.4965 to 0.7211)	
14 Months	0.9746 (0.9015 to 0.9936)	0.6420 (0.5275 to 0.7356)	1.0000 (1.0000 to 1.0000)	0.6197 (0.4965 to 0.7211)	
16 Months	0.9746 (0.9015 to 0.9936)	0.6420 (0.5275 to 0.7356)	1.0000 (1.0000 to 1.0000)	0.6197 (0.4965 to 0.7211)	
Number of patients at risk[b]					
2 Months	85	51	56	44	
4 Months	81	49	53	41	
6 Months	71	44	46	37	
8 Months	65	40	40	37	
10 Months	63	37	38	34	
12 Months	55	31	31	32	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.3 Treatment emergent adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	34	19	19	21	
16 Months	17	7	9	8	
Insomnia (days)					
Number (%) of events	9 (10.2)	6 (7.4)	3 (4.9)	7 (9.9)	0.2470
Number (%) of patients censored	79 (89.8)	75 (92.6)	58 (95.1)	64 (90.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4650		0.3606	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.24 to 1.92)		1.86 (0.48 to 7.20)	
P-value	-	0.4678		0.3684	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.2 Treatment emergent adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	2	2	135	143	
4 Months	2	2	127	136	
6 Months	2	1	109	120	
8 Months	2	1	99	114	
10 Months	1	1	96	106	
12 Months	1	0	82	94	
14 Months	1	0	51	65	
16 Months	0	0	24	28	
Infusion related reaction (days)					
Number (%) of events	0 (0.0)	1 (50.0)	2 (1.4)	55 (36.7)	0.9901
Number (%) of patients censored	2 (100.0)	1 (50.0)	145 (98.6)	95 (63.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1643 (0.1643 to NC)	NC (NC to NC)	0.1314 (0.0657 to 0.1643)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.2 Treatment emergent adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		<.0001	
Hazard ratio (95% CI) vs Pd	-	NC		32.49 (7.92 to 133.27)	
P-value	-	0.9990		<.0001	
Hazard ratio inverted (95% CI) vs IPd			0.03 (0.01 to 0.13)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9930 (0.9511 to 0.9990)	0.6333 (0.5508 to 0.7048)	
4 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9930 (0.9511 to 0.9990)	0.6333 (0.5508 to 0.7048)	
6 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9930 (0.9511 to 0.9990)	0.6333 (0.5508 to 0.7048)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.2 Treatment emergent adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9842 (0.9380 to 0.9961)	0.6333 (0.5508 to 0.7048)	
10 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9842 (0.9380 to 0.9961)	0.6333 (0.5508 to 0.7048)	
12 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9842 (0.9380 to 0.9961)	0.6333 (0.5508 to 0.7048)	
14 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9842 (0.9380 to 0.9961)	0.6333 (0.5508 to 0.7048)	
16 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9842 (0.9380 to 0.9961)	0.6333 (0.5508 to 0.7048)	
Number of patients at risk[b]					
2 Months	2	1	139	94	
4 Months	2	1	132	89	
6 Months	2	1	115	80	
8 Months	2	1	103	76	
10 Months	1	1	100	70	
12 Months	1	0	85	63	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.2 Treatment emergent adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	1	0	52	40	
16 Months	0	0	26	15	
Insomnia (days)					
Number (%) of events	0 (0.0)	1 (50.0)	12 (8.2)	12 (8.0)	0.9908
Number (%) of patients censored	2 (100.0)	1 (50.0)	135 (91.8)	138 (92.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1971 (0.1971 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (0.1971 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.1971 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.8250	
Hazard ratio (95% CI) vs Pd	-	NC		0.91 (0.41 to 2.03)	
P-value	-	0.9990		0.8249	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.3 Treatment emergent adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	90	100	37	30	
4 Months	87	96	33	29	
6 Months	71	84	32	27	
8 Months	65	78	28	27	
10 Months	63	71	27	26	
12 Months	54	61	23	24	
14 Months	34	43	12	15	
16 Months	16	18	6	5	
Infusion related reaction (days)					
Number (%) of events	0 (0.0)	30 (29.1)	1 (2.5)	17 (53.1)	0.7417
Number (%) of patients censored	98 (100.0)	73 (70.9)	39 (97.5)	15 (46.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1643 (0.0986 to NC)	NC (NC to NC)	0.0986 (0.0657 to 0.1643)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.3 Treatment emergent adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	0.1971 (0.1314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Pd	-	NC		28.68 (3.81 to 216.05)	
P-value	-	0.9861		0.0011	
Hazard ratio inverted (95% CI) vs IPd			0.03 (0.00 to 0.26)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.7087 (0.6106 to 0.7864)	0.9744 (0.8316 to 0.9963)	0.4688 (0.2915 to 0.6277)	
4 Months	1.0000 (1.0000 to 1.0000)	0.7087 (0.6106 to 0.7864)	0.9744 (0.8316 to 0.9963)	0.4688 (0.2915 to 0.6277)	
6 Months	1.0000 (1.0000 to 1.0000)	0.7087 (0.6106 to 0.7864)	0.9744 (0.8316 to 0.9963)	0.4688 (0.2915 to 0.6277)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.3 Treatment emergent adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	1.0000 (1.0000 to 1.0000)	0.7087 (0.6106 to 0.7864)	0.9744 (0.8316 to 0.9963)	0.4688 (0.2915 to 0.6277)	
10 Months	1.0000 (1.0000 to 1.0000)	0.7087 (0.6106 to 0.7864)	0.9744 (0.8316 to 0.9963)	0.4688 (0.2915 to 0.6277)	
12 Months	1.0000 (1.0000 to 1.0000)	0.7087 (0.6106 to 0.7864)	0.9744 (0.8316 to 0.9963)	0.4688 (0.2915 to 0.6277)	
14 Months	1.0000 (1.0000 to 1.0000)	0.7087 (0.6106 to 0.7864)	0.9744 (0.8316 to 0.9963)	0.4688 (0.2915 to 0.6277)	
16 Months	1.0000 (1.0000 to 1.0000)	0.7087 (0.6106 to 0.7864)	0.9744 (0.8316 to 0.9963)	0.4688 (0.2915 to 0.6277)	
Number of patients at risk[b]					
2 Months	94	72	37	15	
4 Months	91	69	34	14	
6 Months	76	63	33	14	
8 Months	69	59	29	14	
10 Months	67	53	28	14	
12 Months	57	47	24	13	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.3 Treatment emergent adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	35	33	13	6	
16 Months	17	14	7	0	
Insomnia (days)					
Number (%) of events	12 (12.2)	7 (6.8)	0 (0.0)	3 (9.4)	0.9999
Number (%) of patients censored	86 (87.8)	96 (93.2)	40 (100.0)	29 (90.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.5195 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1470		0.0573	
Hazard ratio (95% CI) vs Pd	-	0.51 (0.20 to 1.29)		NC	
P-value	-	0.1547		0.9956	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.3 Treatment emergent adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	89	98	47	46	
4 Months	86	94	42	43	
6 Months	70	82	40	38	
8 Months	64	76	36	38	
10 Months	62	69	34	37	
12 Months	53	59	29	34	
14 Months	33	42	18	23	
16 Months	15	18	8	10	
Infusion related reaction (days)					
Number (%) of events	0 (0.0)	30 (29.7)	2 (3.9)	26 (52.0)	0.9890
Number (%) of patients censored	97 (100.0)	71 (70.3)	49 (96.1)	24 (48.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1643 (0.0986 to NC)	NC (NC to NC)	0.0657 (0.0657 to 0.1314)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.3 Treatment emergent adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	0.1971 (0.1314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Pd	-	NC		18.02 (4.27 to 76.15)	
P-value	-	0.9861		<.0001	
Hazard ratio inverted (95% CI) vs IPd			0.06 (0.01 to 0.23)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.7030 (0.6035 to 0.7819)	0.9796 (0.8638 to 0.9971)	0.4800 (0.3371 to 0.6093)	
4 Months	1.0000 (1.0000 to 1.0000)	0.7030 (0.6035 to 0.7819)	0.9796 (0.8638 to 0.9971)	0.4800 (0.3371 to 0.6093)	
6 Months	1.0000 (1.0000 to 1.0000)	0.7030 (0.6035 to 0.7819)	0.9796 (0.8638 to 0.9971)	0.4800 (0.3371 to 0.6093)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.3 Treatment emergent adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	1.0000 (1.0000 to 1.0000)	0.7030 (0.6035 to 0.7819)	0.9557 (0.8334 to 0.9888)	0.4800 (0.3371 to 0.6093)	
10 Months	1.0000 (1.0000 to 1.0000)	0.7030 (0.6035 to 0.7819)	0.9557 (0.8334 to 0.9888)	0.4800 (0.3371 to 0.6093)	
12 Months	1.0000 (1.0000 to 1.0000)	0.7030 (0.6035 to 0.7819)	0.9557 (0.8334 to 0.9888)	0.4800 (0.3371 to 0.6093)	
14 Months	1.0000 (1.0000 to 1.0000)	0.7030 (0.6035 to 0.7819)	0.9557 (0.8334 to 0.9888)	0.4800 (0.3371 to 0.6093)	
16 Months	1.0000 (1.0000 to 1.0000)	0.7030 (0.6035 to 0.7819)	0.9557 (0.8334 to 0.9888)	0.4800 (0.3371 to 0.6093)	
Number of patients at risk[b]					
2 Months	93	70	47	24	
4 Months	90	67	43	22	
6 Months	75	61	41	19	
8 Months	68	57	36	19	
10 Months	66	51	34	19	
12 Months	56	45	29	17	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.3 Treatment emergent adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	34	32	18	8	
16 Months	16	14	9	1	
Insomnia (days)					
Number (%) of events	12 (12.4)	6 (5.9)	0 (0.0)	7 (14.0)	0.9862
Number (%) of patients censored	85 (87.6)	95 (94.1)	51 (100.0)	43 (86.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.8337 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0924		0.0067	
Hazard ratio (95% CI) vs Pd	-	0.44 (0.17 to 1.18)		NC	
P-value	-	0.1017		0.9933	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.2 Treatment emergent adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	9	13	128	132	
4 Months	7	12	122	126	
6 Months	5	10	106	111	
8 Months	2	9	99	106	
10 Months	2	9	95	98	
12 Months	2	7	81	87	
14 Months	2	6	50	59	
16 Months	0	4	24	24	
Infusion related reaction (days)					
Number (%) of events	0 (0.0)	6 (42.9)	2 (1.4)	50 (36.2)	0.9903
Number (%) of patients censored	10 (100.0)	8 (57.1)	137 (98.6)	88 (63.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0657 to NC)	NC (NC to NC)	0.1314 (0.0986 to 0.1971)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.2 Treatment emergent adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (0.0657 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0250		<.0001	
Hazard ratio (95% CI) vs Pd	-	NC		30.36 (7.38 to 124.84)	
P-value	-	0.9961		<.0001	
Hazard ratio inverted (95% CI) vs IPd			0.03 (0.01 to 0.14)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.5714 (0.2840 to 0.7797)	0.9926 (0.9486 to 0.9990)	0.6377 (0.5516 to 0.7116)	
4 Months	1.0000 (1.0000 to 1.0000)	0.5714 (0.2840 to 0.7797)	0.9926 (0.9486 to 0.9990)	0.6377 (0.5516 to 0.7116)	
6 Months	1.0000 (1.0000 to 1.0000)	0.5714 (0.2840 to 0.7797)	0.9926 (0.9486 to 0.9990)	0.6377 (0.5516 to 0.7116)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.2 Treatment emergent adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	1.0000 (1.0000 to 1.0000)	0.5714 (0.2840 to 0.7797)	0.9837 (0.9358 to 0.9959)	0.6377 (0.5516 to 0.7116)	
10 Months	1.0000 (1.0000 to 1.0000)	0.5714 (0.2840 to 0.7797)	0.9837 (0.9358 to 0.9959)	0.6377 (0.5516 to 0.7116)	
12 Months	1.0000 (1.0000 to 1.0000)	0.5714 (0.2840 to 0.7797)	0.9837 (0.9358 to 0.9959)	0.6377 (0.5516 to 0.7116)	
14 Months	1.0000 (1.0000 to 1.0000)	0.5714 (0.2840 to 0.7797)	0.9837 (0.9358 to 0.9959)	0.6377 (0.5516 to 0.7116)	
16 Months	1.0000 (1.0000 to 1.0000)	0.5714 (0.2840 to 0.7797)	0.9837 (0.9358 to 0.9959)	0.6377 (0.5516 to 0.7116)	
Number of patients at risk[b]					
2 Months	9	8	132	87	
4 Months	7	7	127	83	
6 Months	5	6	112	75	
8 Months	2	5	103	72	
10 Months	2	5	99	66	
12 Months	2	4	84	59	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.2 Treatment emergent adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	2	3	51	37	
16 Months	0	2	26	13	
Insomnia (days)					
Number (%) of events	1 (10.0)	2 (14.3)	11 (7.9)	11 (8.0)	0.8564
Number (%) of patients censored	9 (90.0)	12 (85.7)	128 (92.1)	127 (92.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (1.2156 to NC)	NC (0.1971 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (1.2156 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.7437		0.9011	
Hazard ratio (95% CI) vs Pd	-	1.49 (0.13 to 16.42)		0.95 (0.41 to 2.19)	
P-value	-	0.7454		0.9010	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.2 Treatment emergent adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	86	82	44	53	
4 Months	82	80	41	50	
6 Months	74	71	33	45	
8 Months	69	68	28	42	
10 Months	66	65	27	37	
12 Months	58	55	23	34	
14 Months	35	39	15	22	
16 Months	15	18	7	9	
Infusion related reaction (days)					
Number (%) of events	1 (1.1)	34 (39.5)	1 (2.1)	18 (33.3)	0.5247
Number (%) of patients censored	93 (98.9)	52 (60.5)	46 (97.9)	36 (66.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0657 to 0.1643)	NC (NC to NC)	0.1314 (0.0657 to NC)	
Median (95% CI)	NC (NC to NC)	NC (0.2300 to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.2 Treatment emergent adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Pd	-	45.63 (6.24 to 333.55)		18.07 (2.41 to 135.48)	
P-value	-	0.0002		0.0049	
Hazard ratio inverted (95% CI) vs IPd	0.02 (0.00 to 0.16)		0.06 (0.01 to 0.41)		
Events probability (95% CI)[b]					
2 Months	0.9891 (0.9253 to 0.9985)	0.6047 (0.4933 to 0.6989)	1.0000 (1.0000 to 1.0000)	0.6667 (0.5243 to 0.7752)	
4 Months	0.9891 (0.9253 to 0.9985)	0.6047 (0.4933 to 0.6989)	1.0000 (1.0000 to 1.0000)	0.6667 (0.5243 to 0.7752)	
6 Months	0.9891 (0.9253 to 0.9985)	0.6047 (0.4933 to 0.6989)	1.0000 (1.0000 to 1.0000)	0.6667 (0.5243 to 0.7752)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.2 Treatment emergent adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.9891 (0.9253 to 0.9985)	0.6047 (0.4933 to 0.6989)	0.9706 (0.8090 to 0.9958)	0.6667 (0.5243 to 0.7752)	
10 Months	0.9891 (0.9253 to 0.9985)	0.6047 (0.4933 to 0.6989)	0.9706 (0.8090 to 0.9958)	0.6667 (0.5243 to 0.7752)	
12 Months	0.9891 (0.9253 to 0.9985)	0.6047 (0.4933 to 0.6989)	0.9706 (0.8090 to 0.9958)	0.6667 (0.5243 to 0.7752)	
14 Months	0.9891 (0.9253 to 0.9985)	0.6047 (0.4933 to 0.6989)	0.9706 (0.8090 to 0.9958)	0.6667 (0.5243 to 0.7752)	
16 Months	0.9891 (0.9253 to 0.9985)	0.6047 (0.4933 to 0.6989)	0.9706 (0.8090 to 0.9958)	0.6667 (0.5243 to 0.7752)	
Number of patients at risk[b]					
2 Months	90	52	44	36	
4 Months	87	52	41	33	
6 Months	79	48	34	29	
8 Months	73	47	28	26	
10 Months	70	44	27	23	
12 Months	62	39	22	20	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.2 Treatment emergent adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	37	24	14	13	
16 Months	17	10	7	4	
Insomnia (days)					
Number (%) of events	6 (6.4)	5 (5.8)	6 (12.8)	8 (14.8)	0.7963
Number (%) of patients censored	88 (93.6)	81 (94.2)	41 (87.2)	46 (85.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.6653 to NC)	NC (6.8337 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8065		0.9373	
Hazard ratio (95% CI) vs Pd	-	0.86 (0.26 to 2.83)		1.04 (0.36 to 3.01)	
P-value	-	0.8067		0.9375	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.2 Treatment emergent adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Infusion related reaction (days)					
Number (%) of events	0 (0.0)	0 (0.0)	2 (1.4)	56 (37.3)	0.9985
Number (%) of patients censored	2 (100.0)	2 (100.0)	145 (98.6)	94 (62.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	0.1314 (0.0657 to 0.1643)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-			<.0001	
Hazard ratio (95% CI) vs Pd	-	NC		33.24 (8.11 to 136.28)	
P-value	-			<.0001	
Hazard ratio inverted (95% CI) vs IPd			0.03 (0.01 to 0.12)		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.2 Treatment emergent adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9930 (0.9511 to 0.9990)	0.6267 (0.5440 to 0.6985)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9930 (0.9511 to 0.9990)	0.6267 (0.5440 to 0.6985)	
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9930 (0.9511 to 0.9990)	0.6267 (0.5440 to 0.6985)	
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9843 (0.9383 to 0.9961)	0.6267 (0.5440 to 0.6985)	
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9843 (0.9383 to 0.9961)	0.6267 (0.5440 to 0.6985)	
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9843 (0.9383 to 0.9961)	0.6267 (0.5440 to 0.6985)	
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9843 (0.9383 to 0.9961)	0.6267 (0.5440 to 0.6985)	
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9843 (0.9383 to 0.9961)	0.6267 (0.5440 to 0.6985)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.2 Treatment emergent adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	2	2	139	93	
4 Months	2	2	132	88	
6 Months	1	2	116	79	
8 Months	0	2	105	75	
10 Months	0	2	101	69	
12 Months	0	2	86	61	
14 Months	0	2	53	38	
16 Months	0	0	26	15	
Insomnia (days)					
Number (%) of events	0 (0.0)	0 (0.0)	12 (8.2)	13 (8.7)	1.0000
Number (%) of patients censored	2 (100.0)	2 (100.0)	135 (91.8)	137 (91.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.3 Treatment emergent adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	102	112	35	33	
4 Months	96	107	33	31	
6 Months	82	96	29	25	
8 Months	75	91	26	24	
10 Months	71	84	26	23	
12 Months	60	76	23	18	
14 Months	38	54	14	11	
16 Months	16	25	8	3	
Infusion related reaction (days)					
Number (%) of events	2 (1.8)	40 (34.2)	0 (0.0)	16 (45.7)	0.9875
Number (%) of patients censored	109 (98.2)	77 (65.8)	38 (100.0)	19 (54.3)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.3 Treatment emergent adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0657 to 0.1971)	NC (NC to NC)	0.0986 (0.0657 to 0.1643)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.0986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Pd	-	22.52 (5.44 to 93.22)		NC	
P-value	-	<.0001		0.9899	
Hazard ratio inverted (95% CI) vs IPd	0.04 (0.01 to 0.18)				
Events probability (95% CI)[b]					
2 Months	0.9907 (0.9355 to 0.9987)	0.6581 (0.5646 to 0.7362)	1.0000 (1.0000 to 1.0000)	0.5429 (0.3661 to 0.6898)	
4 Months	0.9907 (0.9355 to 0.9987)	0.6581 (0.5646 to 0.7362)	1.0000 (1.0000 to 1.0000)	0.5429 (0.3661 to 0.6898)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.3 Treatment emergent adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9907 (0.9355 to 0.9987)	0.6581 (0.5646 to 0.7362)	1.0000 (1.0000 to 1.0000)	0.5429 (0.3661 to 0.6898)	
8 Months	0.9791 (0.9185 to 0.9948)	0.6581 (0.5646 to 0.7362)	1.0000 (1.0000 to 1.0000)	0.5429 (0.3661 to 0.6898)	
10 Months	0.9791 (0.9185 to 0.9948)	0.6581 (0.5646 to 0.7362)	1.0000 (1.0000 to 1.0000)	0.5429 (0.3661 to 0.6898)	
12 Months	0.9791 (0.9185 to 0.9948)	0.6581 (0.5646 to 0.7362)	1.0000 (1.0000 to 1.0000)	0.5429 (0.3661 to 0.6898)	
14 Months	0.9791 (0.9185 to 0.9948)	0.6581 (0.5646 to 0.7362)	1.0000 (1.0000 to 1.0000)	0.5429 (0.3661 to 0.6898)	
16 Months	0.9791 (0.9185 to 0.9948)	0.6581 (0.5646 to 0.7362)	1.0000 (1.0000 to 1.0000)	0.5429 (0.3661 to 0.6898)	
Number of patients at risk[b]					
2 Months	104	76	37	19	
4 Months	99	74	35	16	
6 Months	86	66	31	15	
8 Months	77	63	28	14	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.3 Treatment emergent adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	73	57	28	14	
12 Months	61	53	25	10	
14 Months	38	34	15	6	
16 Months	17	15	9	0	
Insomnia (days)					
Number (%) of events	9 (8.1)	10 (8.5)	3 (7.9)	3 (8.6)	0.9377
Number (%) of patients censored	102 (91.9)	107 (91.5)	35 (92.1)	32 (91.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.7433 to NC)	NC (6.8008 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9715		0.9477	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.2 Treatment emergent adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	128	138	9	7	
4 Months	120	131	9	7	
6 Months	103	115	8	6	
8 Months	93	111	8	4	
10 Months	89	104	8	3	
12 Months	75	91	8	3	
14 Months	47	63	5	2	
16 Months	22	28	2	0	
Infusion related reaction (days)					
Number (%) of events	2 (1.4)	55 (37.9)	0 (0.0)	1 (14.3)	0.9917
Number (%) of patients censored	138 (98.6)	90 (62.1)	9 (100.0)	6 (85.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0657 to 0.1643)	NC (NC to NC)	NC (0.0329 to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.2 Treatment emergent adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.0329 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		0.2568	
Hazard ratio (95% CI) vs Pd	-	32.27 (7.87 to 132.38)		NC	
P-value	-	<.0001		0.9984	
Hazard ratio inverted (95% CI) vs IPd	0.03 (0.01 to 0.13)				
Events probability (95% CI)[b]					
2 Months	0.9926 (0.9486 to 0.9990)	0.6207 (0.5365 to 0.6940)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
4 Months	0.9926 (0.9486 to 0.9990)	0.6207 (0.5365 to 0.6940)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
6 Months	0.9926 (0.9486 to 0.9990)	0.6207 (0.5365 to 0.6940)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.2 Treatment emergent adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.9833 (0.9344 to 0.9958)	0.6207 (0.5365 to 0.6940)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
10 Months	0.9833 (0.9344 to 0.9958)	0.6207 (0.5365 to 0.6940)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
12 Months	0.9833 (0.9344 to 0.9958)	0.6207 (0.5365 to 0.6940)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
14 Months	0.9833 (0.9344 to 0.9958)	0.6207 (0.5365 to 0.6940)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
16 Months	0.9833 (0.9344 to 0.9958)	0.6207 (0.5365 to 0.6940)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
Number of patients at risk[b]					
2 Months	132	89	9	6	
4 Months	125	84	9	6	
6 Months	108	75	9	6	
8 Months	96	73	9	4	
10 Months	92	67	9	4	
12 Months	78	59	8	4	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.2 Treatment emergent adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	48	37	5	3	
16 Months	24	15	2	0	
Insomnia (days)					
Number (%) of events	10 (7.1)	12 (8.3)	2 (22.2)	1 (14.3)	0.6686
Number (%) of patients censored	130 (92.9)	133 (91.7)	7 (77.8)	6 (85.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.2628 to NC)	NC (0.9199 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.2628 to NC)	NC (0.9199 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8475		0.6989	
Hazard ratio (95% CI) vs Pd	-	1.09 (0.47 to 2.51)		0.63 (0.06 to 6.90)	
P-value	-	0.8480		0.7015	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.3 Treatment emergent adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
2 Months	79	87	58	58	
4 Months	75	81	54	57	
6 Months	66	69	45	52	
8 Months	59	66	42	49	
10 Months	59	62	38	45	
12 Months	50	56	33	38	
14 Months	31	37	21	28	
16 Months	13	14	11	14	
Infusion related reaction (days)					
Number (%) of events	1 (1.1)	44 (48.4)	1 (1.6)	12 (19.7)	0.3261
Number (%) of patients censored	86 (98.9)	47 (51.6)	61 (98.4)	49 (80.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1314)	NC (NC to NC)	NC (0.1314 to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_llen_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.3 Treatment emergent adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	<.0001		0.0013	
Hazard ratio (95% CI) vs Pd	-	54.63 (7.52 to 396.69)		13.21 (1.72 to 101.62)	
P-value	-	<.0001		0.0132	
Hazard ratio inverted (95% CI) vs IPd	0.02 (0.00 to 0.13)		0.08 (0.01 to 0.58)		
Events probability (95% CI)[b]					
2 Months	0.9882 (0.9194 to 0.9983)	0.5165 (0.4096 to 0.6132)	1.0000 (1.0000 to 1.0000)	0.8033 (0.6797 to 0.8831)	
4 Months	0.9882 (0.9194 to 0.9983)	0.5165 (0.4096 to 0.6132)	1.0000 (1.0000 to 1.0000)	0.8033 (0.6797 to 0.8831)	
6 Months	0.9882 (0.9194 to 0.9983)	0.5165 (0.4096 to 0.6132)	1.0000 (1.0000 to 1.0000)	0.8033 (0.6797 to 0.8831)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.3 Treatment emergent adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
8 Months	0.9882 (0.9194 to 0.9983)	0.5165 (0.4096 to 0.6132)	0.9787 (0.8584 to 0.9970)	0.8033 (0.6797 to 0.8831)	
10 Months	0.9882 (0.9194 to 0.9983)	0.5165 (0.4096 to 0.6132)	0.9787 (0.8584 to 0.9970)	0.8033 (0.6797 to 0.8831)	
12 Months	0.9882 (0.9194 to 0.9983)	0.5165 (0.4096 to 0.6132)	0.9787 (0.8584 to 0.9970)	0.8033 (0.6797 to 0.8831)	
14 Months	0.9882 (0.9194 to 0.9983)	0.5165 (0.4096 to 0.6132)	0.9787 (0.8584 to 0.9970)	0.8033 (0.6797 to 0.8831)	
16 Months	0.9882 (0.9194 to 0.9983)	0.5165 (0.4096 to 0.6132)	0.9787 (0.8584 to 0.9970)	0.8033 (0.6797 to 0.8831)	
Number of patients at risk[b]					
2 Months	82	46	59	49	
4 Months	79	41	55	49	
6 Months	70	37	47	44	
8 Months	62	36	43	41	
10 Months	62	34	39	37	
12 Months	53	30	33	33	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.3 Treatment emergent adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	33	15	20	25	
16 Months	15	3	11	12	
Insomnia (days)					
Number (%) of events	4 (4.6)	5 (5.5)	8 (12.9)	8 (13.1)	0.7589
Number (%) of patients censored	83 (95.4)	86 (94.5)	54 (87.1)	53 (86.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.6653 to NC)	NC (9.7906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.8263		0.8577	
Hazard ratio (95% CI) vs Pd	-	1.16 (0.31 to 4.31)		0.91 (0.34 to 2.44)	
P-value	-	0.8265		0.8576	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	52	43	44	53	17	24	
8 Months	47	39	40	52	15	24	
10 Months	44	39	38	50	14	23	
12 Months	39	34	34	44	10	20	
14 Months	24	22	20	30	7	15	
16 Months	13	10	8	12	3	4	
Bronchitis (days)							
Number (%) of events	7 (10.3)	11 (20.4)	5 (9.4)	17 (25.8)	1 (3.6)	8 (25.0)	0.5291
Number (%) of patients censored	61 (89.7)	43 (79.6)	48 (90.6)	49 (74.2)	27 (96.4)	24 (75.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (12.4517 to NC)	NC (4.5667 to NC)	NC (NC to NC)	6.6694 (3.3183 to NC)	NC (11.4333 to NC)	10.5462 (0.8542 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1226		0.0332		0.0312	
Hazard ratio (95% CI) vs Pd	-	2.08 (0.80 to 5.36)		2.82 (1.04 to 7.64)		7.09 (0.89 to 56.72)	
P-value	-	0.1310		0.0417		0.0649	
Hazard ratio inverted (95% CI) vs IPd			0.35 (0.13 to 0.96)				
Events probability (95% CI)[b]							
2 Months	0.9704 (0.8867 to 0.9925)	0.9441 (0.8365 to 0.9816)	0.9608 (0.8522 to 0.9900)	0.8925 (0.7877 to 0.9473)	1.0000 (1.0000 to 1.0000)	0.8438 (0.6646 to 0.9318)	
4 Months	0.9704 (0.8867 to 0.9925)	0.8862 (0.7639 to 0.9472)	0.9190 (0.7982 to 0.9688)	0.8299 (0.7138 to 0.9020)	1.0000 (1.0000 to 1.0000)	0.7775 (0.5887 to 0.8873)	
6 Months	0.9180 (0.8135 to 0.9652)	0.7990 (0.6573 to 0.8869)	0.9190 (0.7982 to 0.9688)	0.7823 (0.6601 to 0.8649)	1.0000 (1.0000 to 1.0000)	0.7775 (0.5887 to 0.8873)	
8 Months	0.8989 (0.7877 to 0.9535)	0.7740 (0.6271 to 0.8688)	0.8954 (0.7661 to 0.9553)	0.7483 (0.6220 to 0.8377)	1.0000 (1.0000 to 1.0000)	0.7775 (0.5887 to 0.8873)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		**[65-75[**		**>= 75**		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.8989 (0.7877 to 0.9535)	0.7740 (0.6271 to 0.8688)	0.8954 (0.7661 to 0.9553)	0.7483 (0.6220 to 0.8377)	1.0000 (1.0000 to 1.0000)	0.7775 (0.5887 to 0.8873)	
12 Months	0.8989 (0.7877 to 0.9535)	0.7740 (0.6271 to 0.8688)	0.8954 (0.7661 to 0.9553)	0.7483 (0.6220 to 0.8377)	0.9167 (0.5390 to 0.9878)	0.7318 (0.5297 to 0.8577)	
14 Months	0.8725 (0.7466 to 0.9383)	0.7740 (0.6271 to 0.8688)	0.8954 (0.7661 to 0.9553)	0.7269 (0.5965 to 0.8213)	0.9167 (0.5390 to 0.9878)	0.7318 (0.5297 to 0.8577)	
16 Months	0.8725 (0.7466 to 0.9383)	0.7740 (0.6271 to 0.8688)	0.8954 (0.7661 to 0.9553)	0.7269 (0.5965 to 0.8213)	0.9167 (0.5390 to 0.9878)	0.7318 (0.5297 to 0.8577)	
Number of patients at risk[b]							
2 Months	64	50	48	57	26	27	
4 Months	60	44	44	53	24	20	
6 Months	50	35	42	46	18	19	
8 Months	44	30	37	44	16	19	
10 Months	42	28	36	41	15	18	
12 Months	36	25	31	36	10	15	
14 Months	21	16	18	24	7	11	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.2 Subgroup analyses by age (IRT)
16.2.7.1.2.2.3 Treatment emergent adverse event according to PT by treatment group according to age (IRT) - Safety population

	< 65		[65-75[		>= 75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	12	9	6	10	4	3	
Constipation (days)							
Number (%) of events	12 (17.6)	9 (16.7)	7 (13.2)	11 (16.7)	7 (25.0)	4 (12.5)	0.4386
Number (%) of patients censored	56 (82.4)	45 (83.3)	46 (86.8)	55 (83.3)	21 (75.0)	28 (87.5)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (2.0698 to NC)	NC (2.3655 to NC)	NC (7.4579 to NC)	NC (7.1951 to NC)	5.5852 (0.6242 to NC)	NC (1.2485 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.5852 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.8047		0.6675		0.1876	
Hazard ratio (95% CI) vs Pd	-	0.90 (0.38 to 2.13)		1.23 (0.48 to 3.17)		0.45 (0.13 to 1.53)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.2 Treatment emergent adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	IPd (N=101)	Pd (N=49)	IPd (N=51)	p-value of treatment-by-sub group interaction[c]
Bronchitis (days)					
Number (%) of events	9 (9.0)	24 (23.8)	4 (8.2)	12 (23.5)	0.8951
Number (%) of patients censored	91 (91.0)	77 (76.2)	45 (91.8)	39 (76.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	12.4846 (4.3039 to NC)	NC (NC to NC)	NC (2.8583 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0064		0.0449	
Hazard ratio (95% CI) vs Pd	-	2.78 (1.29 to 5.98)		3.01 (0.97 to 9.33)	
P-value	-	0.0090		0.0564	
Hazard ratio inverted (95% CI) vs IPd	0.36 (0.17 to 0.77)				
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.2 Treatment emergent adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9797 (0.9212 to 0.9949)	0.9001 (0.8222 to 0.9449)	0.9583 (0.8435 to 0.9894)	0.9020 (0.7804 to 0.9580)	
4 Months	0.9684 (0.9051 to 0.9897)	0.8473 (0.7593 to 0.9050)	0.9366 (0.8159 to 0.9791)	0.8218 (0.6854 to 0.9030)	
6 Months	0.9321 (0.8546 to 0.9690)	0.8017 (0.7064 to 0.8689)	0.9366 (0.8159 to 0.9791)	0.7596 (0.6153 to 0.8558)	
8 Months	0.9054 (0.8190 to 0.9518)	0.7649 (0.6643 to 0.8390)	0.9366 (0.8159 to 0.9791)	0.7596 (0.6153 to 0.8558)	
10 Months	0.9054 (0.8190 to 0.9518)	0.7649 (0.6643 to 0.8390)	0.9366 (0.8159 to 0.9791)	0.7596 (0.6153 to 0.8558)	
12 Months	0.9054 (0.8190 to 0.9518)	0.7513 (0.6485 to 0.8279)	0.9019 (0.7521 to 0.9632)	0.7596 (0.6153 to 0.8558)	
14 Months	0.8866 (0.7903 to 0.9403)	0.7356 (0.6298 to 0.8155)	0.9019 (0.7521 to 0.9632)	0.7596 (0.6153 to 0.8558)	
16 Months	0.8866 (0.7903 to 0.9403)	0.7356 (0.6298 to 0.8155)	0.9019 (0.7521 to 0.9632)	0.7596 (0.6153 to 0.8558)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.3 Subgroup analyses by prior lines (IRT)
16.2.7.1.2.3.2 Treatment emergent adverse event according to PT by treatment group according to prior lines (IRT) - Safety population

	2 or 3 previous lines of therapy		> 3 previous lines of therapy		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	92	89	46	45	
4 Months	86	76	42	41	
6 Months	73	66	37	34	
8 Months	65	62	32	31	
10 Months	64	57	29	30	
12 Months	52	50	25	26	
14 Months	30	34	16	17	
16 Months	12	15	10	7	
Constipation (days)					
Number (%) of events	17 (17.0)	14 (13.9)	9 (18.4)	10 (19.6)	0.6656
Number (%) of patients censored	83 (83.0)	87 (86.1)	40 (81.6)	41 (80.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (5.5852 to NC)	NC (NC to NC)	NC (0.6242 to NC)	NC (2.3984 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_plne_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.3 Treatment emergent adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
Bronchitis (days)					
Number (%) of events	9 (13.2)	24 (27.3)	4 (4.9)	12 (18.8)	0.4286
Number (%) of patients censored	59 (86.8)	64 (72.7)	77 (95.1)	52 (81.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (7.7207 to NC)	5.0595 (3.6797 to NC)	NC (NC to NC)	NC (3.3183 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0325		0.0122	
Hazard ratio (95% CI) vs Pd	-	2.26 (1.05 to 4.85)		3.83 (1.24 to 11.88)	
P-value	-	0.0375		0.0200	
Hazard ratio inverted (95% CI) vs IPd	0.44 (0.21 to 0.95)		0.26 (0.08 to 0.81)		
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_sex_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.3 Treatment emergent adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9697 (0.8842 to 0.9923)	0.9083 (0.8249 to 0.9530)	0.9748 (0.9030 to 0.9936)	0.8904 (0.7837 to 0.9462)	
4 Months	0.9376 (0.8422 to 0.9761)	0.8235 (0.7242 to 0.8897)	0.9748 (0.9030 to 0.9936)	0.8583 (0.7452 to 0.9236)	
6 Months	0.9038 (0.7980 to 0.9557)	0.7336 (0.6234 to 0.8162)	0.9601 (0.8808 to 0.9870)	0.8583 (0.7452 to 0.9236)	
8 Months	0.8665 (0.7498 to 0.9312)	0.7054 (0.5923 to 0.7924)	0.9601 (0.8808 to 0.9870)	0.8400 (0.7226 to 0.9107)	
10 Months	0.8665 (0.7498 to 0.9312)	0.7054 (0.5923 to 0.7924)	0.9601 (0.8808 to 0.9870)	0.8400 (0.7226 to 0.9107)	
12 Months	0.8665 (0.7498 to 0.9312)	0.7054 (0.5923 to 0.7924)	0.9396 (0.8435 to 0.9775)	0.8190 (0.6956 to 0.8960)	
14 Months	0.8394 (0.7096 to 0.9146)	0.7054 (0.5923 to 0.7924)	0.9396 (0.8435 to 0.9775)	0.7949 (0.6639 to 0.8793)	
16 Months	0.8394 (0.7096 to 0.9146)	0.7054 (0.5923 to 0.7924)	0.9396 (0.8435 to 0.9775)	0.7949 (0.6639 to 0.8793)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_sex_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.4 Subgroup analyses by gender
16.2.7.1.2.4.3 Treatment emergent adverse event according to PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	63	78	75	56	
4 Months	58	66	70	51	
6 Months	50	53	60	47	
8 Months	46	49	51	44	
10 Months	43	45	50	42	
12 Months	34	40	43	36	
14 Months	22	27	24	24	
16 Months	11	12	11	10	
Constipation (days)					
Number (%) of events	16 (23.5)	18 (20.5)	10 (12.3)	6 (9.4)	0.8120
Number (%) of patients censored	52 (76.5)	70 (79.5)	71 (87.7)	58 (90.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (0.7228 to NC)	NC (2.3984 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_sex_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.2 Treatment emergent adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Bronchitis (days)					
Number (%) of events	11 (9.0)	29 (25.0)	0 (0.0)	3 (12.5)	0.9897
Number (%) of patients censored	111 (91.0)	87 (75.0)	19 (100.0)	21 (87.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	10.5462 (4.3696 to NC)	NC (NC to NC)	NC (0.8542 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0020		0.1093	
Hazard ratio (95% CI) vs Pd	-	2.85 (1.42 to 5.70)		NC	
P-value	-	0.0031		0.9972	
Hazard ratio inverted (95% CI) vs IPd	0.35 (0.18 to 0.70)				
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.2 Treatment emergent adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9748 (0.9240 to 0.9918)	0.9052 (0.8353 to 0.9463)	1.0000 (1.0000 to 1.0000)	0.9167 (0.7061 to 0.9785)	
4 Months	0.9566 (0.8988 to 0.9817)	0.8345 (0.7528 to 0.8911)	1.0000 (1.0000 to 1.0000)	0.9167 (0.7061 to 0.9785)	
6 Months	0.9270 (0.8590 to 0.9629)	0.7777 (0.6886 to 0.8441)	1.0000 (1.0000 to 1.0000)	0.8708 (0.6502 to 0.9565)	
8 Months	0.9044 (0.8287 to 0.9477)	0.7573 (0.6659 to 0.8270)	1.0000 (1.0000 to 1.0000)	0.8708 (0.6502 to 0.9565)	
10 Months	0.9044 (0.8287 to 0.9477)	0.7573 (0.6659 to 0.8270)	1.0000 (1.0000 to 1.0000)	0.8708 (0.6502 to 0.9565)	
12 Months	0.8909 (0.8099 to 0.9386)	0.7457 (0.6525 to 0.8174)	1.0000 (1.0000 to 1.0000)	0.8708 (0.6502 to 0.9565)	
14 Months	0.8909 (0.8099 to 0.9386)	0.7324 (0.6367 to 0.8066)	1.0000 (1.0000 to 1.0000)	0.8708 (0.6502 to 0.9565)	
16 Months	0.8909 (0.8099 to 0.9386)	0.7324 (0.6367 to 0.8066)	1.0000 (1.0000 to 1.0000)	0.8708 (0.6502 to 0.9565)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.5 Subgroup analyses by race
16.2.7.1.2.5.2 Treatment emergent adverse event according to PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	113	105	19	21	
4 Months	104	92	19	20	
6 Months	87	77	19	19	
8 Months	75	72	18	18	
10 Months	72	67	17	17	
12 Months	62	58	13	15	
14 Months	42	38	3	11	
16 Months	20	18	1	3	
Constipation (days)					
Number (%) of events	20 (16.4)	19 (16.4)	5 (26.3)	4 (16.7)	0.4998
Number (%) of patients censored	102 (83.6)	97 (83.6)	14 (73.7)	20 (83.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (7.4579 to NC)	NC (12.1889 to NC)	3.9754 (0.3614 to NC)	NC (0.7556 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.9754 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.3 Treatment emergent adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
Bronchitis (days)					
Number (%) of events	0 (0.0)	1 (25.0)	9 (6.9)	28 (21.9)	0.9890
Number (%) of patients censored	3 (100.0)	3 (75.0)	121 (93.1)	100 (78.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.1971 to NC)	NC (NC to NC)	NC (4.5010 to NC)	
Median (95% CI)	NC (NC to NC)	NC (0.1971 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.1971 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3865		0.0009	
Hazard ratio (95% CI) vs Pd	-	NC		3.32 (1.57 to 7.05)	
P-value	-	0.9984		0.0017	
Hazard ratio inverted (95% CI) vs IPd			0.30 (0.14 to 0.64)		
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.3 Treatment emergent adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9766 (0.9291 to 0.9924)	0.9061 (0.8406 to 0.9456)	
4 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9681 (0.9173 to 0.9879)	0.8494 (0.7740 to 0.9012)	
6 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9505 (0.8930 to 0.9775)	0.8069 (0.7256 to 0.8663)	
8 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9303 (0.8648 to 0.9647)	0.7883 (0.7045 to 0.8509)	
10 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9303 (0.8648 to 0.9647)	0.7883 (0.7045 to 0.8509)	
12 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9179 (0.8466 to 0.9569)	0.7776 (0.6920 to 0.8422)	
14 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9179 (0.8466 to 0.9569)	0.7651 (0.6767 to 0.8323)	
16 Months	1.0000 (1.0000 to 1.0000)	0.7500 (0.1279 to 0.9605)	0.9179 (0.8466 to 0.9569)	0.7651 (0.6767 to 0.8323)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.6 Subgroup analyses by ethnic origin
16.2.7.1.2.6.3 Treatment emergent adverse event according to PT by treatment group according to ethnic origin - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	2	3	122	115	
4 Months	2	3	115	102	
6 Months	1	3	100	88	
8 Months	1	3	87	82	
10 Months	1	3	83	76	
12 Months	0	3	69	65	
14 Months	0	3	42	43	
16 Months	0	1	20	19	
Constipation (days)					
Number (%) of events	0 (0.0)	0 (0.0)	22 (16.9)	21 (16.4)	1.0000
Number (%) of patients censored	3 (100.0)	4 (100.0)	108 (83.1)	107 (83.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.4579 to NC)	NC (12.1889 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
4 Months	60	43	19	27	5	7	15	19	32	37	
6 Months	55	37	15	24	5	6	15	19	23	34	
8 Months	46	36	15	22	5	6	15	18	21	33	
10 Months	45	36	14	21	5	5	14	18	18	32	
12 Months	41	30	13	18	3	5	11	16	15	29	
14 Months	29	18	9	12	1	2	2	12	10	23	
16 Months	13	4	3	4	0	1	1	5	7	12	
Bronchitis (days)											
Number (%) of events	7 (9.5)	16 (29.1)	3 (15.0)	11 (39.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (9.5)	3 (8.6)	7 (17.1)	0.9630
Number (%) of patients censored	67 (90.5)	39 (70.9)	17 (85.0)	17 (60.7)	5 (100.0)	7 (100.0)	15 (100.0)	19 (90.5)	32 (91.4)	34 (82.9)	
Kaplan-Meier estimates of event in months											

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_greg_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
25% quantile (95% CI)	NC (NC to NC)	4.9610 (1.8727 to NC)	NC (0.4928 to NC)	4.3696 (0.7228 to 12.4846)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.8542 to NC)	NC (6.5051 to NC)	NC (3.6797 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.5010 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd											
Log-Rank test p-value[a] vs Pd	-	0.0034		0.0896				0.2263		0.3540	
Hazard ratio (95% CI) vs Pd	-	3.48 (1.43 to 8.47)		2.89 (0.80 to 10.39)		NC		NC		1.88 (0.48 to 7.28)	
P-value	-	0.0059		0.1048				0.9978		0.3620	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**Pd (N=5)**	**IPd (N=7)**	**Pd (N=15)**	**IPd (N=21)**	**Pd (N=35)**	**IPd (N=41)**	**p-value of treatment-by-subgroup interaction[c]**
Hazard ratio inverted (95% CI) vs IPd	0.29 (0.12 to 0.70)										
Events probability (95% CI)[b]											
2 Months	0.9724 (0.8940 to 0.9930)	0.8520 (0.7256 to 0.9231)	0.8947 (0.6408 to 0.9726)	0.8929 (0.7036 to 0.9641)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9048 (0.6700 to 0.9753)	1.0000 (1.0000 to 1.0000)	0.9512 (0.8187 to 0.9876)	
4 Months	0.9570 (0.8722 to 0.9859)	0.7724 (0.6334 to 0.8641)	0.8947 (0.6408 to 0.9726)	0.8199 (0.6199 to 0.9208)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9048 (0.6700 to 0.9753)	0.9688 (0.7982 to 0.9955)	0.8761 (0.7276 to 0.9465)	
6 Months	0.9240 (0.8262 to 0.9678)	0.7042 (0.5561 to 0.8109)	0.8947 (0.6408 to 0.9726)	0.7081 (0.4998 to 0.8421)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9048 (0.6700 to 0.9753)	0.9365 (0.7690 to 0.9837)	0.8504 (0.6967 to 0.9299)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
8 Months	0.9051 (0.7996 to 0.9565)	0.6791 (0.5278 to 0.7911)	0.8947 (0.6408 to 0.9726)	0.6664 (0.4554 to 0.8111)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9048 (0.6700 to 0.9753)	0.8896 (0.6887 to 0.9640)	0.8229 (0.6636 to 0.9115)	
10 Months	0.9051 (0.7996 to 0.9565)	0.6791 (0.5278 to 0.7911)	0.8947 (0.6408 to 0.9726)	0.6664 (0.4554 to 0.8111)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9048 (0.6700 to 0.9753)	0.8896 (0.6887 to 0.9640)	0.8229 (0.6636 to 0.9115)	
12 Months	0.9051 (0.7996 to 0.9565)	0.6791 (0.5278 to 0.7911)	0.8259 (0.5465 to 0.9413)	0.6188 (0.4038 to 0.7757)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9048 (0.6700 to 0.9753)	0.8896 (0.6887 to 0.9640)	0.8229 (0.6636 to 0.9115)	
14 Months	0.8800 (0.7600 to 0.9422)	0.6791 (0.5278 to 0.7911)	0.8259 (0.5465 to 0.9413)	0.5501 (0.3217 to 0.7298)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9048 (0.6700 to 0.9753)	0.8896 (0.6887 to 0.9640)	0.8229 (0.6636 to 0.9115)	
16 Months	0.8800 (0.7600 to 0.9422)	0.6791 (0.5278 to 0.7911)	0.8259 (0.5465 to 0.9413)	0.5501 (0.3217 to 0.7298)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9048 (0.6700 to 0.9753)	0.8896 (0.6887 to 0.9640)	0.8229 (0.6636 to 0.9115)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.7 Subgroup analyses by geographical region
16.2.7.1.2.7.2 Treatment emergent adverse event according to PT by treatment group according to geographical region - Safety population

	Western Europe		Eastern Europe		North America		Asia		Other Countries		
	Pd (N=74)	IPd (N=55)	Pd (N=20)	IPd (N=28)	Pd (N=5)	IPd (N=7)	Pd (N=15)	IPd (N=21)	Pd (N=35)	IPd (N=41)	p-value of treatment-by-subgroup interaction[c]
Number of patients at risk[b]											
2 Months	67	45	17	25	5	7	15	18	34	39	
4 Months	60	36	17	22	5	7	15	17	31	35	
6 Months	55	29	14	17	5	6	15	17	21	31	
8 Months	45	27	14	15	5	6	15	16	18	29	
10 Months	45	25	13	14	5	5	14	16	16	27	
12 Months	39	21	11	11	3	5	11	14	13	25	
14 Months	26	13	7	5	1	2	2	10	10	21	
16 Months	11	4	3	3	0	1	1	3	7	11	
Constipation (days)											
Number (%) of events	13 (17.6)	9 (16.4)	1 (5.0)	2 (7.1)	1 (20.0)	2 (28.6)	4 (26.7)	4 (19.0)	7 (20.0)	7 (17.1)	0.9625

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.3 Treatment emergent adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
Bronchitis (days)					
Number (%) of events	7 (7.4)	18 (23.4)	6 (10.9)	18 (24.0)	0.5510
Number (%) of patients censored	87 (92.6)	59 (76.6)	49 (89.1)	57 (76.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	7.4908 (3.6797 to NC)	NC (11.4333 to NC)	12.4846 (3.3183 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0039		0.0725	
Hazard ratio (95% CI) vs Pd	-	3.35 (1.40 to 8.02)		2.28 (0.90 to 5.74)	
P-value	-	0.0066		0.0808	
Hazard ratio inverted (95% CI) vs IPd	0.30 (0.12 to 0.71)				
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.3 Treatment emergent adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9784 (0.9162 to 0.9945)	0.8948 (0.8006 to 0.9460)	0.9630 (0.8599 to 0.9906)	0.9067 (0.8142 to 0.9544)	
4 Months	0.9664 (0.8994 to 0.9891)	0.8254 (0.7181 to 0.8948)	0.9437 (0.8355 to 0.9815)	0.8513 (0.7474 to 0.9148)	
6 Months	0.9407 (0.8628 to 0.9750)	0.7648 (0.6484 to 0.8471)	0.9236 (0.8090 to 0.9707)	0.8087 (0.6982 to 0.8821)	
8 Months	0.9257 (0.8411 to 0.9662)	0.7478 (0.6287 to 0.8336)	0.8999 (0.7749 to 0.9574)	0.7779 (0.6627 to 0.8578)	
10 Months	0.9257 (0.8411 to 0.9662)	0.7478 (0.6287 to 0.8336)	0.8999 (0.7749 to 0.9574)	0.7779 (0.6627 to 0.8578)	
12 Months	0.9257 (0.8411 to 0.9662)	0.7478 (0.6287 to 0.8336)	0.8709 (0.7310 to 0.9409)	0.7606 (0.6424 to 0.8443)	
14 Months	0.9056 (0.8083 to 0.9549)	0.7478 (0.6287 to 0.8336)	0.8709 (0.7310 to 0.9409)	0.7400 (0.6172 to 0.8288)	
16 Months	0.9056 (0.8083 to 0.9549)	0.7478 (0.6287 to 0.8336)	0.8709 (0.7310 to 0.9409)	0.7400 (0.6172 to 0.8288)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.8 Subgroup analyses by regulatory region
16.2.7.1.2.8.3 Treatment emergent adverse event according to PT by treatment group according to regulatory region - Safety population

	Western Countries		Other Countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	87	67	51	67	
4 Months	79	57	49	60	
6 Months	71	47	39	53	
8 Months	59	44	38	49	
10 Months	57	41	36	46	
12 Months	49	36	28	40	
14 Months	31	24	15	27	
16 Months	13	9	9	13	
Constipation (days)					
Number (%) of events	21 (22.3)	15 (19.5)	5 (9.1)	9 (12.0)	0.5268
Number (%) of patients censored	73 (77.7)	62 (80.5)	50 (90.9)	66 (88.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (0.8871 to NC)	NC (2.3655 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.2 Treatment emergent adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
Bronchitis (days)					
Number (%) of events	12 (8.9)	32 (23.5)	1 (7.1)	4 (25.0)	0.5688
Number (%) of patients censored	123 (91.1)	104 (76.5)	13 (92.9)	12 (75.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	12.4846 (4.5667 to NC)	NC (4.7310 to NC)	3.9097 (0.1971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.9097 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0023		0.1110	
Hazard ratio (95% CI) vs Pd	-	2.69 (1.39 to 5.23)		5.06 (0.56 to 45.95)	
P-value	-	0.0034		0.1500	
Hazard ratio inverted (95% CI) vs IPd	0.37 (0.19 to 0.72)				
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.2 Treatment emergent adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9696 (0.9209 to 0.9885)	0.9117 (0.8498 to 0.9489)	1.0000 (1.0000 to 1.0000)	0.8021 (0.5012 to 0.9320)	
4 Months	0.9531 (0.8986 to 0.9787)	0.8513 (0.7790 to 0.9014)	1.0000 (1.0000 to 1.0000)	0.7018 (0.3723 to 0.8808)	
6 Months	0.9358 (0.8755 to 0.9674)	0.7959 (0.7165 to 0.8554)	0.9091 (0.5081 to 0.9867)	0.7018 (0.3723 to 0.8808)	
8 Months	0.9163 (0.8494 to 0.9543)	0.7706 (0.6882 to 0.8338)	0.9091 (0.5081 to 0.9867)	0.7018 (0.3723 to 0.8808)	
10 Months	0.9163 (0.8494 to 0.9543)	0.7706 (0.6882 to 0.8338)	0.9091 (0.5081 to 0.9867)	0.7018 (0.3723 to 0.8808)	
12 Months	0.9044 (0.8327 to 0.9463)	0.7611 (0.6774 to 0.8259)	0.9091 (0.5081 to 0.9867)	0.7018 (0.3723 to 0.8808)	
14 Months	0.8913 (0.8142 to 0.9376)	0.7499 (0.6642 to 0.8167)	0.9091 (0.5081 to 0.9867)	0.7018 (0.3723 to 0.8808)	
16 Months	0.8913 (0.8142 to 0.9376)	0.7499 (0.6642 to 0.8167)	0.9091 (0.5081 to 0.9867)	0.7018 (0.3723 to 0.8808)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.9 Subgroup analyses by baseline ECOG PS
16.2.7.1.2.9.2 Treatment emergent adverse event according to PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	124	123	14	11	
4 Months	115	110	13	7	
6 Months	101	96	9	4	
8 Months	89	89	8	4	
10 Months	86	83	7	4	
12 Months	72	72	5	4	
14 Months	43	49	3	2	
16 Months	20	21	2	1	
Constipation (days)					
Number (%) of events	25 (18.5)	23 (16.9)	1 (7.1)	1 (6.3)	0.9157
Number (%) of patients censored	110 (81.5)	113 (83.1)	13 (92.9)	15 (93.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (4.6653 to NC)	NC (12.1889 to NC)	NC (0.6242 to NC)	NC (0.2957 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_ecog_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	48	54	44	41	19	22	
8 Months	45	53	39	40	16	19	
10 Months	42	52	37	39	15	18	
12 Months	39	47	29	32	13	16	
14 Months	24	31	18	22	9	11	
16 Months	14	14	7	6	3	6	
Bronchitis (days)							
Number (%) of events	7 (13.7)	13 (20.6)	4 (7.3)	14 (26.4)	1 (2.5)	9 (27.3)	0.1992
Number (%) of patients censored	44 (86.3)	50 (79.4)	51 (92.7)	39 (73.6)	39 (97.5)	24 (72.7)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (12.4517 to NC)	NC (3.2526 to NC)	NC (NC to NC)	7.4908 (3.9097 to NC)	NC (NC to NC)	4.3696 (0.8542 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.5010 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2788		0.0103		0.0043	
Hazard ratio (95% CI) vs Pd	-	1.65 (0.66 to 4.14)		3.86 (1.27 to 11.73)		10.99 (1.39 to 86.75)	
P-value	-	0.2839		0.0173		0.0230	
Hazard ratio inverted (95% CI) vs IPd			0.26 (0.09 to 0.79)		0.09 (0.01 to 0.72)		
Events probability (95% CI)[b]							
2 Months	0.9804 (0.8689 to 0.9972)	0.8889 (0.7810 to 0.9454)	0.9630 (0.8599 to 0.9906)	0.9434 (0.8347 to 0.9814)	0.9722 (0.8187 to 0.9960)	0.8446 (0.6660 to 0.9322)	
4 Months	0.9608 (0.8522 to 0.9900)	0.8245 (0.7055 to 0.8988)	0.9441 (0.8365 to 0.9816)	0.8629 (0.7335 to 0.9323)	0.9722 (0.8187 to 0.9960)	0.8108 (0.6260 to 0.9104)	
6 Months	0.9007 (0.7778 to 0.9574)	0.8077 (0.6861 to 0.8859)	0.9441 (0.8365 to 0.9816)	0.7998 (0.6592 to 0.8871)	0.9722 (0.8187 to 0.9960)	0.6965 (0.4946 to 0.8305)	
8 Months	0.8803 (0.7526 to 0.9444)	0.8077 (0.6861 to 0.8859)	0.9441 (0.8365 to 0.9816)	0.7332 (0.5841 to 0.8360)	0.9722 (0.8187 to 0.9960)	0.6965 (0.4946 to 0.8305)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.8803 (0.7526 to 0.9444)	0.8077 (0.6861 to 0.8859)	0.9441 (0.8365 to 0.9816)	0.7332 (0.5841 to 0.8360)	0.9722 (0.8187 to 0.9960)	0.6965 (0.4946 to 0.8305)	
12 Months	0.8803 (0.7526 to 0.9444)	0.7889 (0.6639 to 0.8718)	0.9115 (0.7729 to 0.9672)	0.7332 (0.5841 to 0.8360)	0.9722 (0.8187 to 0.9960)	0.6965 (0.4946 to 0.8305)	
14 Months	0.8544 (0.7171 to 0.9282)	0.7889 (0.6639 to 0.8718)	0.9115 (0.7729 to 0.9672)	0.7038 (0.5485 to 0.8143)	0.9722 (0.8187 to 0.9960)	0.6965 (0.4946 to 0.8305)	
16 Months	0.8544 (0.7171 to 0.9282)	0.7889 (0.6639 to 0.8718)	0.9115 (0.7729 to 0.9672)	0.7038 (0.5485 to 0.8143)	0.9722 (0.8187 to 0.9960)	0.6965 (0.4946 to 0.8305)	
Number of patients at risk[b]							
2 Months	50	56	51	48	34	27	
4 Months	48	51	50	41	28	22	
6 Months	45	46	43	36	20	15	
8 Months	41	45	38	32	17	13	
10 Months	40	43	36	29	16	12	
12 Months	36	37	26	25	14	11	
14 Months	21	25	15	15	10	8	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.10 Subgroup analyses by ISS staging
16.2.7.1.2.10.2 Treatment emergent adverse event according to PT by treatment group according to ISS staging - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=63)**	**Pd (N=55)**	**IPd (N=53)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	12	14	6	4	4	4	
Constipation (days)							
Number (%) of events	10 (19.6)	9 (14.3)	7 (12.7)	9 (17.0)	7 (17.5)	4 (12.1)	0.5211
Number (%) of patients censored	41 (80.4)	54 (85.7)	48 (87.3)	44 (83.0)	33 (82.5)	29 (87.9)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (0.8214 to NC)	NC (7.1951 to NC)	NC (3.9754 to NC)	NC (3.7782 to NC)	NC (0.4271 to NC)	NC (2.3655 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.4528		0.5726		0.3902	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.29 to 1.75)		1.33 (0.49 to 3.57)		0.59 (0.17 to 2.01)	
P-value	-	0.4550		0.5739		0.3957	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.2 Treatment emergent adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	31	36	76	75	6	9	
8 Months	30	36	67	72	5	7	
10 Months	28	36	63	70	5	6	
12 Months	26	33	53	59	4	6	
14 Months	14	20	34	41	3	6	
16 Months	9	10	15	14	0	2	
Bronchitis (days)							
Number (%) of events	3 (9.7)	7 (17.9)	9 (9.3)	27 (27.6)	1 (4.8)	2 (13.3)	0.8701
Number (%) of patients censored	28 (90.3)	32 (82.1)	88 (90.7)	71 (72.4)	20 (95.2)	13 (86.7)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (7.7207 to NC)	NC (3.2526 to NC)	NC (NC to NC)	6.6694 (3.9097 to NC)	NC (1.3470 to NC)	NC (1.8727 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.2 Treatment emergent adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.2663		0.0016		0.4787	
Hazard ratio (95% CI) vs Pd	-	2.12 (0.55 to 8.19)		3.16 (1.49 to 6.73)		2.32 (0.21 to 25.71)	
P-value	-	0.2776		0.0028		0.4915	
Hazard ratio inverted (95% CI) vs IPd			0.32 (0.15 to 0.67)				
Events probability (95% CI)[b]							
2 Months	1.0000 (1.0000 to 1.0000)	0.9231 (0.7802 to 0.9745)	0.9686 (0.9059 to 0.9898)	0.8875 (0.8061 to 0.9361)	0.9444 (0.6664 to 0.9920)	0.9286 (0.5908 to 0.9896)	
4 Months	1.0000 (1.0000 to 1.0000)	0.8440 (0.6851 to 0.9267)	0.9467 (0.8767 to 0.9775)	0.8343 (0.7437 to 0.8951)	0.9444 (0.6664 to 0.9920)	0.8512 (0.5234 to 0.9607)	
6 Months	0.9355 (0.7659 to 0.9835)	0.8158 (0.6517 to 0.9078)	0.9349 (0.8606 to 0.9703)	0.7678 (0.6687 to 0.8407)	0.9444 (0.6664 to 0.9920)	0.8512 (0.5234 to 0.9607)	
8 Months	0.9032 (0.7293 to 0.9677)	0.8158 (0.6517 to 0.9078)	0.9217 (0.8423 to 0.9621)	0.7314 (0.6282 to 0.8102)	0.9444 (0.6664 to 0.9920)	0.8512 (0.5234 to 0.9607)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.2 Treatment emergent adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
10 Months	0.9032 (0.7293 to 0.9677)	0.8158 (0.6517 to 0.9078)	0.9217 (0.8423 to 0.9621)	0.7314 (0.6282 to 0.8102)	0.9444 (0.6664 to 0.9920)	0.8512 (0.5234 to 0.9607)	
12 Months	0.9032 (0.7293 to 0.9677)	0.8158 (0.6517 to 0.9078)	0.9037 (0.8136 to 0.9515)	0.7173 (0.6121 to 0.7986)	0.9444 (0.6664 to 0.9920)	0.8512 (0.5234 to 0.9607)	
14 Months	0.9032 (0.7293 to 0.9677)	0.8158 (0.6517 to 0.9078)	0.8827 (0.7806 to 0.9390)	0.7014 (0.5934 to 0.7858)	0.9444 (0.6664 to 0.9920)	0.8512 (0.5234 to 0.9607)	
16 Months	0.9032 (0.7293 to 0.9677)	0.8158 (0.6517 to 0.9078)	0.8827 (0.7806 to 0.9390)	0.7014 (0.5934 to 0.7858)	0.9444 (0.6664 to 0.9920)	0.8512 (0.5234 to 0.9607)	
Number of patients at risk[b]							
2 Months	31	36	91	85	16	13	
4 Months	31	32	86	76	11	9	
6 Months	29	29	74	64	7	7	
8 Months	27	29	64	59	6	5	
10 Months	27	29	60	54	6	4	
12 Months	25	26	47	46	5	4	
14 Months	14	17	28	30	4	4	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.11 Subgroup analyses by R-ISS stage
16.2.7.1.2.11.2 Treatment emergent adverse event according to PT by treatment group according to R-ISS stage - Safety population

	I		II		III		
	Pd (N=31)	**IPd (N=39)**	**Pd (N=97)**	**IPd (N=98)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	8	9	13	12	1	1	
Constipation (days)							
Number (%) of events	7 (22.6)	4 (10.3)	14 (14.4)	18 (18.4)	5 (23.8)	2 (13.3)	0.2148
Number (%) of patients censored	24 (77.4)	35 (89.7)	83 (85.6)	80 (81.6)	16 (76.2)	13 (86.7)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (0.6571 to NC)	NC (2.3984 to NC)	NC (NC to NC)	NC (7.1951 to NC)	3.8439 (0.1643 to NC)	NC (2.3655 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.8439 to NC)	NC (4.7639 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Log-Rank test p-value[a] vs Pd	-	0.1734		0.5251		0.2527	
Hazard ratio (95% CI) vs Pd	-	0.44 (0.13 to 1.49)		1.25 (0.62 to 2.52)		0.39 (0.08 to 2.06)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.2 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
Bronchitis (days)					
Number (%) of events	3 (14.3)	3 (21.4)	6 (6.5)	26 (22.4)	0.3863
Number (%) of patients censored	18 (85.7)	11 (78.6)	87 (93.5)	90 (77.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	12.4517 (3.9425 to NC)	7.4908 (1.2485 to NC)	NC (NC to NC)	NC (4.5010 to NC)	
Median (95% CI)	NC (4.8624 to NC)	NC (2.8583 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (7.4908 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.4584		0.0023	
Hazard ratio (95% CI) vs Pd	-	1.84 (0.36 to 9.35)		3.64 (1.50 to 8.84)	
P-value	-	0.4647		0.0043	
Hazard ratio inverted (95% CI) vs IPd			0.27 (0.11 to 0.67)		
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.2 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	0.9231 (0.5664 to 0.9888)	0.9565 (0.8883 to 0.9835)	0.9052 (0.8353 to 0.9463)	
4 Months	0.9333 (0.6126 to 0.9903)	0.8392 (0.4940 to 0.9573)	0.9565 (0.8883 to 0.9835)	0.8430 (0.7623 to 0.8981)	
6 Months	0.8296 (0.4571 to 0.9564)	0.8392 (0.4940 to 0.9573)	0.9446 (0.8718 to 0.9766)	0.7964 (0.7095 to 0.8599)	
8 Months	0.8296 (0.4571 to 0.9564)	0.6713 (0.2458 to 0.8930)	0.9307 (0.8515 to 0.9684)	0.7865 (0.6982 to 0.8516)	
10 Months	0.8296 (0.4571 to 0.9564)	0.6713 (0.2458 to 0.8930)	0.9307 (0.8515 to 0.9684)	0.7865 (0.6982 to 0.8516)	
12 Months	0.8296 (0.4571 to 0.9564)	0.6713 (0.2458 to 0.8930)	0.9307 (0.8515 to 0.9684)	0.7754 (0.6854 to 0.8426)	
14 Months	0.7259 (0.3566 to 0.9053)	0.6713 (0.2458 to 0.8930)	0.9307 (0.8515 to 0.9684)	0.7625 (0.6699 to 0.8323)	
16 Months	0.7259 (0.3566 to 0.9053)	0.6713 (0.2458 to 0.8930)	0.9307 (0.8515 to 0.9684)	0.7625 (0.6699 to 0.8323)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.12 Subgroup analyses by cytogenetic abnormality (del17p)
16.2.7.1.2.12.2 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality (del17p) - Safety population

	Yes		No		
	Pd (N=21)	**IPd (N=14)**	**Pd (N=93)**	**IPd (N=116)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	18	11	87	105	
4 Months	14	7	83	93	
6 Months	8	6	73	80	
8 Months	8	4	65	77	
10 Months	8	3	62	72	
12 Months	8	3	51	62	
14 Months	6	2	33	43	
16 Months	2	1	16	18	
Constipation (days)					
Number (%) of events	4 (19.0)	1 (7.1)	14 (15.1)	22 (19.0)	0.2580
Number (%) of patients censored	17 (81.0)	13 (92.9)	79 (84.9)	94 (81.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (0.1643 to NC)	NC (1.3142 to NC)	NC (7.4579 to NC)	NC (7.1951 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.3 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
Bronchitis (days)					
Number (%) of events	4 (11.8)	3 (13.0)	5 (6.6)	25 (24.3)	0.1436
Number (%) of patients censored	30 (88.2)	20 (87.0)	71 (93.4)	78 (75.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (4.8624 to NC)	NC (1.2485 to NC)	NC (NC to NC)	10.5462 (3.6797 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.9304		0.0021	
Hazard ratio (95% CI) vs Pd	-	1.07 (0.24 to 4.78)		4.02 (1.54 to 10.50)	
P-value	-	0.9300		0.0045	
Hazard ratio inverted (95% CI) vs IPd			0.25 (0.10 to 0.65)		
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.3 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9706 (0.8090 to 0.9958)	0.9545 (0.7187 to 0.9935)	0.9598 (0.8806 to 0.9869)	0.8932 (0.8155 to 0.9394)	
4 Months	0.9333 (0.7560 to 0.9831)	0.9068 (0.6758 to 0.9759)	0.9598 (0.8806 to 0.9869)	0.8229 (0.7335 to 0.8845)	
6 Months	0.8866 (0.6816 to 0.9629)	0.9068 (0.6758 to 0.9759)	0.9455 (0.8611 to 0.9792)	0.7698 (0.6739 to 0.8408)	
8 Months	0.8866 (0.6816 to 0.9629)	0.8371 (0.5649 to 0.9461)	0.9289 (0.8369 to 0.9699)	0.7583 (0.6609 to 0.8312)	
10 Months	0.8866 (0.6816 to 0.9629)	0.8371 (0.5649 to 0.9461)	0.9289 (0.8369 to 0.9699)	0.7583 (0.6609 to 0.8312)	
12 Months	0.8866 (0.6816 to 0.9629)	0.8371 (0.5649 to 0.9461)	0.9289 (0.8369 to 0.9699)	0.7454 (0.6461 to 0.8207)	
14 Months	0.8127 (0.5488 to 0.9308)	0.8371 (0.5649 to 0.9461)	0.9289 (0.8369 to 0.9699)	0.7454 (0.6461 to 0.8207)	
16 Months	0.8127 (0.5488 to 0.9308)	0.8371 (0.5649 to 0.9461)	0.9289 (0.8369 to 0.9699)	0.7454 (0.6461 to 0.8207)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.13 Subgroup analyses by cytogenetic abnormality
16.2.7.1.2.13.3 Treatment emergent adverse event according to PT by treatment group according to cytogenetic abnormality - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	30	20	71	92	
4 Months	25	16	70	80	
6 Months	17	15	62	67	
8 Months	17	12	54	65	
10 Months	17	11	51	60	
12 Months	14	9	43	52	
14 Months	9	6	29	37	
16 Months	5	2	13	16	
Constipation (days)					
Number (%) of events	6 (17.6)	5 (21.7)	11 (14.5)	18 (17.5)	0.9550
Number (%) of patients censored	28 (82.4)	18 (78.3)	65 (85.5)	85 (82.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (0.5585 to NC)	NC (0.5585 to NC)	NC (7.4579 to NC)	NC (7.4579 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.3 Treatment emergent adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
Bronchitis (days)					
Number (%) of events	10 (11.4)	21 (25.9)	3 (4.9)	15 (21.1)	0.4553
Number (%) of patients censored	78 (88.6)	60 (74.1)	58 (95.1)	56 (78.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	6.0123 (3.6797 to NC)	NC (NC to NC)	NC (3.2526 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0138		0.0130	
Hazard ratio (95% CI) vs Pd	-	2.49 (1.17 to 5.30)		4.23 (1.22 to 14.63)	
P-value	-	0.0174		0.0226	
Hazard ratio inverted (95% CI) vs IPd	0.40 (0.19 to 0.85)		0.24 (0.07 to 0.82)		
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.3 Treatment emergent adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9658 (0.8976 to 0.9888)	0.9251 (0.8409 to 0.9657)	0.9825 (0.8819 to 0.9975)	0.8730 (0.7702 to 0.9318)	
4 Months	0.9537 (0.8813 to 0.9824)	0.8474 (0.7468 to 0.9104)	0.9636 (0.8619 to 0.9908)	0.8283 (0.7173 to 0.8987)	
6 Months	0.9139 (0.8274 to 0.9581)	0.7511 (0.6373 to 0.8337)	0.9636 (0.8619 to 0.9908)	0.8283 (0.7173 to 0.8987)	
8 Months	0.8992 (0.8077 to 0.9485)	0.7213 (0.6043 to 0.8090)	0.9412 (0.8273 to 0.9808)	0.8111 (0.6963 to 0.8859)	
10 Months	0.8992 (0.8077 to 0.9485)	0.7213 (0.6043 to 0.8090)	0.9412 (0.8273 to 0.9808)	0.8111 (0.6963 to 0.8859)	
12 Months	0.8822 (0.7842 to 0.9375)	0.7213 (0.6043 to 0.8090)	0.9412 (0.8273 to 0.9808)	0.7926 (0.6738 to 0.8721)	
14 Months	0.8635 (0.7582 to 0.9251)	0.7213 (0.6043 to 0.8090)	0.9412 (0.8273 to 0.9808)	0.7728 (0.6496 to 0.8573)	
16 Months	0.8635 (0.7582 to 0.9251)	0.7213 (0.6043 to 0.8090)	0.9412 (0.8273 to 0.9808)	0.7728 (0.6496 to 0.8573)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.14 Subgroup analyses by previous autologous stem-cell
16.2.7.1.2.14.3 Treatment emergent adverse event according to PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	83	73	55	61	
4 Months	77	63	51	54	
6 Months	66	52	44	48	
8 Months	60	46	37	47	
10 Months	58	42	35	45	
12 Months	49	36	28	40	
14 Months	29	24	17	27	
16 Months	14	11	8	11	
Constipation (days)					
Number (%) of events	15 (17.0)	13 (16.0)	11 (18.0)	11 (15.5)	0.7630
Number (%) of patients censored	73 (83.0)	68 (84.0)	50 (82.0)	60 (84.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (3.9754 to NC)	NC (3.7782 to NC)	NC (1.0513 to NC)	NC (7.4579 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.2 Treatment emergent adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Bronchitis (days)					
Number (%) of events	0 (0.0)	1 (50.0)	13 (8.8)	35 (23.3)	0.9861
Number (%) of patients censored	2 (100.0)	1 (50.0)	134 (91.2)	115 (76.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	4.5667 (4.5667 to NC)	NC (NC to NC)	12.4846 (4.3696 to NC)	
Median (95% CI)	NC (NC to NC)	NC (4.5667 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (4.5667 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.0010	
Hazard ratio (95% CI) vs Pd	-	NC		2.77 (1.47 to 5.24)	
P-value	-	0.9990		0.0017	
Hazard ratio inverted (95% CI) vs IPd			0.36 (0.19 to 0.68)		
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.2 Treatment emergent adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9721 (0.9274 to 0.9894)	0.8993 (0.8384 to 0.9380)	
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9570 (0.9068 to 0.9805)	0.8361 (0.7654 to 0.8871)	
6 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9329 (0.8748 to 0.9646)	0.7911 (0.7147 to 0.8492)	
8 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9146 (0.8505 to 0.9520)	0.7667 (0.6874 to 0.8285)	
10 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9146 (0.8505 to 0.9520)	0.7667 (0.6874 to 0.8285)	
12 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9034 (0.8349 to 0.9445)	0.7576 (0.6770 to 0.8208)	
14 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.8909 (0.8172 to 0.9360)	0.7471 (0.6646 to 0.8121)	
16 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.8909 (0.8172 to 0.9360)	0.7471 (0.6646 to 0.8121)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_allt_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.15 Subgroup analyses by previous allogenic transplantation
16.2.7.1.2.15.2 Treatment emergent adverse event according to PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	2	2	136	132	
4 Months	2	2	126	115	
6 Months	2	1	108	99	
8 Months	2	1	95	92	
10 Months	1	1	92	86	
12 Months	1	1	76	75	
14 Months	1	0	45	51	
16 Months	0	0	22	22	
Constipation (days)					
Number (%) of events	0 (0.0)	0 (0.0)	26 (17.7)	24 (16.0)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	121 (82.3)	126 (84.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.5852 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_allt_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.3 Treatment emergent adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
Bronchitis (days)					
Number (%) of events	7 (7.1)	24 (23.3)	6 (15.0)	7 (21.9)	0.4271
Number (%) of patients censored	91 (92.9)	79 (76.7)	34 (85.0)	25 (78.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	12.4846 (4.3039 to NC)	NC (4.8624 to NC)	NC (1.8727 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0022		0.5684	
Hazard ratio (95% CI) vs Pd	-	3.45 (1.49 to 8.00)		1.37 (0.46 to 4.09)	
P-value	-	0.0040		0.5700	
Hazard ratio inverted (95% CI) vs IPd	0.29 (0.12 to 0.67)				
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_semm_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.3 Treatment emergent adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9685 (0.9056 to 0.9897)	0.9119 (0.8376 to 0.9532)	0.9750 (0.8355 to 0.9964)	0.9052 (0.7340 to 0.9684)	
4 Months	0.9575 (0.8907 to 0.9838)	0.8413 (0.7540 to 0.8996)	0.9463 (0.8012 to 0.9864)	0.8728 (0.6957 to 0.9503)	
6 Months	0.9455 (0.8739 to 0.9770)	0.7878 (0.6931 to 0.8563)	0.8853 (0.7214 to 0.9555)	0.8393 (0.6557 to 0.9298)	
8 Months	0.9455 (0.8739 to 0.9770)	0.7648 (0.6671 to 0.8373)	0.8181 (0.6367 to 0.9146)	0.8057 (0.6173 to 0.9078)	
10 Months	0.9455 (0.8739 to 0.9770)	0.7648 (0.6671 to 0.8373)	0.8181 (0.6367 to 0.9146)	0.8057 (0.6173 to 0.9078)	
12 Months	0.9290 (0.8464 to 0.9680)	0.7648 (0.6671 to 0.8373)	0.8181 (0.6367 to 0.9146)	0.7673 (0.5714 to 0.8822)	
14 Months	0.9104 (0.8169 to 0.9573)	0.7492 (0.6479 to 0.8252)	0.8181 (0.6367 to 0.9146)	0.7673 (0.5714 to 0.8822)	
16 Months	0.9104 (0.8169 to 0.9573)	0.7492 (0.6479 to 0.8252)	0.8181 (0.6367 to 0.9146)	0.7673 (0.5714 to 0.8822)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.16 Subgroup analyses by MM type at SE
16.2.7.1.2.16.3 Treatment emergent adverse event according to PT by treatment group according to MM type at SE - Safety population

	Ig G		Ig A		
	Pd (N=98)	**IPd (N=103)**	**Pd (N=40)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	91	93	37	28	
4 Months	87	81	32	26	
6 Months	73	70	29	25	
8 Months	66	64	23	24	
10 Months	64	59	22	23	
12 Months	53	51	18	20	
14 Months	30	36	10	11	
16 Months	14	15	6	4	
Constipation (days)					
Number (%) of events	19 (19.4)	15 (14.6)	6 (15.0)	7 (21.9)	0.5322
Number (%) of patients censored	79 (80.6)	88 (85.4)	34 (85.0)	25 (78.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (3.8439 to NC)	NC (NC to NC)	NC (0.8871 to NC)	NC (0.4271 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.3 Treatment emergent adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
Bronchitis (days)					
Number (%) of events	6 (6.2)	22 (21.8)	6 (11.8)	13 (26.0)	0.4919
Number (%) of patients censored	91 (93.8)	79 (78.2)	45 (88.2)	37 (74.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (4.3039 to NC)	NC (6.5051 to NC)	6.6694 (2.1684 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0023		0.0738	
Hazard ratio (95% CI) vs Pd	-	3.70 (1.50 to 9.12)		2.35 (0.89 to 6.20)	
P-value	-	0.0045		0.0829	
Hazard ratio inverted (95% CI) vs IPd	0.27 (0.11 to 0.67)				
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.3 Treatment emergent adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9682 (0.9046 to 0.9896)	0.9102 (0.8345 to 0.9522)	0.9804 (0.8689 to 0.9972)	0.8791 (0.7504 to 0.9438)	
4 Months	0.9682 (0.9046 to 0.9896)	0.8482 (0.7608 to 0.9056)	0.9576 (0.8402 to 0.9893)	0.8152 (0.6745 to 0.8994)	
6 Months	0.9561 (0.8870 to 0.9833)	0.8048 (0.7109 to 0.8709)	0.9097 (0.7762 to 0.9653)	0.7685 (0.6200 to 0.8650)	
8 Months	0.9561 (0.8870 to 0.9833)	0.7813 (0.6840 to 0.8518)	0.8568 (0.7069 to 0.9335)	0.7429 (0.5901 to 0.8458)	
10 Months	0.9561 (0.8870 to 0.9833)	0.7813 (0.6840 to 0.8518)	0.8568 (0.7069 to 0.9335)	0.7429 (0.5901 to 0.8458)	
12 Months	0.9393 (0.8577 to 0.9748)	0.7813 (0.6840 to 0.8518)	0.8568 (0.7069 to 0.9335)	0.7143 (0.5562 to 0.8245)	
14 Months	0.9205 (0.8271 to 0.9645)	0.7653 (0.6641 to 0.8397)	0.8568 (0.7069 to 0.9335)	0.7143 (0.5562 to 0.8245)	
16 Months	0.9205 (0.8271 to 0.9645)	0.7653 (0.6641 to 0.8397)	0.8568 (0.7069 to 0.9335)	0.7143 (0.5562 to 0.8245)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.17 Subgroup analyses by MM type at initial diagnosis
16.2.7.1.2.17.3 Treatment emergent adverse event according to PT by treatment group according to MM type at initial diagnosis - Safety population

	IGG		NON-IGG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	90	91	47	42	
4 Months	87	80	41	36	
6 Months	73	70	37	30	
8 Months	66	64	31	29	
10 Months	64	59	29	28	
12 Months	53	51	24	25	
14 Months	30	36	16	15	
16 Months	14	15	8	7	
Constipation (days)					
Number (%) of events	19 (19.6)	13 (12.9)	7 (13.7)	10 (20.0)	0.1586
Number (%) of patients censored	78 (80.4)	88 (87.1)	44 (86.3)	40 (80.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (3.8439 to NC)	NC (NC to NC)	NC (0.8871 to NC)	NC (2.3655 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.2 Treatment emergent adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
Bronchitis (days)					
Number (%) of events	0 (0.0)	3 (21.4)	13 (9.4)	33 (23.9)	0.9841
Number (%) of patients censored	10 (100.0)	11 (78.6)	126 (90.6)	105 (76.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.6899 to NC)	NC (NC to NC)	12.4846 (4.3696 to NC)	
Median (95% CI)	NC (NC to NC)	NC (4.5667 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.1818		0.0013	
Hazard ratio (95% CI) vs Pd	-	NC		2.74 (1.44 to 5.20)	
P-value	-	0.9974		0.0021	
Hazard ratio inverted (95% CI) vs IPd			0.37 (0.19 to 0.69)		
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.2 Treatment emergent adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	0.9706 (0.9236 to 0.9889)	0.9050 (0.8420 to 0.9437)	
4 Months	1.0000 (1.0000 to 1.0000)	0.8571 (0.5394 to 0.9622)	0.9550 (0.9025 to 0.9795)	0.8362 (0.7619 to 0.8890)	
6 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	0.9302 (0.8699 to 0.9631)	0.7876 (0.7070 to 0.8483)	
8 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	0.9117 (0.8457 to 0.9503)	0.7613 (0.6776 to 0.8260)	
10 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	0.9117 (0.8457 to 0.9503)	0.7613 (0.6776 to 0.8260)	
12 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	0.9004 (0.8302 to 0.9426)	0.7514 (0.6664 to 0.8177)	
14 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	0.8877 (0.8124 to 0.9340)	0.7398 (0.6527 to 0.8083)	
16 Months	1.0000 (1.0000 to 1.0000)	0.7792 (0.4590 to 0.9232)	0.8877 (0.8124 to 0.9340)	0.7398 (0.6527 to 0.8083)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.18 Subgroup analyses by existing plasmacytoma
16.2.7.1.2.18.2 Treatment emergent adverse event according to PT by treatment group according to existing plasmacytoma - Safety population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=139)**	**IPd (N=138)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	9	12	129	122	
4 Months	7	11	121	106	
6 Months	5	9	105	91	
8 Months	2	8	95	85	
10 Months	2	8	91	79	
12 Months	2	7	75	69	
14 Months	2	6	44	45	
16 Months	0	5	22	17	
Constipation (days)					
Number (%) of events	0 (0.0)	1 (7.1)	26 (18.7)	23 (16.7)	0.9882
Number (%) of patients censored	10 (100.0)	13 (92.9)	113 (81.3)	115 (83.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (7.1951 to NC)	NC (4.6653 to NC)	NC (12.1889 to NC)	
Median (95% CI)	NC (NC to NC)	NC (7.1951 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.2 Treatment emergent adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
Bronchitis (days)					
Number (%) of events	9 (9.6)	21 (24.4)	2 (4.3)	11 (20.4)	0.4818
Number (%) of patients censored	85 (90.4)	65 (75.6)	45 (95.7)	43 (79.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	10.5462 (4.3696 to NC)	NC (NC to NC)	NC (2.4969 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0103		0.0254	
Hazard ratio (95% CI) vs Pd	-	2.67 (1.22 to 5.83)		4.74 (1.05 to 21.40)	
P-value	-	0.0137		0.0429	
Hazard ratio inverted (95% CI) vs IPd	0.37 (0.17 to 0.82)		0.21 (0.05 to 0.95)		
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_crcl_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.2 Treatment emergent adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9894 (0.9269 to 0.9985)	0.9186 (0.8368 to 0.9603)	0.9556 (0.8338 to 0.9887)	0.8889 (0.7693 to 0.9485)	
4 Months	0.9666 (0.9000 to 0.9891)	0.8471 (0.7513 to 0.9083)	0.9556 (0.8338 to 0.9887)	0.8510 (0.7240 to 0.9226)	
6 Months	0.9297 (0.8500 to 0.9679)	0.7859 (0.6818 to 0.8594)	0.9556 (0.8338 to 0.9887)	0.8100 (0.6751 to 0.8931)	
8 Months	0.9034 (0.8155 to 0.9506)	0.7597 (0.6523 to 0.8380)	0.9556 (0.8338 to 0.9887)	0.8100 (0.6751 to 0.8931)	
10 Months	0.9034 (0.8155 to 0.9506)	0.7597 (0.6523 to 0.8380)	0.9556 (0.8338 to 0.9887)	0.8100 (0.6751 to 0.8931)	
12 Months	0.8878 (0.7943 to 0.9403)	0.7456 (0.6364 to 0.8264)	0.9556 (0.8338 to 0.9887)	0.8100 (0.6751 to 0.8931)	
14 Months	0.8878 (0.7943 to 0.9403)	0.7456 (0.6364 to 0.8264)	0.9556 (0.8338 to 0.9887)	0.7800 (0.6340 to 0.8733)	
16 Months	0.8878 (0.7943 to 0.9403)	0.7456 (0.6364 to 0.8264)	0.9556 (0.8338 to 0.9887)	0.7800 (0.6340 to 0.8733)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.19 Subgroup analyses by baseline creatinine clearance
16.2.7.1.2.19.2 Treatment emergent adverse event according to PT by treatment group according to baseline creatinine clearance - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	90	78	42	48	
4 Months	84	70	39	42	
6 Months	73	61	33	35	
8 Months	65	57	28	33	
10 Months	62	55	27	29	
12 Months	53	46	22	27	
14 Months	31	33	14	16	
16 Months	14	14	7	7	
Constipation (days)					
Number (%) of events	17 (18.1)	16 (18.6)	8 (17.0)	7 (13.0)	0.6182
Number (%) of patients censored	77 (81.9)	70 (81.4)	39 (83.0)	47 (87.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (2.0698 to NC)	NC (7.1951 to NC)	NC (3.8439 to NC)	NC (4.7639 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.2 Treatment emergent adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
14 Months	0	2	51	65	
16 Months	0	0	24	26	
Bronchitis (days)					
Number (%) of events	0 (0.0)	1 (50.0)	13 (8.8)	35 (23.3)	0.9883
Number (%) of patients censored	2 (100.0)	1 (50.0)	134 (91.2)	115 (76.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.8871 (0.8871 to NC)	NC (NC to NC)	12.4846 (4.5010 to NC)	
Median (95% CI)	NC (NC to NC)	NC (0.8871 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (0.8871 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.3173		0.0010	
Hazard ratio (95% CI) vs Pd	-	NC		2.78 (1.47 to 5.25)	
P-value	-	0.9990		0.0016	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.2 Treatment emergent adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IPd			0.36 (0.19 to 0.68)		
Events probability (95% CI)[b]					
2 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9721 (0.9274 to 0.9894)	0.9060 (0.8464 to 0.9432)	
4 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9570 (0.9068 to 0.9805)	0.8428 (0.7729 to 0.8927)	
6 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9331 (0.8751 to 0.9647)	0.7905 (0.7139 to 0.8488)	
8 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9151 (0.8513 to 0.9522)	0.7661 (0.6866 to 0.8280)	
10 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9151 (0.8513 to 0.9522)	0.7661 (0.6866 to 0.8280)	
12 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.9040 (0.8360 to 0.9448)	0.7570 (0.6762 to 0.8203)	
14 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.8917 (0.8185 to 0.9364)	0.7463 (0.6636 to 0.8116)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.20 Subgroup analyses by previous therapy with anti-CD38 mAB
16.2.7.1.2.20.2 Treatment emergent adverse event according to PT by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[c]**
16 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.0060 to 0.9104)	0.8917 (0.8185 to 0.9364)	0.7463 (0.6636 to 0.8116)	
Number of patients at risk[b]					
2 Months	2	1	136	133	
4 Months	2	1	126	116	
6 Months	1	1	109	99	
8 Months	0	1	97	92	
10 Months	0	1	93	86	
12 Months	0	1	77	75	
14 Months	0	1	46	50	
16 Months	0	0	22	22	
Constipation (days)					
Number (%) of events	0 (0.0)	0 (0.0)	26 (17.7)	24 (16.0)	0.9999
Number (%) of patients censored	2 (100.0)	2 (100.0)	121 (82.3)	126 (84.0)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.3 Treatment emergent adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
Bronchitis (days)					
Number (%) of events	10 (9.0)	28 (23.9)	3 (7.9)	8 (22.9)	0.8563
Number (%) of patients censored	101 (91.0)	89 (76.1)	35 (92.1)	27 (77.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	10.5462 (4.3039 to NC)	NC (NC to NC)	12.4846 (1.9384 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0040		0.0732	
Hazard ratio (95% CI) vs Pd	-	2.76 (1.34 to 5.68)		3.16 (0.84 to 11.90)	
P-value	-	0.0058		0.0897	
Hazard ratio inverted (95% CI) vs IPd	0.36 (0.18 to 0.75)				
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.3 Treatment emergent adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9725 (0.9171 to 0.9910)	0.9054 (0.8356 to 0.9465)	0.9730 (0.8232 to 0.9961)	0.8839 (0.7196 to 0.9548)	
4 Months	0.9524 (0.8893 to 0.9799)	0.8341 (0.7523 to 0.8909)	0.9730 (0.8232 to 0.9961)	0.8545 (0.6849 to 0.9367)	
6 Months	0.9416 (0.8743 to 0.9734)	0.7873 (0.6994 to 0.8522)	0.9122 (0.7513 to 0.9709)	0.7861 (0.6013 to 0.8924)	
8 Months	0.9170 (0.8398 to 0.9579)	0.7562 (0.6644 to 0.8262)	0.9122 (0.7513 to 0.9709)	0.7861 (0.6013 to 0.8924)	
10 Months	0.9170 (0.8398 to 0.9579)	0.7562 (0.6644 to 0.8262)	0.9122 (0.7513 to 0.9709)	0.7861 (0.6013 to 0.8924)	
12 Months	0.9014 (0.8167 to 0.9482)	0.7444 (0.6507 to 0.8165)	0.9122 (0.7513 to 0.9709)	0.7861 (0.6013 to 0.8924)	
14 Months	0.8837 (0.7905 to 0.9371)	0.7444 (0.6507 to 0.8165)	0.9122 (0.7513 to 0.9709)	0.7370 (0.5338 to 0.8621)	
16 Months	0.8837 (0.7905 to 0.9371)	0.7444 (0.6507 to 0.8165)	0.9122 (0.7513 to 0.9709)	0.7370 (0.5338 to 0.8621)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.21 Subgroup analyses by refractory to PI status
16.2.7.1.2.21.3 Treatment emergent adverse event according to PT by treatment group according to refractory to PI status - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	102	104	36	30	
4 Months	94	91	34	26	
6 Months	81	77	29	23	
8 Months	71	71	26	22	
10 Months	67	65	26	22	
12 Months	54	58	23	18	
14 Months	32	39	14	12	
16 Months	13	20	9	2	
Constipation (days)					
Number (%) of events	22 (19.8)	19 (16.2)	4 (10.5)	5 (14.3)	0.4627
Number (%) of patients censored	89 (80.2)	98 (83.8)	34 (89.5)	30 (85.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (3.8439 to NC)	NC (12.1889 to NC)	NC (0.7885 to NC)	NC (1.3142 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.2 Treatment emergent adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Bronchitis (days)					
Number (%) of events	13 (9.3)	35 (24.1)	0 (0.0)	1 (14.3)	0.9883
Number (%) of patients censored	127 (90.7)	110 (75.9)	9 (100.0)	6 (85.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	10.5462 (4.3696 to NC)	NC (NC to NC)	NC (4.3039 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.3039 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0013		0.2568	
Hazard ratio (95% CI) vs Pd	-	2.73 (1.44 to 5.15)		NC	
P-value	-	0.0020		0.9984	
Hazard ratio inverted (95% CI) vs IPd	0.37 (0.19 to 0.69)				
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.2 Treatment emergent adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9707 (0.9238 to 0.9889)	0.8957 (0.8330 to 0.9358)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9548 (0.9020 to 0.9794)	0.8303 (0.7575 to 0.8829)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9292 (0.8680 to 0.9626)	0.7834 (0.7047 to 0.8434)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
8 Months	0.9096 (0.8420 to 0.9492)	0.7579 (0.6762 to 0.8218)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
10 Months	0.9096 (0.8420 to 0.9492)	0.7579 (0.6762 to 0.8218)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
12 Months	0.8975 (0.8249 to 0.9410)	0.7485 (0.6654 to 0.8138)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
14 Months	0.8839 (0.8056 to 0.9319)	0.7373 (0.6522 to 0.8046)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
16 Months	0.8839 (0.8056 to 0.9319)	0.7373 (0.6522 to 0.8046)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_refr1_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.22 Subgroup analyses by refractory to IMID status
16.2.7.1.2.22.2 Treatment emergent adverse event according to PT by treatment group according to refractory to IMID status - Safety population

	Yes		No		
	Pd (N=140)	**IPd (N=145)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	129	127	9	7	
4 Months	119	110	9	7	
6 Months	101	94	9	6	
8 Months	88	88	9	5	
10 Months	84	82	9	5	
12 Months	69	71	8	5	
14 Months	41	48	5	3	
16 Months	20	22	2	0	
Constipation (days)					
Number (%) of events	26 (18.6)	23 (15.9)	0 (0.0)	1 (14.3)	0.9867
Number (%) of patients censored	114 (81.4)	122 (84.1)	9 (100.0)	6 (85.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (4.6653 to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.4928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.4928 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_refr1_s_t_x.rtf (16FEB2021 22:52)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.3 Treatment emergent adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
Bronchitis (days)					
Number (%) of events	9 (10.3)	21 (23.1)	4 (6.5)	15 (24.6)	0.5322
Number (%) of patients censored	78 (89.7)	70 (76.9)	58 (93.5)	46 (75.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (3.3183 to NC)	NC (NC to NC)	12.4846 (4.3039 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test p-value[a] vs Pd	-	0.0197		0.0114	
Hazard ratio (95% CI) vs Pd	-	2.46 (1.12 to 5.36)		3.76 (1.25 to 11.34)	
P-value	-	0.0242		0.0185	
Hazard ratio inverted (95% CI) vs IPd	0.41 (0.19 to 0.89)		0.27 (0.09 to 0.80)		
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_llen_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.3 Treatment emergent adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	0.9765 (0.9092 to 0.9941)	0.8778 (0.7902 to 0.9304)	0.9669 (0.8740 to 0.9916)	0.9344 (0.8347 to 0.9749)	
4 Months	0.9638 (0.8918 to 0.9882)	0.8194 (0.7220 to 0.8853)	0.9490 (0.8499 to 0.9833)	0.8671 (0.7516 to 0.9312)	
6 Months	0.9238 (0.8379 to 0.9651)	0.7673 (0.6620 to 0.8435)	0.9490 (0.8499 to 0.9833)	0.8154 (0.6912 to 0.8933)	
8 Months	0.8935 (0.7974 to 0.9455)	0.7531 (0.6457 to 0.8320)	0.9490 (0.8499 to 0.9833)	0.7779 (0.6477 to 0.8647)	
10 Months	0.8935 (0.7974 to 0.9455)	0.7531 (0.6457 to 0.8320)	0.9490 (0.8499 to 0.9833)	0.7779 (0.6477 to 0.8647)	
12 Months	0.8935 (0.7974 to 0.9455)	0.7531 (0.6457 to 0.8320)	0.9211 (0.7973 to 0.9706)	0.7562 (0.6220 to 0.8484)	
14 Months	0.8727 (0.7664 to 0.9327)	0.7531 (0.6457 to 0.8320)	0.9211 (0.7973 to 0.9706)	0.7310 (0.5909 to 0.8298)	
16 Months	0.8727 (0.7664 to 0.9327)	0.7531 (0.6457 to 0.8320)	0.9211 (0.7973 to 0.9706)	0.7310 (0.5909 to 0.8298)	

Number of patients at risk[b]

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_llen_s_t_x.rtf (16FEB2021 22:51)

16.2.7.1 Safety endpoints
16.2.7.1.2 Analysis according to SOC/PT
16.2.7.1.2.23 Subgroup analyses by refractory to lenalidomide in last previous regimen
16.2.7.1.2.23.3 Treatment emergent adverse event according to PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[c]**
2 Months	81	78	57	56	
4 Months	76	66	52	51	
6 Months	65	56	45	44	
8 Months	55	53	42	40	
10 Months	55	50	38	37	
12 Months	46	45	31	31	
14 Months	27	30	19	21	
16 Months	11	11	11	11	
Constipation (days)					
Number (%) of events	15 (17.2)	15 (16.5)	11 (17.7)	9 (14.8)	0.7608
Number (%) of patients censored	72 (82.8)	76 (83.5)	51 (82.3)	52 (85.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (4.6653 to NC)	NC (7.4579 to NC)	NC (0.6899 to NC)	NC (2.3655 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_de_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_llen_s_t_x.rtf (16FEB2021 22:51)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.1 Overall survival by treatment group - ITT population

Overall Survival	**Pd (N=153)**	**IPd (N=154)**
Number (%) of deaths	105 (68.6)	93 (60.4)
Number (%) of patients censored	48 (31.4)	61 (39.6)
Kaplan-Meier estimates of Overall Survival in months		
25% quantile (95% CI)	6.6037 (5.0267 to 10.0862)	10.6448 (7.6879 to 15.3101)
Median (95% CI)	17.7084 (14.3901 to 26.2177)	24.5749 (20.3039 to 31.3101)
75% quantile (95% CI)	37.8152 (30.9158 to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test two-sided p-value[b] vs Pd	-	0.0561
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.76 (0.57 to 1.01)
P-value	-	0.0568
Overall Survival probability (95% CI)[c]		
3 Months	0.90 (0.84 to 0.94)	0.95 (0.91 to 0.98)
6 Months	0.78 (0.71 to 0.84)	0.84 (0.77 to 0.89)

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio
Cut-off date: 01OCT2020 HR<1 favors IPd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a]Stratified on age (<75 years versus >=75 years) and number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] Two-sided significance level is set to 0.05.
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_i_t_x.rtf (17NOV2020 15:03)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.2 Overall survival by treatment group according to age - ITT population

	<65		[65-75[		>=75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-subgroup interaction[a]**
Number (%) of deaths	41 (58.6)	33 (61.1)	39 (72.2)	40 (58.8)	25 (86.2)	20 (62.5)	0.2045
Number (%) of patients censored	29 (41.4)	21 (38.9)	15 (27.8)	28 (41.2)	4 (13.8)	12 (37.5)	
Kaplan-Meier estimates of OS in months							
25% quantile (95% CI)	7.3922 (4.4682 to 11.5647)	8.4435 (4.8296 to 16.5585)	10.0862 (4.5996 to 14.4887)	12.9117 (6.8665 to 18.4312)	4.7639 (1.2485 to 7.2936)	10.3819 (3.3511 to 16.1971)	
Median (95% CI)	25.6263 (13.4045 to 36.2382)	25.4620 (16.3285 to 36.1068)	19.8111 (14.3901 to 29.9302)	26.8747 (20.2710 to NC)	10.2505 (4.8953 to 17.3470)	19.9754 (14.1930 to NC)	
75% quantile (95% CI)	NC (36.2382 to NC)	NC (36.1068 to NC)	37.0924 (29.7331 to NC)	NC (NC to NC)	20.9610 (13.9630 to 37.8152)	NC (24.1807 to NC)	
Comparison vs. Pd							
Log-Rank test two-sided p-value[b] vs Pd	-	0.8883	-	0.1171	-	0.0220	

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_agegr1_i_t_x.rtf (17NOV2020 15:06)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.2 Overall survival by treatment group according to age - ITT population

	<65		[65-75[		>=75		
	Pd (N=70)	**IPd (N=54)**	**Pd (N=54)**	**IPd (N=68)**	**Pd (N=29)**	**IPd (N=32)**	**p-value of treatment-by-subgroup interaction[a]**
Hazard ratio (95% CI) vs Pd	-	0.97 (0.61 to 1.53)	-	0.70 (0.45 to 1.09)	-	0.51 (0.28 to 0.92)	
P-value	-	0.8885	-	0.1189	-	0.0245	
Overall Survival probability (95% CI)							
3 Months	0.93 (0.84 to 0.97)	0.96 (0.86 to 0.99)	0.91 (0.79 to 0.96)	0.96 (0.87 to 0.99)	0.83 (0.63 to 0.92)	0.94 (0.77 to 0.98)	
6 Months	0.79 (0.68 to 0.87)	0.83 (0.70 to 0.91)	0.85 (0.72 to 0.92)	0.87 (0.76 to 0.93)	0.62 (0.42 to 0.77)	0.81 (0.62 to 0.91)	
9 Months	0.73 (0.61 to 0.82)	0.74 (0.60 to 0.84)	0.76 (0.62 to 0.85)	0.84 (0.72 to 0.91)	0.52 (0.33 to 0.68)	0.78 (0.59 to 0.89)	
12 Months	0.64 (0.51 to 0.74)	0.70 (0.56 to 0.80)	0.74 (0.60 to 0.84)	0.76 (0.64 to 0.85)	0.48 (0.29 to 0.65)	0.71 (0.52 to 0.84)	
15 Months	0.61 (0.48 to 0.72)	0.66 (0.52 to 0.77)	0.62 (0.48 to 0.74)	0.72 (0.59 to 0.81)	0.37 (0.20 to 0.54)	0.68 (0.48 to 0.81)	
18 Months	0.55 (0.42 to 0.66)	0.60 (0.46 to 0.72)	0.55 (0.41 to 0.67)	0.66 (0.53 to 0.76)	0.30 (0.14 to 0.47)	0.54 (0.35 to 0.70)	
21 Months	0.53 (0.40 to 0.64)	0.58 (0.44 to 0.70)	0.49 (0.35 to 0.62)	0.61 (0.48 to 0.72)	0.22 (0.09 to 0.39)	0.47 (0.29 to 0.64)	
24 Months	0.52 (0.39 to 0.63)	0.54 (0.40 to 0.67)	0.49 (0.35 to 0.62)	0.52 (0.39 to 0.63)	0.22 (0.09 to 0.39)	0.44 (0.26 to 0.61)	
27 Months	0.47 (0.34 to 0.58)	0.47 (0.33 to 0.59)	0.43 (0.30 to 0.56)	0.49 (0.36 to 0.60)	0.18 (0.07 to 0.35)	0.41 (0.23 to 0.57)	
30 Months	0.41 (0.29 to 0.52)	0.43 (0.29 to 0.56)	0.36 (0.23 to 0.48)	0.46 (0.34 to 0.57)	0.18 (0.07 to 0.35)	0.37 (0.21 to 0.54)	
33 Months	0.39 (0.27 to 0.51)	0.41 (0.27 to 0.54)	0.30 (0.18 to 0.42)	0.44 (0.32 to 0.56)	0.15 (0.05 to 0.30)	0.37 (0.21 to 0.54)	
36 Months	0.39 (0.27 to 0.51)	0.38 (0.25 to 0.51)	0.26 (0.14 to 0.39)	0.39 (0.27 to 0.50)	0.15 (0.05 to 0.30)	0.33 (0.17 to 0.50)	

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_agegr1_i_t_x.rtf (17NOV2020 15:06)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.3 Overall survival by treatment group according to number of prior lines of therapy (IRT) - ITT population

	2 or 3		>3		
	Pd (N=101)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=52)**	**p-value of treatment-by-sub group interaction[a]**
Number (%) of deaths	69 (68.3)	59 (57.8)	36 (69.2)	34 (65.4)	0.7839
Number (%) of patients censored	32 (31.7)	43 (42.2)	16 (30.8)	18 (34.6)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	7.8193 (4.5667 to 12.4517)	11.3676 (5.9466 to 16.3285)	5.1581 (4.4682 to 9.0678)	10.6448 (4.8953 to 14.9815)	
Median (95% CI)	19.9097 (15.5729 to 27.5318)	25.2320 (19.9754 to 33.9055)	14.9815 (8.5092 to 29.1088)	24.5749 (14.4559 to 29.5688)	
75% quantile (95% CI)	NC (30.9158 to NC)	NC (NC to NC)	37.8152 (25.6263 to NC)	NC (29.5688 to NC)	
Comparison vs. Pd					
Log-Rank test two-sided p-value[b] vs Pd	-	0.0897	-	0.4208	
Hazard ratio (95% CI) vs Pd	-	0.74 (0.52 to 1.05)	-	0.82 (0.51 to 1.32)	
P-value	-	0.0909	-	0.4215	
Overall Survival probability (95% CI)					

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_stratum2_i_t_x.rtf (17NOV2020 15:06)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.4 Overall survival by treatment group according to gender - ITT population

	Male		Female		
	Pd (N=70)	**IPd (N=89)**	**Pd (N=83)**	**IPd (N=65)**	**p-value of treatment-by-sub group interaction[a]**
Number (%) of deaths	49 (70.0)	52 (58.4)	56 (67.5)	41 (63.1)	0.6951
Number (%) of patients censored	21 (30.0)	37 (41.6)	27 (32.5)	24 (36.9)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	10.0205 (4.5667 to 14.3244)	9.5934 (4.8953 to 15.5729)	6.0452 (4.1396 to 7.9507)	11.3676 (6.3409 to 17.2813)	
Median (95% CI)	20.9610 (14.3573 to 27.5975)	24.5749 (18.7269 to 33.9055)	17.1499 (11.2361 to 26.3162)	25.2320 (17.7084 to 33.6756)	
75% quantile (95% CI)	37.0924 (29.6016 to NC)	NC (NC to NC)	37.8152 (32.8214 to NC)	NC (33.6756 to NC)	
Comparison vs. Pd					
Log-Rank test two-sided p-value[b] vs Pd	-	0.1063	-	0.2874	
Hazard ratio (95% CI) vs Pd	-	0.73 (0.49 to 1.07)	-	0.80 (0.54 to 1.20)	
P-value	-	0.1078	-	0.2883	
Overall Survival probability (95% CI)					

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_sex_i_t_x.rtf (17NOV2020 15:07)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.5 Overall survival by treatment group according to race - ITT population

	White		Other		
	Pd (N=126)	**IPd (N=118)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[a]**
Number (%) of deaths	89 (70.6)	71 (60.2)	8 (42.1)	13 (54.2)	0.1108
Number (%) of patients censored	37 (29.4)	47 (39.8)	11 (57.9)	11 (45.8)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	6.2423 (4.5667 to 9.0678)	11.3676 (8.3121 to 15.5729)	22.7023 (6.4723 to 37.0924)	16.1971 (1.4784 to 21.3881)	
Median (95% CI)	17.7084 (14.3244 to 26.2177)	25.7577 (21.1253 to 33.6756)	37.0924 (22.7023 to 37.0924)	25.3306 (17.2813 to NC)	
75% quantile (95% CI)	37.8152 (29.9302 to NC)	NC (NC to NC)	37.0924 (NC to NC)	NC (29.4045 to NC)	
Comparison vs. Pd					
Log-Rank test two-sided p-value[b] vs Pd	-	0.0207	-	0.3415	
Hazard ratio (95% CI) vs Pd	-	0.69 (0.51 to 0.95)	-	1.53 (0.63 to 3.70)	
P-value	-	0.0214	-	0.3450	
Overall Survival probability (95% CI)					

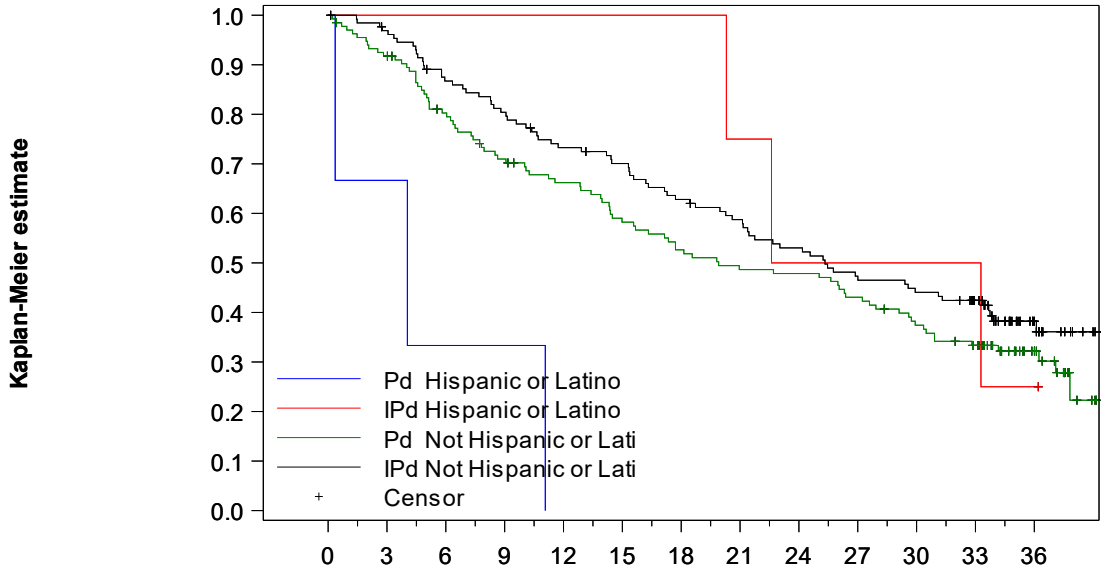
OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_racegr2_i_t_x.rtf (17NOV2020 15:07)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.6 Overall survival by treatment group according to ethnicity - ITT population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=134)**	**IPd (N=130)**	**p-value of treatment-by-sub group interaction[a]**
Number (%) of deaths	3 (100.0)	3 (75.0)	89 (66.4)	77 (59.2)	0.0304
Number (%) of patients censored	0 (0.0)	1 (25.0)	45 (33.6)	53 (40.8)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	0.3614 (0.3614 to 11.0719)	21.4538 (20.3039 to 33.2813)	7.3922 (5.1253 to 11.2361)	10.7105 (8.3121 to 15.5729)	
Median (95% CI)	4.0411 (0.3614 to 11.0719)	27.9425 (20.3039 to NC)	19.9097 (14.9815 to 27.5975)	25.3306 (20.5996 to 33.4456)	
75% quantile (95% CI)	11.0719 (0.3614 to 11.0719)	NC (20.3039 to NC)	37.8152 (34.1684 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test two-sided p-value[b] vs Pd	-	0.0101	-	0.1131	
Hazard ratio (95% CI) vs Pd	-	NC (NC to NC)	-	0.78 (0.58 to 1.06)	
P-value	-	0.9975	-	0.1136	

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_ethnic_i_t_x.rtf (17NOV2020 15:07)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.7 Overall survival by treatment group according to ethnicity - Kaplan-Meier curves - ITT population



Number at Risk

Pd Hispanic or Latino	3	2	1	1	0	0	0	0	0	0	0	0	0
IPd Hispanic or Latino	4	4	4	4	4	4	4	3	2	2	2	2	1
Pd Not Hispanic or Lati	134	122	104	91	83	73	66	61	60	54	46	37	19
IPd Not Hispanic or Lati	130	124	110	102	92	87	78	72	65	58	54	45	19

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.8 Overall survival by treatment group according to geographical region - ITT population

	Western Europe		Eastern Europe		
	Pd (N=76)	**IPd (N=55)**	**Pd (N=20)**	**IPd (N=28)**	**p-value of treatment-by-sub group interaction[a]**
Number (%) of deaths	52 (68.4)	33 (60.0)	15 (75.0)	19 (67.9)	0.4348
Number (%) of patients censored	24 (31.6)	22 (40.0)	5 (25.0)	9 (32.1)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	7.2936 (4.0411 to 11.2361)	8.2793 (4.3368 to 15.5729)	6.8337 (0.2300 to 14.9815)	10.2505 (4.4682 to 16.3285)	
Median (95% CI)	18.1355 (14.3244 to 27.2361)	24.1807 (15.5729 to 33.9055)	16.7392 (5.0267 to 36.2382)	20.7146 (11.7290 to 33.7413)	
75% quantile (95% CI)	NC (27.5975 to NC)	NC (33.9055 to NC)	36.2382 (17.1499 to 37.8152)	NC (29.5688 to NC)	
Comparison vs. Pd					
Log-Rank test two-sided p-value[b] vs Pd	-	0.2551	-	0.6839	
Hazard ratio (95% CI) vs Pd	-	0.78 (0.50 to 1.20)	-	0.87 (0.44 to 1.71)	
P-value	-	0.2564	-	0.6842	

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_region1_i_t_x.rtf (17NOV2020 15:07)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.9 Overall survival by treatment group according to regulatory region - ITT population

	Western Countries		Other Countries		
	Pd (N=97)	**IPd (N=77)**	**Pd (N=56)**	**IPd (N=77)**	**p-value of treatment-by-sub group interaction[a]**
Number (%) of deaths	67 (69.1)	45 (58.4)	38 (67.9)	48 (62.3)	0.5267
Number (%) of patients censored	30 (30.9)	32 (41.6)	18 (32.1)	29 (37.7)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	6.6037 (4.5667 to 10.3819)	10.3819 (5.7823 to 16.5585)	7.1622 (4.4682 to 13.8973)	11.7290 (7.6879 to 16.1971)	
Median (95% CI)	17.5441 (13.4045 to 26.2177)	25.2320 (17.9055 to 33.9055)	22.7023 (13.8973 to 34.1684)	24.5749 (17.2813 to 33.4456)	
75% quantile (95% CI)	NC (27.9261 to NC)	NC (NC to NC)	37.0924 (34.1684 to NC)	NC (33.7413 to NC)	
Comparison vs. Pd					
Log-Rank test two-sided p-value[b] vs Pd	-	0.0707	-	0.4201	
Hazard ratio (95% CI) vs Pd	-	0.71 (0.48 to 1.03)	-	0.84 (0.55 to 1.29)	
P-value	-	0.0721	-	0.4207	
Overall Survival probability (95% CI)					

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_region2_i_t_x.rtf (17NOV2020 15:08)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.10 Overall survival by treatment group according to baseline ECOG PS - ITT population

	0 or 1		2		
	Pd (N=137)	**IPd (N=138)**	**Pd (N=16)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[a]**
Number (%) of deaths	93 (67.9)	81 (58.7)	12 (75.0)	12 (75.0)	0.7252
Number (%) of patients censored	44 (32.1)	57 (41.3)	4 (25.0)	4 (25.0)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	7.3922 (5.0267 to 11.0719)	12.9117 (8.4435 to 15.5729)	4.4682 (0.6899 to 8.5092)	3.3511 (0.3614 to 17.7084)	
Median (95% CI)	19.9097 (15.6715 to 26.3819)	25.4620 (20.5996 to 33.6756)	13.9630 (4.4682 to 15.5729)	17.7084 (3.3511 to 33.4456)	
75% quantile (95% CI)	37.8152 (32.8214 to NC)	NC (NC to NC)	30.3573 (13.9630 to NC)	33.4456 (17.7084 to NC)	
Comparison vs. Pd					
Log-Rank test two-sided p-value[b] vs Pd	-	0.0507	-	0.7415	
Hazard ratio (95% CI) vs Pd	-	0.74 (0.55 to 1.00)	-	0.87 (0.39 to 1.96)	
P-value	-	0.0515	-	0.7417	
Overall Survival probability (95% CI)					

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_ecoblg1_i_t_x.rtf (17NOV2020 15:08)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.11 Overall survival by treatment group according to ISS staging at study entry - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=62)**	**Pd (N=56)**	**IPd (N=55)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-subgroup interaction[a]**
Number (%) of deaths	29 (56.9)	31 (50.0)	38 (67.9)	33 (60.0)	35 (81.4)	28 (82.4)	0.6840
Number (%) of patients censored	22 (43.1)	31 (50.0)	18 (32.1)	22 (40.0)	8 (18.6)	6 (17.6)	
Kaplan-Meier estimates of OS in months							
25% quantile (95% CI)	17.3470 (11.5647 to 26.3162)	17.9055 (10.6448 to 22.6694)	9.0678 (4.8953 to 13.9630)	10.3819 (5.8809 to 17.1499)	2.8255 (1.2485 to 4.4682)	4.8296 (3.0554 to 9.5934)	
Median (95% CI)	32.8214 (26.0534 to NC)	33.6756 (22.6694 to NC)	17.1499 (12.4517 to 26.2177)	25.2320 (17.1499 to NC)	5.1581 (4.1396 to 12.8789)	13.6674 (6.3409 to 21.1253)	
75% quantile (95% CI)	NC (37.0924 to NC)	NC (NC to NC)	37.8152 (22.7023 to NC)	NC (33.9055 to NC)	20.9610 (8.6407 to NC)	28.2218 (15.5729 to NC)	
Comparison vs. Pd							
Log-Rank test two-sided p-value[b] vs Pd	-	0.9023	-	0.1467	-	0.2627	

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_seisstg_i_t_x.rtf (17NOV2020 15:08)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.11 Overall survival by treatment group according to ISS staging at study entry - ITT population

	I		II		III		
	Pd (N=51)	**IPd (N=62)**	**Pd (N=56)**	**IPd (N=55)**	**Pd (N=43)**	**IPd (N=34)**	**p-value of treatment-by-subgroup interaction[a]**
Hazard ratio (95% CI) vs Pd	-	0.97 (0.58 to 1.61)	-	0.71 (0.44 to 1.13)	-	0.75 (0.46 to 1.24)	
P-value	-	0.9022	-	0.1486	-	0.2643	
Overall Survival probability (95% CI)							
3 Months	1.00 (1.00 to 1.00)	0.98 (0.89 to 1.00)	0.96 (0.86 to 0.99)	0.95 (0.84 to 0.98)	0.72 (0.56 to 0.83)	0.91 (0.75 to 0.97)	
6 Months	0.98 (0.87 to 1.00)	0.90 (0.79 to 0.95)	0.83 (0.70 to 0.91)	0.85 (0.73 to 0.92)	0.48 (0.32 to 0.62)	0.71 (0.52 to 0.83)	
9 Months	0.90 (0.78 to 0.96)	0.88 (0.77 to 0.94)	0.76 (0.62 to 0.85)	0.78 (0.64 to 0.87)	0.38 (0.24 to 0.53)	0.62 (0.43 to 0.76)	
12 Months	0.86 (0.73 to 0.93)	0.83 (0.71 to 0.91)	0.66 (0.51 to 0.77)	0.72 (0.58 to 0.82)	0.36 (0.22 to 0.50)	0.53 (0.35 to 0.68)	
15 Months	0.80 (0.67 to 0.89)	0.82 (0.69 to 0.89)	0.56 (0.41 to 0.68)	0.66 (0.52 to 0.77)	0.31 (0.18 to 0.45)	0.47 (0.30 to 0.62)	
18 Months	0.73 (0.58 to 0.83)	0.73 (0.60 to 0.83)	0.48 (0.34 to 0.61)	0.63 (0.48 to 0.74)	0.26 (0.14 to 0.40)	0.34 (0.19 to 0.50)	
21 Months	0.71 (0.56 to 0.81)	0.70 (0.57 to 0.80)	0.40 (0.27 to 0.53)	0.57 (0.43 to 0.69)	0.23 (0.12 to 0.37)	0.34 (0.19 to 0.50)	
24 Months	0.71 (0.56 to 0.81)	0.62 (0.48 to 0.73)	0.38 (0.25 to 0.51)	0.53 (0.39 to 0.65)	0.23 (0.12 to 0.37)	0.28 (0.14 to 0.44)	
27 Months	0.61 (0.46 to 0.73)	0.56 (0.43 to 0.68)	0.36 (0.23 to 0.49)	0.47 (0.34 to 0.60)	0.21 (0.10 to 0.34)	0.25 (0.12 to 0.41)	
30 Months	0.51 (0.36 to 0.63)	0.53 (0.40 to 0.65)	0.32 (0.20 to 0.45)	0.44 (0.30 to 0.56)	0.18 (0.08 to 0.31)	0.22 (0.10 to 0.37)	
33 Months	0.49 (0.34 to 0.62)	0.53 (0.40 to 0.65)	0.28 (0.16 to 0.41)	0.40 (0.27 to 0.53)	0.15 (0.06 to 0.28)	0.22 (0.10 to 0.37)	
36 Months	0.46 (0.32 to 0.59)	0.45 (0.32 to 0.58)	0.28 (0.16 to 0.41)	0.37 (0.24 to 0.50)	0.15 (0.06 to 0.28)	0.19 (0.08 to 0.34)	

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_seisstg_i_t_x.rtf (17NOV2020 15:08)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.12 Overall survival by treatment group according to R-ISS staging - ITT population

	I		II		III		
	Pd (N=38)	**IPd (N=43)**	**Pd (N=84)**	**IPd (N=87)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-subgroup interaction[a]**
Number (%) of deaths	20 (52.6)	19 (44.2)	57 (67.9)	55 (63.2)	22 (91.7)	13 (81.3)	0.4439
Number (%) of patients censored	18 (47.4)	24 (55.8)	27 (32.1)	32 (36.8)	2 (8.3)	3 (18.8)	
Kaplan-Meier estimates of OS in months							
25% quantile (95% CI)	26.0534 (14.3901 to 29.1088)	21.3881 (10.6448 to 25.7577)	7.7207 (5.1581 to 10.3819)	10.7105 (7.6879 to 14.9815)	1.9713 (0.2300 to 2.8912)	3.4333 (0.3614 to 6.3409)	
Median (95% CI)	34.1684 (27.5975 to NC)	NC (24.5749 to NC)	17.1499 (12.4517 to 20.9610)	21.7166 (17.1499 to 31.1129)	4.0411 (2.0041 to 6.3737)	6.6858 (3.3511 to 21.1253)	
75% quantile (95% CI)	NC (36.2382 to NC)	NC (NC to NC)	37.8152 (27.2361 to NC)	NC (33.7413 to NC)	10.2505 (4.1396 to 25.6263)	21.1253 (6.3409 to 36.1068)	
Comparison vs. Pd							
Log-Rank test two-sided p-value[b] vs Pd	-	0.7728	-	0.2171	-	0.1042	

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_serisstg_i_t_x.rtf (17NOV2020 15:08)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.12 Overall survival by treatment group according to R-ISS staging - ITT population

	I		II		III		
	Pd (N=38)	**IPd (N=43)**	**Pd (N=84)**	**IPd (N=87)**	**Pd (N=24)**	**IPd (N=16)**	**p-value of treatment-by-subgroup interaction[a]**
Hazard ratio (95% CI) vs Pd	-	0.91 (0.49 to 1.71)	-	0.79 (0.55 to 1.15)	-	0.56 (0.28 to 1.14)	
P-value	-	0.7728	-	0.2181	-	0.1090	
Overall Survival probability (95% CI)							
3 Months	1.00 (1.00 to 1.00)	0.98 (0.85 to 1.00)	0.95 (0.88 to 0.98)	0.95 (0.88 to 0.98)	0.58 (0.36 to 0.75)	0.88 (0.59 to 0.97)	
6 Months	0.97 (0.83 to 1.00)	0.93 (0.80 to 0.98)	0.82 (0.72 to 0.89)	0.85 (0.75 to 0.91)	0.31 (0.14 to 0.50)	0.56 (0.30 to 0.76)	
9 Months	0.95 (0.81 to 0.99)	0.93 (0.80 to 0.98)	0.71 (0.59 to 0.79)	0.79 (0.68 to 0.86)	0.27 (0.11 to 0.46)	0.44 (0.20 to 0.66)	
12 Months	0.95 (0.81 to 0.99)	0.86 (0.72 to 0.93)	0.62 (0.50 to 0.71)	0.73 (0.62 to 0.81)	0.22 (0.08 to 0.41)	0.38 (0.15 to 0.60)	
15 Months	0.89 (0.74 to 0.96)	0.86 (0.72 to 0.93)	0.54 (0.42 to 0.64)	0.65 (0.54 to 0.75)	0.18 (0.06 to 0.36)	0.38 (0.15 to 0.60)	
18 Months	0.84 (0.68 to 0.93)	0.79 (0.64 to 0.89)	0.45 (0.34 to 0.55)	0.58 (0.47 to 0.68)	0.13 (0.03 to 0.30)	0.30 (0.10 to 0.53)	
21 Months	0.82 (0.65 to 0.91)	0.77 (0.61 to 0.87)	0.38 (0.28 to 0.49)	0.53 (0.42 to 0.63)	0.13 (0.03 to 0.30)	0.30 (0.10 to 0.53)	
24 Months	0.82 (0.65 to 0.91)	0.67 (0.51 to 0.79)	0.37 (0.27 to 0.48)	0.48 (0.37 to 0.59)	0.13 (0.03 to 0.30)	0.23 (0.06 to 0.46)	
27 Months	0.68 (0.51 to 0.81)	0.62 (0.46 to 0.75)	0.36 (0.26 to 0.46)	0.44 (0.33 to 0.54)	0.09 (0.02 to 0.25)	0.23 (0.06 to 0.46)	
30 Months	0.55 (0.38 to 0.69)	0.58 (0.41 to 0.71)	0.33 (0.23 to 0.44)	0.40 (0.29 to 0.50)	0.04 (0.00 to 0.19)	0.23 (0.06 to 0.46)	
33 Months	0.52 (0.35 to 0.67)	0.58 (0.41 to 0.71)	0.31 (0.21 to 0.41)	0.38 (0.27 to 0.48)	0.04 (0.00 to 0.19)	0.23 (0.06 to 0.46)	
36 Months	0.48 (0.31 to 0.64)	0.54 (0.37 to 0.68)	0.31 (0.21 to 0.41)	0.33 (0.23 to 0.43)	0.04 (0.00 to 0.19)	0.23 (0.06 to 0.46)	

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_serisstg_i_t_x.rtf (17NOV2020 15:08)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.13 Overall survival by treatment group according to cytogenetic abnormality (del(170), t(4,14), t(14,16)) - ITT population

	At least one		None		
	Pd (N=36)	**IPd (N=24)**	**Pd (N=78)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[a]**
Number (%) of deaths	27 (75.0)	16 (66.7)	47 (60.3)	63 (61.2)	0.8676
Number (%) of patients censored	9 (25.0)	8 (33.3)	31 (39.7)	40 (38.8)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	4.0411 (2.0041 to 10.2505)	4.4682 (0.3614 to 9.1335)	7.9507 (5.1581 to 12.4517)	14.1930 (8.4435 to 17.1499)	
Median (95% CI)	15.5729 (4.7639 to 20.6324)	15.3758 (4.8953 to 29.4045)	20.9610 (14.3244 to 37.0924)	25.3306 (20.3039 to 33.6756)	
75% quantile (95% CI)	29.7331 (17.3470 to NC)	NC (17.9055 to NC)	37.8152 (37.0924 to NC)	NC (36.1068 to NC)	
Comparison vs. Pd					
Log-Rank test two-sided p-value[b] vs Pd	-	0.6607	-	0.5855	
Hazard ratio (95% CI) vs Pd	-	0.87 (0.47 to 1.62)	-	0.90 (0.62 to 1.31)	
P-value	-	0.6609	-	0.5856	
Overall Survival probability (95% CI)					

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_carebl_i_t_x.rtf (17NOV2020 15:08)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.14 Overall survival by treatment group according to cytogenetic abnormality del(17p) - ITT population

	Yes		No		
	Pd (N=23)	**IPd (N=14)**	**Pd (N=95)**	**IPd (N=118)**	**p-value of treatment-by-sub group interaction[a]**
Number (%) of deaths	17 (73.9)	8 (57.1)	60 (63.2)	73 (61.9)	0.5409
Number (%) of patients censored	6 (26.1)	6 (42.9)	35 (36.8)	45 (38.1)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	3.7454 (0.2300 to 4.1396)	3.5154 (0.3614 to 6.3409)	7.8193 (5.1253 to 11.2361)	14.2587 (8.8049 to 16.3285)	
Median (95% CI)	16.1314 (3.7454 to 27.5318)	6.3409 (3.3511 to NC)	18.5626 (13.9630 to 30.4887)	24.1807 (20.2710 to 31.1129)	
75% quantile (95% CI)	29.7331 (16.1314 to NC)	NC (6.3409 to NC)	37.8152 (36.2382 to NC)	NC (36.1068 to NC)	
Comparison vs. Pd					
Log-Rank test two-sided p-value[b] vs Pd	-	0.3652	-	0.4438	
Hazard ratio (95% CI) vs Pd	-	0.68 (0.29 to 1.58)	-	0.87 (0.62 to 1.23)	
P-value	-	0.3682	-	0.4442	
Overall Survival probability (95% CI)					

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_del17bl_i_t_x.rtf (17NOV2020 15:09)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.15 Overall survival by treatment group according to previous autologous stem-cell - ITT population

	Yes		No		
	Pd (N=90)	**IPd (N=83)**	**Pd (N=63)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[a]**
Number (%) of deaths	61 (67.8)	52 (62.7)	44 (69.8)	41 (57.7)	0.1602
Number (%) of patients censored	29 (32.2)	31 (37.3)	19 (30.2)	30 (42.3)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	9.0678 (4.5996 to 13.8973)	9.1335 (5.7823 to 15.3429)	5.1581 (2.5955 to 8.5092)	14.4230 (5.9466 to 17.2813)	
Median (95% CI)	25.6263 (14.9815 to 27.5975)	22.6037 (17.7084 to 29.4045)	15.6715 (8.5092 to 20.9610)	29.9302 (18.4312 to 36.1068)	
75% quantile (95% CI)	NC (30.9158 to NC)	NC (33.2813 to NC)	37.8152 (25.0349 to NC)	NC (36.1068 to NC)	
Comparison vs. Pd					
Log-Rank test two-sided p-value[b] vs Pd	-	0.6131	-	0.0184	
Hazard ratio (95% CI) vs Pd	-	0.91 (0.63 to 1.32)	-	0.60 (0.39 to 0.92)	
P-value	-	0.6140	-	0.0197	
Overall Survival probability (95% CI)					

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_auttpfl_i_t_x.rtf (17NOV2020 15:09)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.16 Overall survival by treatment group according to previous allogenic transplantation - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[a]**
Number (%) of deaths	1 (50.0)	0 (0.0)	104 (68.9)	93 (61.2)	0.9736
Number (%) of patients censored	1 (50.0)	2 (100.0)	47 (31.1)	59 (38.8)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	29.1088 (NC to NC)	NC (NC to NC)	6.6037 (4.8953 to 10.0862)	10.6448 (7.0308 to 15.3101)	
Median (95% CI)	29.1088 (NC to NC)	NC (NC to NC)	17.7084 (14.3901 to 26.0534)	24.5749 (20.2710 to 31.1129)	
75% quantile (95% CI)	29.1088 (NC to NC)	NC (NC to NC)	37.8152 (30.9158 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test two-sided p-value[b] vs Pd	-	0.3173	-	0.0627	
Hazard ratio (95% CI) vs Pd	-	NC (NC to NC)	-	0.77 (0.58 to 1.01)	
P-value	-	1.0000	-	0.0634	
Overall Survival probability (95% CI)					

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_alltpfl_i_t_x.rtf (17NOV2020 15:09)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.17 Overall survival by treatment group according to MM type - ITT population

	IgG		Non-IgG		
	Pd (N=100)	**IPd (N=102)**	**Pd (N=52)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[a]**
Number (%) of deaths	64 (64.0)	59 (57.8)	40 (76.9)	34 (66.7)	0.9962
Number (%) of patients censored	36 (36.0)	43 (42.2)	12 (23.1)	17 (33.3)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	6.3737 (4.5996 to 10.2505)	10.7105 (7.6879 to 16.1971)	7.3922 (2.5955 to 14.3573)	10.0862 (4.8624 to 15.3758)	
Median (95% CI)	17.3470 (12.8789 to 29.1088)	25.4620 (20.5996 to 33.7413)	18.5626 (14.3244 to 25.9877)	21.7495 (15.3101 to 33.6756)	
75% quantile (95% CI)	37.8152 (36.2382 to NC)	NC (NC to NC)	30.9158 (25.9877 to NC)	NC (33.4456 to NC)	
Comparison vs. Pd					
Log-Rank test two-sided p-value[b] vs Pd	-	0.1503	-	0.2531	
Hazard ratio (95% CI) vs Pd	-	0.77 (0.54 to 1.10)	-	0.77 (0.48 to 1.21)	
P-value	-	0.1514	-	0.2540	
Overall Survival probability (95% CI)					

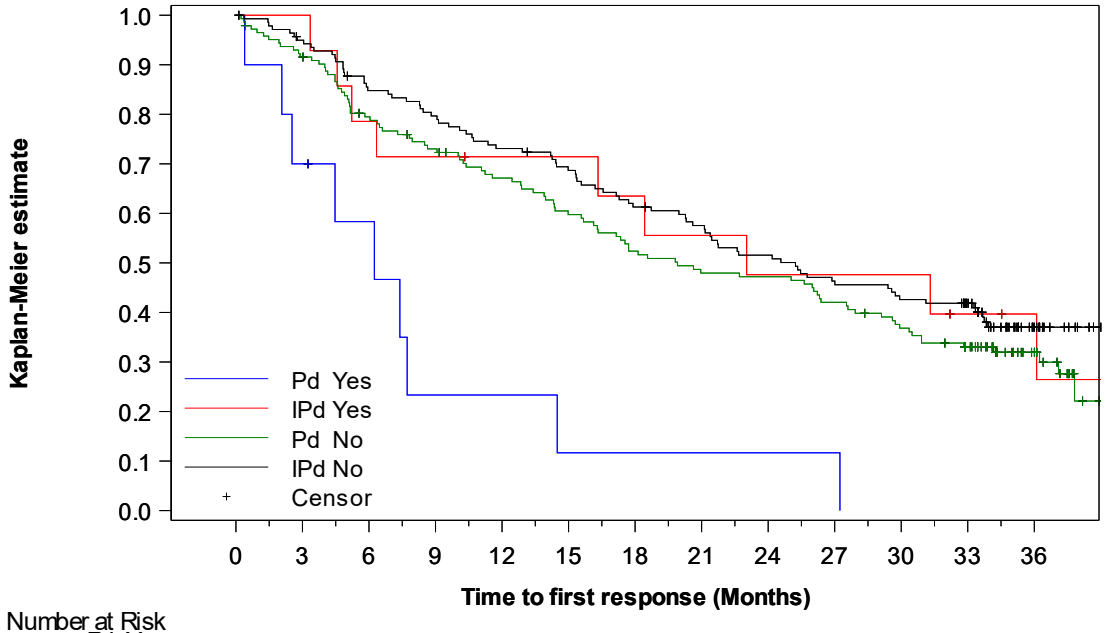
OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_dghcgr1_i_t_x.rtf (17NOV2020 15:09)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.18 Overall survival by treatment group according to existing plasmacytoma - ITT population

	Yes		No		
	Pd (N=10)	**IPd (N=14)**	**Pd (N=143)**	**IPd (N=140)**	**p-value of treatment-by-sub group interaction[a]**
Number (%) of deaths	9 (90.0)	9 (64.3)	96 (67.1)	84 (60.0)	0.0162
Number (%) of patients censored	1 (10.0)	5 (35.7)	47 (32.9)	56 (40.0)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	2.5298 (0.3943 to 6.2423)	6.3409 (3.3511 to 23.0308)	7.9507 (5.0924 to 11.2361)	10.7105 (8.2793 to 15.3429)	
Median (95% CI)	6.2423 (0.3943 to 14.4887)	23.0308 (5.2238 to NC)	19.9097 (15.6715 to 27.5318)	25.2320 (20.3039 to 31.1129)	
75% quantile (95% CI)	7.7207 (4.4682 to 27.2361)	NC (23.0308 to NC)	37.8152 (34.1684 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test two-sided p-value[b] vs Pd	-	0.0042	-	0.1363	
Hazard ratio (95% CI) vs Pd	-	0.25 (0.09 to 0.69)	-	0.80 (0.60 to 1.07)	
P-value	-	0.0074	-	0.1368	
Overall Survival probability (95% CI)					

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_mrictifl_i_t_x.rtf (17NOV2020 15:09)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.19 Overall survival by treatment group according to existing plasmacytoma - Kaplan-Meier curves - ITT population



Number at Risk

Pd Yes	10	7	5	2	2	1	1	1	1	1	0	0	0
IPd Yes	14	14	11	10	9	9	8	7	6	6	6	4	3
Pd No	143	130	111	101	91	81	71	65	64	57	49	40	20
IPd No	140	131	116	109	100	93	83	77	69	62	57	49	19

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.20 Overall survival by treatment group according to baseline creatinine clearance (MDRD) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=96)	**IPd (N=87)**	**Pd (N=49)**	**IPd (N=55)**	**p-value of treatment-by-sub group interaction[a]**
Number (%) of deaths	59 (61.5)	41 (47.1)	38 (77.6)	43 (78.2)	0.4662
Number (%) of patients censored	37 (38.5)	46 (52.9)	11 (22.4)	12 (21.8)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	12.4517 (6.0452 to 15.6715)	17.1499 (10.6448 to 23.0308)	5.1253 (2.0041 to 7.2936)	8.3121 (4.8296 to 11.7290)	
Median (95% CI)	27.5318 (19.8111 to 32.8214)	33.7413 (25.4620 to NC)	12.8789 (6.6037 to 17.7084)	17.7084 (11.7290 to 22.6037)	
75% quantile (95% CI)	37.8152 (36.2382 to NC)	NC (NC to NC)	27.5975 (16.3285 to NC)	33.2813 (21.7495 to NC)	
Comparison vs. Pd					
Log-Rank test two-sided p-value[b] vs Pd	-	0.0352	-	0.3702	
Hazard ratio (95% CI) vs Pd	-	0.65 (0.44 to 0.97)	-	0.82 (0.53 to 1.27)	
P-value	-	0.0366	-	0.3710	

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_crclgr2_i_t_x.rtf (17NOV2020 15:10)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.21 Overall survival by treatment group according to previous therapy with anti-CD38 mAB - ITT population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=151)**	**IPd (N=152)**	**p-value of treatment-by-sub group interaction[a]**
Number (%) of deaths	2 (100.0)	2 (100.0)	103 (68.2)	91 (59.9)	0.1577
Number (%) of patients censored	0 (0.0)	0 (0.0)	48 (31.8)	61 (40.1)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	4.0411 (4.0411 to 6.6037)	23.0308 (23.0308 to 33.9055)	7.3922 (5.0267 to 10.3819)	10.6448 (7.0308 to 15.3101)	
Median (95% CI)	5.3224 (4.0411 to 6.6037)	28.4682 (23.0308 to 33.9055)	18.1355 (14.4887 to 26.3162)	24.5749 (20.2710 to 31.3101)	
75% quantile (95% CI)	6.6037 (4.0411 to 6.6037)	33.9055 (23.0308 to 33.9055)	37.8152 (30.9158 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test two-sided p-value[b] vs Pd	-	0.0896	-	0.0653	
Hazard ratio (95% CI) vs Pd	-	NC (NC to NC)	-	0.77 (0.58 to 1.02)	
P-value	-	0.9985	-	0.0661	

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_prmabfl_i_t_x.rtf (17NOV2020 15:10)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.22 Overall survival by treatment group according to refractory to PI - ITT population

	Yes		No		
	Pd (N=115)	**IPd (N=118)**	**Pd (N=38)**	**IPd (N=36)**	**p-value of treatment-by-sub group interaction[a]**
Number (%) of deaths	79 (68.7)	74 (62.7)	26 (68.4)	19 (52.8)	0.8757
Number (%) of patients censored	36 (31.3)	44 (37.3)	12 (31.6)	17 (47.2)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	6.4723 (4.5667 to 10.0205)	10.6448 (7.6879 to 15.3101)	7.9507 (4.0082 to 19.9097)	10.3984 (2.7598 to 17.7084)	
Median (95% CI)	16.2957 (13.4045 to 25.0349)	25.2320 (20.2710 to 31.1129)	26.3491 (14.4887 to 36.2382)	24.1807 (16.1971 to NC)	
75% quantile (95% CI)	37.8152 (29.6016 to NC)	NC (36.1068 to NC)	37.0924 (30.9158 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test two-sided p-value[b] vs Pd	-	0.0619	-	0.4770	
Hazard ratio (95% CI) vs Pd	-	0.74 (0.54 to 1.02)	-	0.81 (0.45 to 1.46)	
P-value	-	0.0629	-	0.4779	
Overall Survival probability (95% CI)					

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_refr4fl_i_t_x.rtf (17NOV2020 15:10)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.23 Overall survival by treatment group according to refractory to IMID - ITT population

	Yes		No		
	Pd (N=144)	**IPd (N=147)**	**Pd (N=9)**	**IPd (N=7)**	**p-value of treatment-by-sub group interaction[a]**
Number (%) of deaths	100 (69.4)	91 (61.9)	5 (55.6)	2 (28.6)	0.6667
Number (%) of patients censored	44 (30.6)	56 (38.1)	4 (44.4)	5 (71.4)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	6.3737 (4.7639 to 9.0678)	10.7105 (7.0308 to 15.3101)	17.7084 (11.2361 to 30.9158)	7.6879 (6.8665 to NC)	
Median (95% CI)	17.5441 (14.3244 to 25.9877)	24.1807 (20.2710 to 29.9302)	30.9158 (11.2361 to NC)	NC (6.8665 to NC)	
75% quantile (95% CI)	37.0924 (30.3573 to NC)	NC (NC to NC)	NC (29.6016 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test two-sided p-value[b] vs Pd	-	0.0541	-	0.4651	
Hazard ratio (95% CI) vs Pd	-	0.76 (0.57 to 1.01)	-	0.55 (0.11 to 2.83)	
P-value	-	0.0549	-	0.4717	

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_refr1fl_i_t_x.rtf (17NOV2020 15:10)

16.2.6 Efficacy response data
16.2.6.1 Secondary efficacy endpoints
16.2.6.1.1 Overall survival
16.2.6.1.1.24 Overall survival by treatment group according to refractory to lenalidomide in last previous regimen - ITT population

	Yes		No		
	Pd (N=88)	**IPd (N=93)**	**Pd (N=65)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[a]**
Number (%) of deaths	63 (71.6)	57 (61.3)	42 (64.6)	36 (59.0)	0.9222
Number (%) of patients censored	25 (28.4)	36 (38.7)	23 (35.4)	25 (41.0)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	7.2936 (4.7639 to 11.5647)	10.6448 (5.2238 to 15.5729)	5.1581 (3.7454 to 11.2361)	11.3676 (7.0308 to 17.1499)	
Median (95% CI)	17.7084 (14.3901 to 26.3162)	22.6694 (18.7269 to 31.1129)	17.7084 (12.8789 to 30.4887)	25.4620 (17.2813 to NC)	
75% quantile (95% CI)	37.0924 (27.5975 to NC)	NC (36.1068 to NC)	37.8152 (30.4887 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Log-Rank test two-sided p-value[b] vs Pd	-	0.1479	-	0.1938	
Hazard ratio (95% CI) vs Pd	-	0.77 (0.54 to 1.10)	-	0.74 (0.48 to 1.16)	
P-value	-	0.1491	-	0.1954	
Overall Survival probability (95% CI)					

OS: Overall survival, CI: Confidence interval, HR: Hazard ratio - Cutoff date = 01OCT2020
[a]Interaction test from the Cox proportional hazard model including the factor, treatment effect and the treatment by factor interaction
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[b] Two-sided significance level is set to 0.05.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_sr_de_os_len_and_ref_i_t_x.rtf (17NOV2020 15:10)

16.2.7.1 Safety endpoints

16.2.7.1.1 Treatment emergent adverse event by treatment group - Safety population

Any treatment emergent adverse event	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	146 (98.0)	151 (99.3)
Number (%) of patients censored	3 (2.0)	1 (0.7)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.1314 (0.1314 to 0.1643)	0.0986 (0.0657 to 0.1314)
Median (95% CI)	0.3285 (0.2628 to 0.4928)	0.1971 (0.1643 to 0.2300)
75% quantile (95% CI)	0.8871 (0.7228 to 1.3470)	0.5585 (0.3943 to 0.7556)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0027
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.4289 (1.1301 to 1.8067)
P-value	-	0.0029
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6998 (0.5535 to 0.8849)	-
probability (95% CI)[c]		
2 Months	0.1111 (0.0664 to 0.1685)	0.0600 (0.0295 to 0.1058)
4 Months	0.0486 (0.0215 to 0.0924)	0.0200 (0.0055 to 0.0530)
6 Months	0.0405 (0.0162 to 0.0826)	0.0133 (0.0026 to 0.0433)
8 Months	0.0324 (0.0113 to 0.0725)	0.0067 (0.0006 to 0.0336)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints

16.2.7.1.1 Treatment emergent adverse event by treatment group - Safety population

Any treatment emergent adverse event	**Pd (N=149)**	**IPd (N=152)**
10 Months	0.0243 (0.0070 to 0.0620)	0.0067 (0.0006 to 0.0336)
12 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
14 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
16 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
18 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
20 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
22 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
24 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
26 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
Number of patients at risk[c]		
2 Months	16	9
4 Months	7	3
6 Months	5	2
8 Months	4	1
10 Months	3	1
12 Months	2	1
14 Months	2	1
16 Months	2	1
18 Months	2	1
20 Months	1	1

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints

16.2.7.1.1 Treatment emergent adverse event by treatment group - Safety population

Any treatment emergent adverse event	**Pd (N=149)**	**IPd (N=152)**
22 Months	1	1
24 Months	1	1
26 Months	1	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints

16.2.7.1.2 Non-progression treatment emergent adverse event by treatment group - Safety population

Any treatment emergent adverse event without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	146 (98.0)	151 (99.3)
Number (%) of patients censored	3 (2.0)	1 (0.7)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.1314 (0.1314 to 0.1643)	0.0986 (0.0657 to 0.1314)
Median (95% CI)	0.3285 (0.2628 to 0.4928)	0.1971 (0.1643 to 0.2300)
75% quantile (95% CI)	0.8871 (0.7228 to 1.3470)	0.5585 (0.3943 to 0.7556)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0027
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.4289 (1.1301 to 1.8067)
P-value	-	0.0029
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6998 (0.5535 to 0.8849)	-
probability (95% CI)[c]		
2 Months	0.1111 (0.0664 to 0.1685)	0.0600 (0.0295 to 0.1058)
4 Months	0.0486 (0.0215 to 0.0924)	0.0200 (0.0055 to 0.0530)
6 Months	0.0405 (0.0162 to 0.0826)	0.0133 (0.0026 to 0.0433)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teaenp_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.2 Non-progression treatment emergent adverse event by treatment group - Safety population

Any treatment emergent adverse event without progression events	**Pd (N=149)**	**IPd (N=152)**
8 Months	0.0324 (0.0113 to 0.0725)	0.0067 (0.0006 to 0.0336)
10 Months	0.0243 (0.0070 to 0.0620)	0.0067 (0.0006 to 0.0336)
12 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
14 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
16 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
18 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
20 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
22 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
24 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
26 Months	0.0162 (0.0033 to 0.0510)	0.0067 (0.0006 to 0.0336)
Number of patients at risk[c]		
2 Months	16	9
4 Months	7	3
6 Months	5	2
8 Months	4	1
10 Months	3	1
12 Months	2	1
14 Months	2	1
16 Months	2	1

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

16.2.7.1 Safety endpoints

16.2.7.1.2 Non-progression treatment emergent adverse event by treatment group - Safety population

Any treatment emergent adverse event without progression events	Pd (N=149)	IPd (N=152)
18 Months	2	1
20 Months	1	1
22 Months	1	1
24 Months	1	1
26 Months	1	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

16.2.7.1 Safety endpoints

16.2.7.1.3 Treatment emergent serious adverse event by treatment group - Safety population

Treatment emergent serious adverse event	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	90 (60.4)	111 (73.0)
Number (%) of patients censored	59 (39.6)	41 (27.0)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	1.3799 (0.7228 to 1.9384)	0.7885 (0.4928 to 1.4127)
Median (95% CI)	6.5708 (3.7782 to 14.9158)	5.9795 (2.7926 to 9.8234)
75% quantile (95% CI)	NC (34.9569 to NC)	26.6119 (18.4312 to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0973
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.2666 (0.9573 to 1.6760)
P-value	-	0.0981
probability (95% CI)[c]		
2 Months	0.6779 (0.5964 to 0.7464)	0.6490 (0.5672 to 0.7192)
4 Months	0.5830 (0.4994 to 0.6574)	0.5554 (0.4724 to 0.6305)
6 Months	0.5131 (0.4296 to 0.5903)	0.4943 (0.4119 to 0.5712)
8 Months	0.4838 (0.4006 to 0.5619)	0.4668 (0.3852 to 0.5442)
10 Months	0.4838 (0.4006 to 0.5619)	0.4119 (0.3324 to 0.4896)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints

16.2.7.1.3 Treatment emergent serious adverse event by treatment group - Safety population

Treatment emergent serious adverse event	**Pd (N=149)**	**IPd (N=152)**
12 Months	0.4679 (0.3848 to 0.5466)	0.3621 (0.2852 to 0.4394)
14 Months	0.4348 (0.3520 to 0.5145)	0.3549 (0.2784 to 0.4321)
16 Months	0.4177 (0.3352 to 0.4980)	0.3399 (0.2643 to 0.4169)
18 Months	0.4177 (0.3352 to 0.4980)	0.3318 (0.2566 to 0.4088)
20 Months	0.4177 (0.3352 to 0.4980)	0.2980 (0.2246 to 0.3747)
22 Months	0.4177 (0.3352 to 0.4980)	0.2807 (0.2085 to 0.3572)
24 Months	0.4073 (0.3245 to 0.4882)	0.2714 (0.1997 to 0.3478)
26 Months	0.3965 (0.3136 to 0.4781)	0.2523 (0.1820 to 0.3286)
Number of patients at risk[c]		
2 Months	100	98
4 Months	86	82
6 Months	72	72
8 Months	63	68
10 Months	62	60
12 Months	57	50
14 Months	51	49
16 Months	48	43
18 Months	44	40
20 Months	42	35
22 Months	40	31

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints

16.2.7.1.3 Treatment emergent serious adverse event by treatment group - Safety population

Treatment emergent serious adverse event	Pd (N=149)	IPd (N=152)
24 Months	38	29
26 Months	36	24

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints

16.2.7.1.4 Non-progression treatment emergent serious adverse event by treatment group - Safety population

Treatment emergent serious adverse event without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	89 (59.7)	111 (73.0)
Number (%) of patients censored	60 (40.3)	41 (27.0)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	1.3799 (0.7228 to 1.9384)	0.7885 (0.4928 to 1.4127)
Median (95% CI)	6.5708 (3.7782 to 14.9158)	6.2752 (2.7926 to 9.9548)
75% quantile (95% CI)	NC (NC to NC)	26.6119 (18.4312 to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0863
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.2780 (0.9649 to 1.6926)
P-value	-	0.0871
probability (95% CI)[c]		
2 Months	0.6779 (0.5964 to 0.7464)	0.6490 (0.5672 to 0.7192)
4 Months	0.5830 (0.4994 to 0.6574)	0.5554 (0.4724 to 0.6305)
6 Months	0.5131 (0.4296 to 0.5903)	0.5011 (0.4187 to 0.5779)
8 Months	0.4838 (0.4006 to 0.5619)	0.4737 (0.3918 to 0.5510)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesaenp_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.4 Non-progression treatment emergent serious adverse event by treatment group - Safety population

Treatment emergent serious adverse event without progression events	**Pd (N=149)**	**IPd (N=152)**
10 Months	0.4838 (0.4006 to 0.5619)	0.4187 (0.3389 to 0.4964)
12 Months	0.4679 (0.3848 to 0.5466)	0.3619 (0.2850 to 0.4392)
14 Months	0.4348 (0.3520 to 0.5145)	0.3547 (0.2782 to 0.4319)
16 Months	0.4177 (0.3352 to 0.4980)	0.3397 (0.2641 to 0.4167)
18 Months	0.4177 (0.3352 to 0.4980)	0.3316 (0.2564 to 0.4086)
20 Months	0.4177 (0.3352 to 0.4980)	0.2978 (0.2245 to 0.3746)
22 Months	0.4177 (0.3352 to 0.4980)	0.2805 (0.2083 to 0.3570)
24 Months	0.4073 (0.3245 to 0.4882)	0.2712 (0.1996 to 0.3476)
26 Months	0.3965 (0.3136 to 0.4781)	0.2521 (0.1818 to 0.3284)
Number of patients at risk[c]		
2 Months	100	98
4 Months	86	82
6 Months	72	73
8 Months	63	69
10 Months	62	61
12 Months	57	50
14 Months	51	49
16 Months	48	43
18 Months	44	40

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesaenp_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.4 Non-progression treatment emergent serious adverse event by treatment group - Safety population

Treatment emergent serious adverse event without progression events	Pd (N=149)	IPd (N=152)
20 Months	42	35
22 Months	40	31
24 Months	38	29
26 Months	36	24

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesaenp_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.5 Treatment emergent adverse event leading to discontinuation of treatment by treatment group - Safety population

Any treatment emergent leading to discontinuation of treatment	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	21 (14.1)	18 (11.8)
Number (%) of patients censored	128 (85.9)	134 (88.2)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3961
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.7616 (0.4052 to 1.4314)
P-value	-	0.3976
probability (95% CI)[c]		
2 Months	0.9120 (0.8533 to 0.9480)	0.9934 (0.9539 to 0.9991)
4 Months	0.9051 (0.8449 to 0.9427)	0.9732 (0.9302 to 0.9899)
6 Months	0.8836 (0.8193 to 0.9260)	0.9522 (0.9023 to 0.9769)
8 Months	0.8755 (0.8094 to 0.9197)	0.9444 (0.8917 to 0.9718)
10 Months	0.8755 (0.8094 to 0.9197)	0.9362 (0.8806 to 0.9664)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints

16.2.7.1.5 Treatment emergent adverse event leading to discontinuation of treatment by treatment group - Safety population

Any treatment emergent leading to discontinuation of treatment	**Pd (N=149)**	**IPd (N=152)**
12 Months	0.8755 (0.8094 to 0.9197)	0.9276 (0.8691 to 0.9605)
14 Months	0.8558 (0.7843 to 0.9050)	0.9276 (0.8691 to 0.9605)
16 Months	0.8558 (0.7843 to 0.9050)	0.8991 (0.8313 to 0.9406)
18 Months	0.8558 (0.7843 to 0.9050)	0.8991 (0.8313 to 0.9406)
20 Months	0.8558 (0.7843 to 0.9050)	0.8783 (0.8045 to 0.9255)
22 Months	0.8558 (0.7843 to 0.9050)	0.8673 (0.7904 to 0.9174)
24 Months	0.8558 (0.7843 to 0.9050)	0.8673 (0.7904 to 0.9174)
26 Months	0.8558 (0.7843 to 0.9050)	0.8673 (0.7904 to 0.9174)
Number of patients at risk[c]		
2 Months	133	148
4 Months	127	139
6 Months	113	126
8 Months	103	120
10 Months	99	113
12 Months	91	105
14 Months	84	104
16 Months	77	93
18 Months	69	87
20 Months	65	82
22 Months	63	73

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints

16.2.7.1.5 Treatment emergent adverse event leading to discontinuation of treatment by treatment group - Safety population

Any treatment emergent leading to discontinuation of treatment	**Pd (N=149)**	**IPd (N=152)**
24 Months	62	71
26 Months	60	65

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints

16.2.7.1.6 Non-progression treatment emergent adverse event leading to discontinuation of treatment by treatment group - Safety population

Any treatment emergent leading to discontinuation of treatment without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	21 (14.1)	16 (10.5)
Number (%) of patients censored	128 (85.9)	136 (89.5)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2527
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.6854 (0.3573 to 1.3144)
P-value	-	0.2555
probability (95% CI)[c]		
2 Months	0.9120 (0.8533 to 0.9480)	0.9934 (0.9539 to 0.9991)
4 Months	0.9051 (0.8449 to 0.9427)	0.9732 (0.9302 to 0.9899)
6 Months	0.8836 (0.8193 to 0.9260)	0.9522 (0.9023 to 0.9769)
8 Months	0.8755 (0.8094 to 0.9197)	0.9522 (0.9023 to 0.9769)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tediscnp_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.6 Non-progression treatment emergent adverse event leading to discontinuation of treatment by treatment group - Safety population

Any treatment emergent leading to discontinuation of treatment without progression events	**Pd (N=149)**	**IPd (N=152)**
10 Months	0.8755 (0.8094 to 0.9197)	0.9440 (0.8909 to 0.9716)
12 Months	0.8755 (0.8094 to 0.9197)	0.9354 (0.8791 to 0.9660)
14 Months	0.8558 (0.7843 to 0.9050)	0.9354 (0.8791 to 0.9660)
16 Months	0.8558 (0.7843 to 0.9050)	0.9068 (0.8405 to 0.9465)
18 Months	0.8558 (0.7843 to 0.9050)	0.9068 (0.8405 to 0.9465)
20 Months	0.8558 (0.7843 to 0.9050)	0.8963 (0.8265 to 0.9391)
22 Months	0.8558 (0.7843 to 0.9050)	0.8851 (0.8116 to 0.9311)
24 Months	0.8558 (0.7843 to 0.9050)	0.8851 (0.8116 to 0.9311)
26 Months	0.8558 (0.7843 to 0.9050)	0.8851 (0.8116 to 0.9311)
Number of patients at risk[c]		
2 Months	133	148
4 Months	127	139
6 Months	113	126
8 Months	103	121
10 Months	99	114
12 Months	91	106
14 Months	84	105
16 Months	77	93
18 Months	69	87

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

16.2.7.1 Safety endpoints

16.2.7.1.6 Non-progression treatment emergent adverse event leading to discontinuation of treatment by treatment group - Safety population

Any treatment emergent leading to discontinuation of treatment without progression events	Pd (N=149)	IPd (N=152)
20 Months	65	82
22 Months	63	73
24 Months	62	71
26 Months	60	65

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

16.2.7.1 Safety endpoints

16.2.7.1.7 Treatment emergent mild adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1,2)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	138 (92.6)	142 (93.4)
Number (%) of patients censored	11 (7.4)	10 (6.6)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.1643 (0.1314 to 0.2628)	0.0986 (0.0657 to 0.1314)
Median (95% CI)	0.4928 (0.3285 to 0.7228)	0.2300 (0.1643 to 0.3285)
75% quantile (95% CI)	1.4456 (0.8871 to 1.8727)	0.8214 (0.6571 to 2.0698)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1222
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.2077 (0.9503 to 1.5347)
P-value	-	0.1227
probability (95% CI)[c]		
2 Months	0.1740 (0.1167 to 0.2410)	0.1854 (0.1281 to 0.2511)
4 Months	0.0908 (0.0501 to 0.1463)	0.1143 (0.0691 to 0.1719)
6 Months	0.0825 (0.0439 to 0.1367)	0.0817 (0.0435 to 0.1352)
8 Months	0.0722 (0.0358 to 0.1256)	0.0545 (0.0238 to 0.1037)
10 Months	0.0619 (0.0282 to 0.1142)	0.0545 (0.0238 to 0.1037)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints

16.2.7.1.7 Treatment emergent mild adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1,2)	**Pd (N=149)**	**IPd (N=152)**
12 Months	0.0495 (0.0193 to 0.1014)	0.0545 (0.0238 to 0.1037)
14 Months	0.0371 (0.0116 to 0.0877)	0.0545 (0.0238 to 0.1037)
16 Months	0.0371 (0.0116 to 0.0877)	0.0454 (0.0180 to 0.0926)
18 Months	0.0371 (0.0116 to 0.0877)	0.0454 (0.0180 to 0.0926)
20 Months	0.0371 (0.0116 to 0.0877)	0.0454 (0.0180 to 0.0926)
22 Months	0.0371 (0.0116 to 0.0877)	0.0454 (0.0180 to 0.0926)
24 Months	0.0371 (0.0116 to 0.0877)	0.0454 (0.0180 to 0.0926)
26 Months	0.0371 (0.0116 to 0.0877)	0.0454 (0.0180 to 0.0926)
Number of patients at risk[c]		
2 Months	23	27
4 Months	12	15
6 Months	8	9
8 Months	7	6
10 Months	5	6
12 Months	4	6
14 Months	3	6
16 Months	3	3
18 Months	3	3
20 Months	2	3
22 Months	2	3

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints

16.2.7.1.7 Treatment emergent mild adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1,2)	**Pd (N=149)**	**IPd (N=152)**
24 Months	2	3
26 Months	1	2

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints

16.2.7.1.8 Non-progression treatment emergent mild adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1,2) without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	138 (92.6)	142 (93.4)
Number (%) of patients censored	11 (7.4)	10 (6.6)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.1643 (0.1314 to 0.2628)	0.0986 (0.0657 to 0.1314)
Median (95% CI)	0.4928 (0.3285 to 0.7228)	0.2300 (0.1643 to 0.3285)
75% quantile (95% CI)	1.4456 (0.8871 to 1.8727)	0.8214 (0.6571 to 2.0698)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1145
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.2129 (0.9541 to 1.5419)
P-value	-	0.1150
probability (95% CI)[c]		
2 Months	0.1740 (0.1167 to 0.2410)	0.1854 (0.1281 to 0.2511)
4 Months	0.0908 (0.0501 to 0.1463)	0.1143 (0.0691 to 0.1719)
6 Months	0.0825 (0.0439 to 0.1367)	0.0817 (0.0435 to 0.1352)
8 Months	0.0722 (0.0358 to 0.1256)	0.0545 (0.0238 to 0.1037)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12np_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.8 Non-progression treatment emergent mild adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1,2) without progression events	**Pd (N=149)**	**IPd (N=152)**
10 Months	0.0619 (0.0282 to 0.1142)	0.0545 (0.0238 to 0.1037)
12 Months	0.0495 (0.0193 to 0.1014)	0.0545 (0.0238 to 0.1037)
14 Months	0.0495 (0.0193 to 0.1014)	0.0545 (0.0238 to 0.1037)
16 Months	0.0495 (0.0193 to 0.1014)	0.0454 (0.0180 to 0.0926)
18 Months	0.0495 (0.0193 to 0.1014)	0.0454 (0.0180 to 0.0926)
20 Months	0.0371 (0.0116 to 0.0877)	0.0454 (0.0180 to 0.0926)
22 Months	0.0371 (0.0116 to 0.0877)	0.0454 (0.0180 to 0.0926)
24 Months	0.0371 (0.0116 to 0.0877)	0.0454 (0.0180 to 0.0926)
26 Months	0.0371 (0.0116 to 0.0877)	0.0454 (0.0180 to 0.0926)
Number of patients at risk[c]		
2 Months	23	27
4 Months	12	15
6 Months	8	9
8 Months	7	6
10 Months	5	6
12 Months	4	6
14 Months	4	6
16 Months	4	3
18 Months	4	3

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

16.2.7.1 Safety endpoints

16.2.7.1.8 Non-progression treatment emergent mild adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1,2) without progression events	Pd (N=149)	IPd (N=152)
20 Months	2	3
22 Months	2	3
24 Months	2	3
26 Months	1	2

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

16.2.7.1 Safety endpoints

16.2.7.1.9 Treatment emergent severe adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	110 (73.8)	135 (88.8)
Number (%) of patients censored	39 (26.2)	17 (11.2)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.5585 (0.3943 to 0.7556)	0.5257 (0.3614 to 0.5585)
Median (95% CI)	1.5770 (0.9856 to 2.9569)	0.8542 (0.7556 to 1.1499)
75% quantile (95% CI)	27.8275 (6.0452 to NC)	3.7782 (2.1355 to 6.1766)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0020
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.4922 (1.1553 to 1.9273)
P-value	-	0.0022
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6702 (0.5189 to 0.8656)	-
probability (95% CI)[c]		
2 Months	0.4701 (0.3877 to 0.5481)	0.3405 (0.2659 to 0.4164)
4 Months	0.3747 (0.2969 to 0.4523)	0.2319 (0.1678 to 0.3024)
6 Months	0.3254 (0.2510 to 0.4018)	0.1888 (0.1302 to 0.2560)
8 Months	0.3034 (0.2306 to 0.3791)	0.1598 (0.1056 to 0.2241)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints

16.2.7.1.9 Treatment emergent severe adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4)	**Pd (N=149)**	**IPd (N=152)**
10 Months	0.3034 (0.2306 to 0.3791)	0.1525 (0.0995 to 0.2160)
12 Months	0.3034 (0.2306 to 0.3791)	0.1445 (0.0928 to 0.2072)
14 Months	0.2863 (0.2146 to 0.3619)	0.1365 (0.0861 to 0.1984)
16 Months	0.2773 (0.2061 to 0.3529)	0.1204 (0.0730 to 0.1805)
18 Months	0.2773 (0.2061 to 0.3529)	0.1204 (0.0730 to 0.1805)
20 Months	0.2773 (0.2061 to 0.3529)	0.1019 (0.0579 to 0.1604)
22 Months	0.2773 (0.2061 to 0.3529)	0.0926 (0.0506 to 0.1500)
24 Months	0.2773 (0.2061 to 0.3529)	0.0926 (0.0506 to 0.1500)
26 Months	0.2532 (0.1822 to 0.3302)	0.0926 (0.0506 to 0.1500)
Number of patients at risk[c]		
2 Months	69	51
4 Months	55	33
6 Months	46	26
8 Months	39	22
10 Months	39	20
12 Months	36	18
14 Months	33	17
16 Months	30	15
18 Months	27	13
20 Months	25	11

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints

16.2.7.1.9 Treatment emergent severe adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4)	Pd (N=149)	IPd (N=152)
22 Months	24	9
24 Months	23	7
26 Months	20	6

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.10 Non-progression treatment emergent severe adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4) without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	110 (73.8)	135 (88.8)
Number (%) of patients censored	39 (26.2)	17 (11.2)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.5585 (0.3943 to 0.7556)	0.5257 (0.3614 to 0.5585)
Median (95% CI)	1.5770 (0.9856 to 2.9569)	0.8542 (0.7556 to 1.1499)
75% quantile (95% CI)	27.8275 (6.0452 to NC)	3.7782 (2.1355 to 6.9651)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0022
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.4866 (1.1510 to 1.9201)
P-value	-	0.0024
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6727 (0.5208 to 0.8688)	-
probability (95% CI)[c]		
2 Months	0.4701 (0.3877 to 0.5481)	0.3405 (0.2659 to 0.4164)
4 Months	0.3747 (0.2969 to 0.4523)	0.2319 (0.1678 to 0.3024)
6 Months	0.3254 (0.2510 to 0.4018)	0.1961 (0.1364 to 0.2639)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34np_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.10 Non-progression treatment emergent severe adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4) without progression events	**Pd (N=149)**	**IPd (N=152)**
8 Months	0.3034 (0.2306 to 0.3791)	0.1670 (0.1116 to 0.2321)
10 Months	0.3034 (0.2306 to 0.3791)	0.1598 (0.1056 to 0.2241)
12 Months	0.3034 (0.2306 to 0.3791)	0.1438 (0.0921 to 0.2066)
14 Months	0.2863 (0.2146 to 0.3619)	0.1358 (0.0855 to 0.1978)
16 Months	0.2773 (0.2061 to 0.3529)	0.1198 (0.0725 to 0.1800)
18 Months	0.2773 (0.2061 to 0.3529)	0.1198 (0.0725 to 0.1800)
20 Months	0.2773 (0.2061 to 0.3529)	0.1014 (0.0575 to 0.1598)
22 Months	0.2773 (0.2061 to 0.3529)	0.0922 (0.0502 to 0.1495)
24 Months	0.2773 (0.2061 to 0.3529)	0.0922 (0.0502 to 0.1495)
26 Months	0.2532 (0.1822 to 0.3302)	0.0922 (0.0502 to 0.1495)
Number of patients at risk[c]		
2 Months	69	51
4 Months	55	33
6 Months	46	27
8 Months	39	23
10 Months	39	21
12 Months	36	18
14 Months	33	17
16 Months	30	15

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34np_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.10 Non-progression treatment emergent severe adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4) without progression events	Pd (N=149)	IPd (N=152)
18 Months	27	13
20 Months	25	11
22 Months	24	9
24 Months	23	7
26 Months	20	6

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

16.2.7.1 Safety endpoints
16.2.7.1.11 Treatment emergent severe adverse event including death by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4,5)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	112 (75.2)	138 (90.8)
Number (%) of patients censored	37 (24.8)	14 (9.2)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.5421 (0.3285 to 0.7556)	0.5257 (0.3614 to 0.5585)
Median (95% CI)	1.5770 (0.9856 to 2.8255)	0.8542 (0.7556 to 1.1499)
75% quantile (95% CI)	24.8706 (5.5852 to NC)	3.6468 (2.1027 to 5.9795)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0015
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5027 (1.1663 to 1.9361)
P-value	-	0.0016
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6655 (0.5165 to 0.8574)	-
probability (95% CI)[c]		
2 Months	0.4662 (0.3842 to 0.5440)	0.3311 (0.2575 to 0.4064)
4 Months	0.3716 (0.2943 to 0.4488)	0.2241 (0.1613 to 0.2936)
6 Months	0.3166 (0.2433 to 0.3922)	0.1825 (0.1252 to 0.2484)
8 Months	0.2951 (0.2236 to 0.3700)	0.1544 (0.1016 to 0.2173)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.11 Treatment emergent severe adverse event including death by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4,5)	**Pd (N=149)**	**IPd (N=152)**
10 Months	0.2951 (0.2236 to 0.3700)	0.1404 (0.0901 to 0.2016)
12 Months	0.2951 (0.2236 to 0.3700)	0.1330 (0.0840 to 0.1933)
14 Months	0.2785 (0.2080 to 0.3531)	0.1256 (0.0780 to 0.1850)
16 Months	0.2698 (0.1999 to 0.3443)	0.1108 (0.0662 to 0.1682)
18 Months	0.2698 (0.1999 to 0.3443)	0.1108 (0.0662 to 0.1682)
20 Months	0.2698 (0.1999 to 0.3443)	0.0938 (0.0526 to 0.1492)
22 Months	0.2698 (0.1999 to 0.3443)	0.0852 (0.0460 to 0.1396)
24 Months	0.2698 (0.1999 to 0.3443)	0.0852 (0.0460 to 0.1396)
26 Months	0.2463 (0.1767 to 0.3222)	0.0852 (0.0460 to 0.1396)
Number of patients at risk[c]		
2 Months	69	50
4 Months	55	33
6 Months	46	26
8 Months	39	22
10 Months	39	20
12 Months	36	18
14 Months	33	17
16 Months	30	15
18 Months	27	13
20 Months	25	11

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.11 Treatment emergent severe adverse event including death by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4,5)	Pd (N=149)	IPd (N=152)
22 Months	24	9
24 Months	23	7
26 Months	20	6

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.12 Non-progression treatment emergent severe adverse event including death by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4,5) without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	112 (75.2)	138 (90.8)
Number (%) of patients censored	37 (24.8)	14 (9.2)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.5421 (0.3285 to 0.7556)	0.5257 (0.3614 to 0.5585)
Median (95% CI)	1.5770 (0.9856 to 2.8255)	0.8542 (0.7556 to 1.1499)
75% quantile (95% CI)	24.8706 (5.5852 to NC)	3.6468 (2.1027 to 6.1766)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0017
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.4972 (1.1621 to 1.9291)
P-value	-	0.0018
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6679 (0.5184 to 0.8605)	-
probability (95% CI)[c]		
2 Months	0.4662 (0.3842 to 0.5440)	0.3311 (0.2575 to 0.4064)
4 Months	0.3716 (0.2943 to 0.4488)	0.2241 (0.1613 to 0.2936)
6 Months	0.3166 (0.2433 to 0.3922)	0.1895 (0.1312 to 0.2561)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

16.2.7.1 Safety endpoints

16.2.7.1.12 Non-progression treatment emergent severe adverse event including death by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4,5) without progression events	**Pd (N=149)**	**IPd (N=152)**
8 Months	0.2951 (0.2236 to 0.3700)	0.1614 (0.1075 to 0.2252)
10 Months	0.2951 (0.2236 to 0.3700)	0.1474 (0.0958 to 0.2095)
12 Months	0.2951 (0.2236 to 0.3700)	0.1327 (0.0837 to 0.1930)
14 Months	0.2785 (0.2080 to 0.3531)	0.1253 (0.0777 to 0.1847)
16 Months	0.2698 (0.1999 to 0.3443)	0.1105 (0.0660 to 0.1679)
18 Months	0.2698 (0.1999 to 0.3443)	0.1105 (0.0660 to 0.1679)
20 Months	0.2698 (0.1999 to 0.3443)	0.0935 (0.0524 to 0.1490)
22 Months	0.2698 (0.1999 to 0.3443)	0.0850 (0.0459 to 0.1393)
24 Months	0.2698 (0.1999 to 0.3443)	0.0850 (0.0459 to 0.1393)
26 Months	0.2463 (0.1767 to 0.3222)	0.0850 (0.0459 to 0.1393)
Number of patients at risk[c]		
2 Months	69	50
4 Months	55	33
6 Months	46	27
8 Months	39	23
10 Months	39	21
12 Months	36	18
14 Months	33	17
16 Months	30	15

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

16.2.7.1 Safety endpoints

16.2.7.1.12 Non-progression treatment emergent severe adverse event including death by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4,5) without progression events	**Pd (N=149)**	**IPd (N=152)**
18 Months	27	13
20 Months	25	11
22 Months	24	9
24 Months	23	7
26 Months	20	6

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

16.2.7.1 Safety endpoints
16.2.7.1.13 Treatment emergent mild (grade 1) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	114 (76.5)	120 (78.9)
Number (%) of patients censored	35 (23.5)	32 (21.1)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.2957 (0.1314 to 0.3943)	0.2957 (0.2300 to 0.4600)
Median (95% CI)	0.8871 (0.7228 to 1.7741)	1.0513 (0.7228 to 2.0370)
75% quantile (95% CI)	8.5421 (3.2197 to 30.3573)	8.3778 (3.7454 to 27.4004)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.7270
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.9548 (0.7368 to 1.2373)
P-value	-	0.7267
probability (95% CI)[c]		
2 Months	0.3898 (0.3101 to 0.4686)	0.4268 (0.3473 to 0.5038)
4 Months	0.2993 (0.2255 to 0.3763)	0.3227 (0.2492 to 0.3984)
6 Months	0.2902 (0.2170 to 0.3672)	0.2685 (0.1988 to 0.3428)
8 Months	0.2702 (0.1979 to 0.3474)	0.2598 (0.1908 to 0.3340)
10 Months	0.2385 (0.1682 to 0.3160)	0.2338 (0.1671 to 0.3072)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev1_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.13 Treatment emergent mild (grade 1) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1)	**Pd (N=149)**	**IPd (N=152)**
12 Months	0.2260 (0.1561 to 0.3039)	0.2245 (0.1585 to 0.2977)
14 Months	0.1883 (0.1214 to 0.2666)	0.2151 (0.1500 to 0.2880)
16 Months	0.1883 (0.1214 to 0.2666)	0.2049 (0.1406 to 0.2777)
18 Months	0.1883 (0.1214 to 0.2666)	0.1941 (0.1308 to 0.2668)
20 Months	0.1883 (0.1214 to 0.2666)	0.1941 (0.1308 to 0.2668)
22 Months	0.1883 (0.1214 to 0.2666)	0.1941 (0.1308 to 0.2668)
24 Months	0.1883 (0.1214 to 0.2666)	0.1820 (0.1195 to 0.2549)
26 Months	0.1883 (0.1214 to 0.2666)	0.1820 (0.1195 to 0.2549)
Number of patients at risk[c]		
2 Months	54	63
4 Months	39	45
6 Months	29	31
8 Months	26	30
10 Months	21	25
12 Months	18	24
14 Months	15	23
16 Months	13	19
18 Months	11	18
20 Months	9	18
22 Months	9	16

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev1_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.13 Treatment emergent mild (grade 1) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1)	Pd (N=149)	IPd (N=152)
24 Months	9	14
26 Months	8	12

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev1_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.14 Non-progression treatment emergent mild (grade 1) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1) without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	113 (75.8)	120 (78.9)
Number (%) of patients censored	36 (24.2)	32 (21.1)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.2957 (0.1314 to 0.3943)	0.2957 (0.2300 to 0.4600)
Median (95% CI)	0.8871 (0.7228 to 1.7741)	1.0513 (0.7228 to 2.0370)
75% quantile (95% CI)	8.5421 (3.2197 to NC)	8.3778 (3.7454 to 27.4004)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.7995
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.9669 (0.7457 to 1.2536)
P-value	-	0.7993
probability (95% CI)[c]		
2 Months	0.3898 (0.3101 to 0.4686)	0.4268 (0.3473 to 0.5038)
4 Months	0.2993 (0.2255 to 0.3763)	0.3227 (0.2492 to 0.3984)
6 Months	0.2902 (0.2170 to 0.3672)	0.2685 (0.1988 to 0.3428)
8 Months	0.2702 (0.1979 to 0.3474)	0.2598 (0.1908 to 0.3340)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev1np_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.14 Non-progression treatment emergent mild (grade 1) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1) without progression events	**Pd (N=149)**	**IPd (N=152)**
10 Months	0.2385 (0.1682 to 0.3160)	0.2338 (0.1671 to 0.3072)
12 Months	0.2260 (0.1561 to 0.3039)	0.2245 (0.1585 to 0.2977)
14 Months	0.2009 (0.1328 to 0.2792)	0.2151 (0.1500 to 0.2880)
16 Months	0.2009 (0.1328 to 0.2792)	0.2049 (0.1406 to 0.2777)
18 Months	0.2009 (0.1328 to 0.2792)	0.1941 (0.1308 to 0.2668)
20 Months	0.2009 (0.1328 to 0.2792)	0.1941 (0.1308 to 0.2668)
22 Months	0.2009 (0.1328 to 0.2792)	0.1941 (0.1308 to 0.2668)
24 Months	0.2009 (0.1328 to 0.2792)	0.1820 (0.1195 to 0.2549)
26 Months	0.2009 (0.1328 to 0.2792)	0.1820 (0.1195 to 0.2549)
Number of patients at risk[c]		
2 Months	54	63
4 Months	39	45
6 Months	29	31
8 Months	26	30
10 Months	21	25
12 Months	18	24
14 Months	16	23
16 Months	14	19
18 Months	12	18

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev1np_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.14 Non-progression treatment emergent mild (grade 1) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1) without progression events	Pd (N=149)	IPd (N=152)
20 Months	10	18
22 Months	10	16
24 Months	10	14
26 Months	9	12

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev1np_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.15 Treatment emergent moderate (grade 2) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 2)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	122 (81.9)	136 (89.5)
Number (%) of patients censored	27 (18.1)	16 (10.5)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.4928 (0.3285 to 0.7228)	0.1314 (0.0986 to 0.1643)
Median (95% CI)	1.6427 (1.0513 to 2.0698)	0.5257 (0.2628 to 0.7885)
75% quantile (95% CI)	3.9754 (2.8255 to 7.8193)	2.5955 (1.4456 to 4.4353)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0007
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5369 (1.1957 to 1.9755)
P-value	-	0.0008
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6507 (0.5062 to 0.8363)	-
probability (95% CI)[c]		
2 Months	0.4539 (0.3705 to 0.5334)	0.2979 (0.2270 to 0.3718)
4 Months	0.2483 (0.1798 to 0.3226)	0.1946 (0.1354 to 0.2619)
6 Months	0.2073 (0.1435 to 0.2793)	0.1493 (0.0967 to 0.2127)
8 Months	0.1682 (0.1089 to 0.2386)	0.1161 (0.0693 to 0.1761)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev2_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.15 Treatment emergent moderate (grade 2) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 2)	**Pd (N=149)**	**IPd (N=152)**
10 Months	0.1682 (0.1089 to 0.2386)	0.0983 (0.0550 to 0.1563)
12 Months	0.1472 (0.0908 to 0.2165)	0.0983 (0.0550 to 0.1563)
14 Months	0.1472 (0.0908 to 0.2165)	0.0874 (0.0462 to 0.1448)
16 Months	0.1472 (0.0908 to 0.2165)	0.0764 (0.0377 to 0.1330)
18 Months	0.1472 (0.0908 to 0.2165)	0.0764 (0.0377 to 0.1330)
20 Months	0.1349 (0.0801 to 0.2041)	0.0764 (0.0377 to 0.1330)
22 Months	0.1349 (0.0801 to 0.2041)	0.0764 (0.0377 to 0.1330)
24 Months	0.1349 (0.0801 to 0.2041)	0.0764 (0.0377 to 0.1330)
26 Months	0.1199 (0.0667 to 0.1899)	0.0764 (0.0377 to 0.1330)
Number of patients at risk[c]		
2 Months	62	44
4 Months	33	27
6 Months	23	18
8 Months	17	13
10 Months	16	10
12 Months	14	9
14 Months	13	8
16 Months	12	5
18 Months	12	4
20 Months	10	4

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev2_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.15 Treatment emergent moderate (grade 2) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 2)	Pd (N=149)	IPd (N=152)
22 Months	9	4
24 Months	9	4
26 Months	7	3

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev2_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.16 Non-progression treatment emergent moderate (grade 2) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 2) without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	122 (81.9)	136 (89.5)
Number (%) of patients censored	27 (18.1)	16 (10.5)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.4928 (0.3285 to 0.7228)	0.1314 (0.0986 to 0.1643)
Median (95% CI)	1.6427 (1.0513 to 2.0698)	0.5257 (0.2628 to 0.7885)
75% quantile (95% CI)	3.9754 (2.8255 to 7.8193)	2.5955 (1.4456 to 4.4353)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0007
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5369 (1.1957 to 1.9755)
P-value	-	0.0008
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6507 (0.5062 to 0.8363)	-
probability (95% CI)[c]		
2 Months	0.4539 (0.3705 to 0.5334)	0.2979 (0.2270 to 0.3718)
4 Months	0.2483 (0.1798 to 0.3226)	0.1946 (0.1354 to 0.2619)
6 Months	0.2073 (0.1435 to 0.2793)	0.1493 (0.0967 to 0.2127)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev2np_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.16 Non-progression treatment emergent moderate (grade 2) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 2) without progression events	**Pd (N=149)**	**IPd (N=152)**
8 Months	0.1682 (0.1089 to 0.2386)	0.1161 (0.0693 to 0.1761)
10 Months	0.1682 (0.1089 to 0.2386)	0.0983 (0.0550 to 0.1563)
12 Months	0.1472 (0.0908 to 0.2165)	0.0983 (0.0550 to 0.1563)
14 Months	0.1472 (0.0908 to 0.2165)	0.0874 (0.0462 to 0.1448)
16 Months	0.1472 (0.0908 to 0.2165)	0.0764 (0.0377 to 0.1330)
18 Months	0.1472 (0.0908 to 0.2165)	0.0764 (0.0377 to 0.1330)
20 Months	0.1349 (0.0801 to 0.2041)	0.0764 (0.0377 to 0.1330)
22 Months	0.1349 (0.0801 to 0.2041)	0.0764 (0.0377 to 0.1330)
24 Months	0.1349 (0.0801 to 0.2041)	0.0764 (0.0377 to 0.1330)
26 Months	0.1199 (0.0667 to 0.1899)	0.0764 (0.0377 to 0.1330)
Number of patients at risk[c]		
2 Months	62	44
4 Months	33	27
6 Months	23	18
8 Months	17	13
10 Months	16	10
12 Months	14	9
14 Months	13	8
16 Months	12	5

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

16.2.7.1 Safety endpoints

16.2.7.1.16 Non-progression treatment emergent moderate (grade 2) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 2) without progression events	**Pd (N=149)**	**IPd (N=152)**
18 Months	12	4
20 Months	10	4
22 Months	9	4
24 Months	9	4
26 Months	7	3

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev2np_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.17 Treatment emergent severe (grade 3) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	95 (63.8)	125 (82.2)
Number (%) of patients censored	54 (36.2)	27 (17.8)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.7885 (0.5585 to 1.1499)	0.7556 (0.4928 to 1.0842)
Median (95% CI)	3.7454 (2.0370 to 8.3450)	2.1355 (1.7084 to 3.1540)
75% quantile (95% CI)	NC (24.8706 to NC)	9.5934 (5.8152 to 15.1458)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0086
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.4340 (1.0945 to 1.8787)
P-value	-	0.0089
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6974 (0.5323 to 0.9137)	-
probability (95% CI)[c]		
2 Months	0.5861 (0.5021 to 0.6607)	0.5206 (0.4378 to 0.5969)
4 Months	0.4896 (0.4064 to 0.5675)	0.3703 (0.2930 to 0.4475)
6 Months	0.4384 (0.3565 to 0.5172)	0.3118 (0.2384 to 0.3879)
8 Months	0.4223 (0.3406 to 0.5015)	0.2747 (0.2044 to 0.3493)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev3_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.17 Treatment emergent severe (grade 3) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3)	**Pd (N=149)**	**IPd (N=152)**
10 Months	0.4135 (0.3319 to 0.4930)	0.2371 (0.1708 to 0.3098)
12 Months	0.4043 (0.3228 to 0.4842)	0.2210 (0.1563 to 0.2928)
14 Months	0.3662 (0.2852 to 0.4474)	0.2040 (0.1412 to 0.2749)
16 Months	0.3557 (0.2748 to 0.4373)	0.1774 (0.1179 to 0.2468)
18 Months	0.3557 (0.2748 to 0.4373)	0.1669 (0.1086 to 0.2361)
20 Months	0.3557 (0.2748 to 0.4373)	0.1356 (0.0817 to 0.2032)
22 Months	0.3557 (0.2748 to 0.4373)	0.1356 (0.0817 to 0.2032)
24 Months	0.3557 (0.2748 to 0.4373)	0.1356 (0.0817 to 0.2032)
26 Months	0.3273 (0.2449 to 0.4120)	0.1356 (0.0817 to 0.2032)
Number of patients at risk[c]		
2 Months	86	78
4 Months	70	52
6 Months	57	42
8 Months	48	37
10 Months	47	31
12 Months	43	26
14 Months	37	24
16 Months	32	19
18 Months	29	16
20 Months	27	13

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints

16.2.7.1.17 Treatment emergent severe (grade 3) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3)	Pd (N=149)	IPd (N=152)
22 Months	26	12
24 Months	25	9
26 Months	22	7

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.18 Non-progression treatment emergent severe (grade 3) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3) without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	95 (63.8)	125 (82.2)
Number (%) of patients censored	54 (36.2)	27 (17.8)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.7885 (0.5585 to 1.1499)	0.7556 (0.4928 to 1.0842)
Median (95% CI)	3.7454 (2.0370 to 8.3450)	2.1355 (1.7084 to 3.1540)
75% quantile (95% CI)	NC (24.8706 to NC)	9.8234 (5.9795 to 15.1458)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0093
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.4285 (1.0902 to 1.8718)
P-value	-	0.0097
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.7000 (0.5342 to 0.9173)	-
probability (95% CI)[c]		
2 Months	0.5861 (0.5021 to 0.6607)	0.5206 (0.4378 to 0.5969)
4 Months	0.4896 (0.4064 to 0.5675)	0.3703 (0.2930 to 0.4475)
6 Months	0.4384 (0.3565 to 0.5172)	0.3192 (0.2452 to 0.3955)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev3np_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.18 Non-progression treatment emergent severe (grade 3) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3) without progression events	**Pd (N=149)**	**IPd (N=152)**
8 Months	0.4223 (0.3406 to 0.5015)	0.2821 (0.2112 to 0.3571)
10 Months	0.4135 (0.3319 to 0.4930)	0.2446 (0.1774 to 0.3177)
12 Months	0.4043 (0.3228 to 0.4842)	0.2205 (0.1559 to 0.2924)
14 Months	0.3662 (0.2852 to 0.4474)	0.2036 (0.1408 to 0.2746)
16 Months	0.3557 (0.2748 to 0.4373)	0.1770 (0.1176 to 0.2465)
18 Months	0.3557 (0.2748 to 0.4373)	0.1666 (0.1083 to 0.2358)
20 Months	0.3557 (0.2748 to 0.4373)	0.1354 (0.0815 to 0.2029)
22 Months	0.3557 (0.2748 to 0.4373)	0.1354 (0.0815 to 0.2029)
24 Months	0.3557 (0.2748 to 0.4373)	0.1354 (0.0815 to 0.2029)
26 Months	0.3273 (0.2449 to 0.4120)	0.1354 (0.0815 to 0.2029)
Number of patients at risk[c]		
2 Months	86	78
4 Months	70	52
6 Months	57	43
8 Months	48	38
10 Months	47	32
12 Months	43	26
14 Months	37	24
16 Months	32	19

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev3np_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.18 Non-progression treatment emergent severe (grade 3) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3) without progression events	Pd (N=149)	IPd (N=152)
18 Months	29	16
20 Months	27	13
22 Months	26	12
24 Months	25	9
26 Months	22	7

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

16.2.7.1 Safety endpoints
16.2.7.1.19 Treatment emergent severe (grade 4) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 4)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	50 (33.6)	69 (45.4)
Number (%) of patients censored	99 (66.4)	83 (54.6)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	2.8255 (0.8542 to 7.6222)	0.7556 (0.5914 to 0.8542)
Median (95% CI)	NC (NC to NC)	NC (7.7207 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0295
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5007 (1.0386 to 2.1683)
P-value	-	0.0306
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6664 (0.4612 to 0.9628)	-
probability (95% CI)[c]		
2 Months	0.7603 (0.6823 to 0.8216)	0.6402 (0.5579 to 0.7112)
4 Months	0.7244 (0.6438 to 0.7897)	0.5993 (0.5162 to 0.6728)
6 Months	0.6944 (0.6118 to 0.7629)	0.5993 (0.5162 to 0.6728)
8 Months	0.6783 (0.5945 to 0.7484)	0.5745 (0.4902 to 0.6499)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev4_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.19 Treatment emergent severe (grade 4) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 4)	**Pd (N=149)**	**IPd (N=152)**
10 Months	0.6783 (0.5945 to 0.7484)	0.5660 (0.4814 to 0.6421)
12 Months	0.6783 (0.5945 to 0.7484)	0.5566 (0.4714 to 0.6335)
14 Months	0.6687 (0.5839 to 0.7401)	0.5566 (0.4714 to 0.6335)
16 Months	0.6687 (0.5839 to 0.7401)	0.5465 (0.4605 to 0.6244)
18 Months	0.6687 (0.5839 to 0.7401)	0.5465 (0.4605 to 0.6244)
20 Months	0.6687 (0.5839 to 0.7401)	0.5465 (0.4605 to 0.6244)
22 Months	0.6687 (0.5839 to 0.7401)	0.5343 (0.4470 to 0.6139)
24 Months	0.6561 (0.5690 to 0.7298)	0.5206 (0.4315 to 0.6024)
26 Months	0.6561 (0.5690 to 0.7298)	0.5206 (0.4315 to 0.6024)
Number of patients at risk[c]		
2 Months	109	95
4 Months	100	85
6 Months	90	75
8 Months	80	69
10 Months	77	62
12 Months	71	58
14 Months	67	57
16 Months	62	53
18 Months	56	49
20 Months	54	47

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints

16.2.7.1.19 Treatment emergent severe (grade 4) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 4)	Pd (N=149)	IPd (N=152)
22 Months	53	41
24 Months	51	38
26 Months	49	36

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.20 Non-progression treatment emergent severe (grade 4) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 4) without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	50 (33.6)	69 (45.4)
Number (%) of patients censored	99 (66.4)	83 (54.6)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	2.8255 (0.8542 to 7.6222)	0.7556 (0.5914 to 0.8542)
Median (95% CI)	NC (NC to NC)	NC (7.7207 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0295
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5007 (1.0386 to 2.1683)
P-value	-	0.0306
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6664 (0.4612 to 0.9628)	-
probability (95% CI)[c]		
2 Months	0.7603 (0.6823 to 0.8216)	0.6402 (0.5579 to 0.7112)
4 Months	0.7244 (0.6438 to 0.7897)	0.5993 (0.5162 to 0.6728)
6 Months	0.6944 (0.6118 to 0.7629)	0.5993 (0.5162 to 0.6728)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev4np_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.20 Non-progression treatment emergent severe (grade 4) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 4) without progression events	**Pd (N=149)**	**IPd (N=152)**
8 Months	0.6783 (0.5945 to 0.7484)	0.5745 (0.4902 to 0.6499)
10 Months	0.6783 (0.5945 to 0.7484)	0.5660 (0.4814 to 0.6421)
12 Months	0.6783 (0.5945 to 0.7484)	0.5566 (0.4714 to 0.6335)
14 Months	0.6687 (0.5839 to 0.7401)	0.5566 (0.4714 to 0.6335)
16 Months	0.6687 (0.5839 to 0.7401)	0.5465 (0.4605 to 0.6244)
18 Months	0.6687 (0.5839 to 0.7401)	0.5465 (0.4605 to 0.6244)
20 Months	0.6687 (0.5839 to 0.7401)	0.5465 (0.4605 to 0.6244)
22 Months	0.6687 (0.5839 to 0.7401)	0.5343 (0.4470 to 0.6139)
24 Months	0.6561 (0.5690 to 0.7298)	0.5206 (0.4315 to 0.6024)
26 Months	0.6561 (0.5690 to 0.7298)	0.5206 (0.4315 to 0.6024)
Number of patients at risk[c]		
2 Months	109	95
4 Months	100	85
6 Months	90	75
8 Months	80	69
10 Months	77	62
12 Months	71	58
14 Months	67	57
16 Months	62	53

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev4np_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.20 Non-progression treatment emergent severe (grade 4) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 4) without progression events	**Pd (N=149)**	**IPd (N=152)**
18 Months	56	49
20 Months	54	47
22 Months	53	41
24 Months	51	38
26 Months	49	36

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev4np_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.21 Treatment emergent severe (grade 5) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 5)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	15 (10.1)	14 (9.2)
Number (%) of patients censored	134 (89.9)	138 (90.8)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6414
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.8407 (0.4052 to 1.7443)
P-value	-	0.6412
probability (95% CI)[c]		
2 Months	0.9530 (0.9040 to 0.9773)	0.9671 (0.9228 to 0.9862)
4 Months	0.9322 (0.8776 to 0.9629)	0.9605 (0.9142 to 0.9820)
6 Months	0.9106 (0.8510 to 0.9471)	0.9331 (0.8793 to 0.9635)
8 Months	0.9106 (0.8510 to 0.9471)	0.9257 (0.8698 to 0.9582)
10 Months	0.9106 (0.8510 to 0.9471)	0.9179 (0.8597 to 0.9526)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev5_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.21 Treatment emergent severe (grade 5) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 5)	**Pd (N=149)**	**IPd (N=152)**
12 Months	0.9106 (0.8510 to 0.9471)	0.9179 (0.8597 to 0.9526)
14 Months	0.9006 (0.8372 to 0.9402)	0.9179 (0.8597 to 0.9526)
16 Months	0.9006 (0.8372 to 0.9402)	0.9179 (0.8597 to 0.9526)
18 Months	0.9006 (0.8372 to 0.9402)	0.9179 (0.8597 to 0.9526)
20 Months	0.9006 (0.8372 to 0.9402)	0.9078 (0.8456 to 0.9457)
22 Months	0.9006 (0.8372 to 0.9402)	0.9078 (0.8456 to 0.9457)
24 Months	0.9006 (0.8372 to 0.9402)	0.9078 (0.8456 to 0.9457)
26 Months	0.9006 (0.8372 to 0.9402)	0.9078 (0.8456 to 0.9457)
Number of patients at risk[c]		
2 Months	141	147
4 Months	132	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints

16.2.7.1.21 Treatment emergent severe (grade 5) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 5)	Pd (N=149)	IPd (N=152)
24 Months	65	75
26 Months	62	69

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.22 Non-progression treatment emergent severe (grade 5) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 5) without progression events	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	15 (10.1)	13 (8.6)
Number (%) of patients censored	134 (89.9)	139 (91.4)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5490
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.7970 (0.3791 to 1.6759)
P-value	-	0.5497
probability (95% CI)[c]		
2 Months	0.9530 (0.9040 to 0.9773)	0.9671 (0.9228 to 0.9862)
4 Months	0.9322 (0.8776 to 0.9629)	0.9605 (0.9142 to 0.9820)
6 Months	0.9106 (0.8510 to 0.9471)	0.9331 (0.8793 to 0.9635)
8 Months	0.9106 (0.8510 to 0.9471)	0.9257 (0.8698 to 0.9582)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev5np_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.22 Non-progression treatment emergent severe (grade 5) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 5) without progression events	**Pd (N=149)**	**IPd (N=152)**
10 Months	0.9106 (0.8510 to 0.9471)	0.9179 (0.8597 to 0.9526)
12 Months	0.9106 (0.8510 to 0.9471)	0.9179 (0.8597 to 0.9526)
14 Months	0.9006 (0.8372 to 0.9402)	0.9179 (0.8597 to 0.9526)
16 Months	0.9006 (0.8372 to 0.9402)	0.9179 (0.8597 to 0.9526)
18 Months	0.9006 (0.8372 to 0.9402)	0.9179 (0.8597 to 0.9526)
20 Months	0.9006 (0.8372 to 0.9402)	0.9179 (0.8597 to 0.9526)
22 Months	0.9006 (0.8372 to 0.9402)	0.9179 (0.8597 to 0.9526)
24 Months	0.9006 (0.8372 to 0.9402)	0.9179 (0.8597 to 0.9526)
26 Months	0.9006 (0.8372 to 0.9402)	0.9179 (0.8597 to 0.9526)
Number of patients at risk[c]		
2 Months	141	147
4 Months	132	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98
18 Months	72	91

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev5np_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.22 Non-progression treatment emergent severe (grade 5) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 5) without progression events	Pd (N=149)	IPd (N=152)
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

16.2.7.1 Safety endpoints
16.2.7.1.23 Treatment emergent adverse event of interest by treatment group - Safety population

Any treatment emergent AESI	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	1 (0.7)	14 (9.2)
Number (%) of patients censored	148 (99.3)	138 (90.8)
Kaplan-Meier estimates of AESI in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0018
Stratified[a] Hazard ratio (95% CI) vs Pd	-	12.4535 (1.6340 to 94.9113)
P-value	-	0.0149
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.0803 (0.0105 to 0.6120)	-
probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	0.9671 (0.9227 to 0.9862)
4 Months	1.0000 (1.0000 to 1.0000)	0.9602 (0.9135 to 0.9819)
6 Months	1.0000 (1.0000 to 1.0000)	0.9451 (0.8930 to 0.9722)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsiae_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.23 Treatment emergent adverse event of interest by treatment group - Safety population

Any treatment emergent AESI	**Pd (N=149)**	**IPd (N=152)**
8 Months	1.0000 (1.0000 to 1.0000)	0.9371 (0.8824 to 0.9669)
10 Months	1.0000 (1.0000 to 1.0000)	0.9371 (0.8824 to 0.9669)
12 Months	1.0000 (1.0000 to 1.0000)	0.9285 (0.8706 to 0.9610)
14 Months	0.9889 (0.9237 to 0.9984)	0.9285 (0.8706 to 0.9610)
16 Months	0.9889 (0.9237 to 0.9984)	0.9285 (0.8706 to 0.9610)
18 Months	0.9889 (0.9237 to 0.9984)	0.9183 (0.8561 to 0.9543)
20 Months	0.9889 (0.9237 to 0.9984)	0.9073 (0.8408 to 0.9469)
22 Months	0.9889 (0.9237 to 0.9984)	0.8957 (0.8246 to 0.9390)
24 Months	0.9889 (0.9237 to 0.9984)	0.8957 (0.8246 to 0.9390)
26 Months	0.9889 (0.9237 to 0.9984)	0.8821 (0.8052 to 0.9300)
Number of patients at risk[c]		
2 Months	142	145
4 Months	134	137
6 Months	117	123
8 Months	106	117
10 Months	102	110
12 Months	93	102
14 Months	86	101
16 Months	79	92

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsiae_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.23 Treatment emergent adverse event of interest by treatment group - Safety population

Any treatment emergent AESI	Pd (N=149)	IPd (N=152)
18 Months	71	84
20 Months	67	80
22 Months	65	73
24 Months	64	70
26 Months	61	64

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy

PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsiae_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.24 Treatment emergent serious adverse event of interest by treatment group - Safety population

Any serious treatment emergent AESI	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	0 (0.0)	11 (7.2)
Number (%) of patients censored	149 (100.0)	141 (92.8)
Kaplan-Meier estimates of AESI in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0021
Stratified[a] Hazard ratio (95% CI) vs Pd	-	. (. to .)
P-value	-	0.9918
probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	0.9671 (0.9227 to 0.9862)
4 Months	1.0000 (1.0000 to 1.0000)	0.9602 (0.9135 to 0.9819)
6 Months	1.0000 (1.0000 to 1.0000)	0.9526 (0.9031 to 0.9772)
8 Months	1.0000 (1.0000 to 1.0000)	0.9447 (0.8922 to 0.9720)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsiser_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.24 Treatment emergent serious adverse event of interest by treatment group - Safety population

Any serious treatment emergent AESI	**Pd (N=149)**	**IPd (N=152)**
10 Months	1.0000 (1.0000 to 1.0000)	0.9447 (0.8922 to 0.9720)
12 Months	1.0000 (1.0000 to 1.0000)	0.9447 (0.8922 to 0.9720)
14 Months	1.0000 (1.0000 to 1.0000)	0.9447 (0.8922 to 0.9720)
16 Months	1.0000 (1.0000 to 1.0000)	0.9447 (0.8922 to 0.9720)
18 Months	1.0000 (1.0000 to 1.0000)	0.9345 (0.8769 to 0.9657)
20 Months	1.0000 (1.0000 to 1.0000)	0.9237 (0.8609 to 0.9588)
22 Months	1.0000 (1.0000 to 1.0000)	0.9237 (0.8609 to 0.9588)
24 Months	1.0000 (1.0000 to 1.0000)	0.9237 (0.8609 to 0.9588)
26 Months	1.0000 (1.0000 to 1.0000)	0.9099 (0.8393 to 0.9504)
Number of patients at risk[c]		
2 Months	142	145
4 Months	134	137
6 Months	117	124
8 Months	106	118
10 Months	102	111
12 Months	93	104
14 Months	87	103
16 Months	80	94
18 Months	72	86

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsiser_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.24 Treatment emergent serious adverse event of interest by treatment group - Safety population

Any serious treatment emergent AESI	**Pd (N=149)**	**IPd (N=152)**
20 Months	68	82
22 Months	66	74
24 Months	65	71
26 Months	62	65

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy

PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsiser_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.25 Treatment emergent severe (grade 3,4) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 3,4)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	0 (0.0)	11 (7.2)
Number (%) of patients censored	149 (100.0)	141 (92.8)
Kaplan-Meier estimates of AESI in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0020
Stratified[a] Hazard ratio (95% CI) vs Pd	-	. (. to .)
P-value	-	0.9918
probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	0.9671 (0.9227 to 0.9862)
4 Months	1.0000 (1.0000 to 1.0000)	0.9671 (0.9227 to 0.9862)
6 Months	1.0000 (1.0000 to 1.0000)	0.9594 (0.9118 to 0.9816)
8 Months	1.0000 (1.0000 to 1.0000)	0.9515 (0.9006 to 0.9766)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsisv34_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.25 Treatment emergent severe (grade 3,4) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 3,4)	**Pd (N=149)**	**IPd (N=152)**
10 Months	1.0000 (1.0000 to 1.0000)	0.9515 (0.9006 to 0.9766)
12 Months	1.0000 (1.0000 to 1.0000)	0.9427 (0.8882 to 0.9711)
14 Months	1.0000 (1.0000 to 1.0000)	0.9427 (0.8882 to 0.9711)
16 Months	1.0000 (1.0000 to 1.0000)	0.9427 (0.8882 to 0.9711)
18 Months	1.0000 (1.0000 to 1.0000)	0.9325 (0.8730 to 0.9647)
20 Months	1.0000 (1.0000 to 1.0000)	0.9215 (0.8571 to 0.9576)
22 Months	1.0000 (1.0000 to 1.0000)	0.9215 (0.8571 to 0.9576)
24 Months	1.0000 (1.0000 to 1.0000)	0.9215 (0.8571 to 0.9576)
26 Months	1.0000 (1.0000 to 1.0000)	0.9215 (0.8571 to 0.9576)
Number of patients at risk[c]		
2 Months	142	145
4 Months	134	138
6 Months	117	124
8 Months	106	118
10 Months	102	111
12 Months	93	103
14 Months	87	102
16 Months	80	93
18 Months	72	85

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy

16.2.7.1 Safety endpoints

16.2.7.1.25 Treatment emergent severe (grade 3,4) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 3,4)	**Pd (N=149)**	**IPd (N=152)**
20 Months	68	81
22 Months	66	73
24 Months	65	70
26 Months	62	65

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy

16.2.7.1 Safety endpoints

16.2.7.1.26 Treatment emergent not severe (grade 1) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 1)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	0 (0.0)	0 (0.0)
Number (%) of patients censored	149 (100.0)	152 (100.0)
Kaplan-Meier estimates of AESI in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Hazard ratio (95% CI) vs Pd	-	. (. to .)
probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy

16.2.7.1 Safety endpoints
16.2.7.1.26 Treatment emergent not severe (grade 1) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 1)	**Pd (N=149)**	**IPd (N=152)**
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
18 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
20 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
22 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
24 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
26 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsisv1_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.26 Treatment emergent not severe (grade 1) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 1)	**Pd (N=149)**	**IPd (N=152)**
24 Months	65	75
26 Months	62	69

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy

16.2.7.1 Safety endpoints
16.2.7.1.27 Treatment emergent not severe (grade 2) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 2)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	1 (0.7)	5 (3.3)
Number (%) of patients censored	148 (99.3)	147 (96.7)
Kaplan-Meier estimates of AESI in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1937
Stratified[a] Hazard ratio (95% CI) vs Pd	-	3.7840 (0.4386 to 32.6442)
P-value	-	0.2261
probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	0.9931 (0.9521 to 0.9990)
6 Months	1.0000 (1.0000 to 1.0000)	0.9778 (0.9327 to 0.9928)
8 Months	1.0000 (1.0000 to 1.0000)	0.9778 (0.9327 to 0.9928)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsisv2_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.27 Treatment emergent not severe (grade 2) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 2)	**Pd (N=149)**	**IPd (N=152)**
10 Months	1.0000 (1.0000 to 1.0000)	0.9778 (0.9327 to 0.9928)
12 Months	1.0000 (1.0000 to 1.0000)	0.9778 (0.9327 to 0.9928)
14 Months	0.9889 (0.9237 to 0.9984)	0.9778 (0.9327 to 0.9928)
16 Months	0.9889 (0.9237 to 0.9984)	0.9778 (0.9327 to 0.9928)
18 Months	0.9889 (0.9237 to 0.9984)	0.9778 (0.9327 to 0.9928)
20 Months	0.9889 (0.9237 to 0.9984)	0.9778 (0.9327 to 0.9928)
22 Months	0.9889 (0.9237 to 0.9984)	0.9660 (0.9098 to 0.9875)
24 Months	0.9889 (0.9237 to 0.9984)	0.9660 (0.9098 to 0.9875)
26 Months	0.9889 (0.9237 to 0.9984)	0.9520 (0.8844 to 0.9805)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	140
6 Months	117	126
8 Months	106	121
10 Months	102	114
12 Months	93	107
14 Months	86	106
16 Months	79	96
18 Months	71	89

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsisv2_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.27 Treatment emergent not severe (grade 2) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 2)	Pd (N=149)	IPd (N=152)
20 Months	67	85
22 Months	65	77
24 Months	64	74
26 Months	61	67

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy

16.2.7.1 Safety endpoints
16.2.7.1.28 Treatment emergent severe (grade 3) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 3)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	0 (0.0)	8 (5.3)
Number (%) of patients censored	149 (100.0)	144 (94.7)
Kaplan-Meier estimates of AESI in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0108
Stratified[a] Hazard ratio (95% CI) vs Pd	-	. (. to .)
P-value	-	0.9931
probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	0.9802 (0.9399 to 0.9936)
4 Months	1.0000 (1.0000 to 1.0000)	0.9802 (0.9399 to 0.9936)
6 Months	1.0000 (1.0000 to 1.0000)	0.9726 (0.9284 to 0.9896)
8 Months	1.0000 (1.0000 to 1.0000)	0.9726 (0.9284 to 0.9896)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsisv3_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.28 Treatment emergent severe (grade 3) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 3)	**Pd (N=149)**	**IPd (N=152)**
10 Months	1.0000 (1.0000 to 1.0000)	0.9726 (0.9284 to 0.9896)
12 Months	1.0000 (1.0000 to 1.0000)	0.9638 (0.9146 to 0.9849)
14 Months	1.0000 (1.0000 to 1.0000)	0.9638 (0.9146 to 0.9849)
16 Months	1.0000 (1.0000 to 1.0000)	0.9638 (0.9146 to 0.9849)
18 Months	1.0000 (1.0000 to 1.0000)	0.9534 (0.8979 to 0.9791)
20 Months	1.0000 (1.0000 to 1.0000)	0.9423 (0.8808 to 0.9726)
22 Months	1.0000 (1.0000 to 1.0000)	0.9423 (0.8808 to 0.9726)
24 Months	1.0000 (1.0000 to 1.0000)	0.9423 (0.8808 to 0.9726)
26 Months	1.0000 (1.0000 to 1.0000)	0.9423 (0.8808 to 0.9726)
Number of patients at risk[c]		
2 Months	142	147
4 Months	134	139
6 Months	117	125
8 Months	106	120
10 Months	102	113
12 Months	93	105
14 Months	87	104
16 Months	80	94
18 Months	72	86

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsisv3_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.28 Treatment emergent severe (grade 3) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 3)	Pd (N=149)	IPd (N=152)
20 Months	68	82
22 Months	66	73
24 Months	65	70
26 Months	62	65

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy

PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsisv3_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.29 Treatment emergent severe (grade 4) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 4)	**Pd (N=149)**	**IPd (N=152)**
Number (%) of events	0 (0.0)	3 (2.0)
Number (%) of patients censored	149 (100.0)	149 (98.0)
Kaplan-Meier estimates of AESI in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0875
Stratified[a] Hazard ratio (95% CI) vs Pd	-	. (. to .)
P-value	-	0.9956
probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	0.9868 (0.9484 to 0.9967)
4 Months	1.0000 (1.0000 to 1.0000)	0.9868 (0.9484 to 0.9967)
6 Months	1.0000 (1.0000 to 1.0000)	0.9868 (0.9484 to 0.9967)
8 Months	1.0000 (1.0000 to 1.0000)	0.9788 (0.9354 to 0.9932)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsisv4_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints
16.2.7.1.29 Treatment emergent severe (grade 4) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 4)	**Pd (N=149)**	**IPd (N=152)**
10 Months	1.0000 (1.0000 to 1.0000)	0.9788 (0.9354 to 0.9932)
12 Months	1.0000 (1.0000 to 1.0000)	0.9788 (0.9354 to 0.9932)
14 Months	1.0000 (1.0000 to 1.0000)	0.9788 (0.9354 to 0.9932)
16 Months	1.0000 (1.0000 to 1.0000)	0.9788 (0.9354 to 0.9932)
18 Months	1.0000 (1.0000 to 1.0000)	0.9788 (0.9354 to 0.9932)
20 Months	1.0000 (1.0000 to 1.0000)	0.9788 (0.9354 to 0.9932)
22 Months	1.0000 (1.0000 to 1.0000)	0.9788 (0.9354 to 0.9932)
24 Months	1.0000 (1.0000 to 1.0000)	0.9788 (0.9354 to 0.9932)
26 Months	1.0000 (1.0000 to 1.0000)	0.9788 (0.9354 to 0.9932)
Number of patients at risk[c]		
2 Months	142	147
4 Months	134	140
6 Months	117	127
8 Months	106	121
10 Months	102	114
12 Months	93	107
14 Months	87	106
16 Months	80	97
18 Months	72	90

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsisv4_s_t_x.rtf (16NOV2020 12:46)

16.2.7.1 Safety endpoints

16.2.7.1.29 Treatment emergent severe (grade 4) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 4)	**Pd (N=149)**	**IPd (N=152)**
20 Months	68	86
22 Months	66	78
24 Months	65	75
26 Months	62	69

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle

[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT

[b] One-sided significance level is 0.025

[c] Estimated using the Kaplan-Meier method

Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy

16.2.7.1 Safety endpoints
16.2.7.1.30 Subgroup analysis
16.2.7.1.30.1 Listing of subgroup interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent adverse event	**Treatment emergent serious adverse event**	**Any treatment emergent by severity (Grade 1,2)**	**Any treatment emergent by severity (Grade 3,4)**	**Any treatment emergent by severity (Grade 3,4,5)**	**Any treatment emergent leading to discontinuation of treatment**
Age	0.2501	0.7615	0.8434	0.4851	0.4811	0.7005
Number of previous lines of therapy (IRT)	0.5772	0.0726	0.8884	0.8552	0.7080	0.1754
Gender	0.5969	0.5475	0.1735	0.7550	0.7574	0.1985
Race	0.9137	0.8949	0.6782	0.4896	0.4629	0.3000
Ethnicity	0.6260	0.8212	0.4291	0.9667	0.4928	0.9850
Geographical region	0.4768	0.6939	0.5449	0.3403	0.3108	0.3794
Regulatory region	0.4045	0.6159	0.7320	0.0978	0.0754	0.0456
ECOG PS	0.5869	0.0012	0.6767	0.5789	0.7319	0.2115
ISS staging at study entry	0.2162	0.6813	0.5485	0.1748	0.1179	0.4473
R-ISS staging	0.4136	0.3972	0.6844	0.0111	0.0164	0.9491
Cytogenetic abnormality	0.2003	0.0508	0.8584	0.0330	0.0111	0.1289
Cytogenetic abnormality del(17p)	0.2734	0.5658	0.8038	0.5660	0.2828	0.3316
Previous autologous stem-cell transplantation	0.8309	0.3771	0.9933	0.7137	0.8736	0.7312
Previous allogenic transplantation	0.7014	0.5644	0.5610	0.6295	0.6328	0.9999
MM type	0.0124	0.2290	0.0132	0.1414	0.1980	0.9805
Existing plasmacytoma	0.8454	0.3182	0.2611	0.4822	0.3233	0.9864
Baseline creatinine clearance	0.2390	0.1542	0.4672	0.2707	0.3448	0.8184
Previous therapy with anti-CD38 mAB	0.3528	0.5015	0.4575	0.0036	0.0035	0.9881
Refractory to PI	0.1579	0.0107	0.1289	0.6877	0.5781	0.8728
Refractory to IMiD	0.7979	0.6478	0.8839	0.5231	0.5173	0.9901
Refractory to lenalidomide in last previous regimen	0.0494	0.2582	0.0352	0.3628	0.2646	0.4620

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.31 Subgroup analysis by regulatory region
16.2.7.1.31.1 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	11 (11.7)	2 (2.6)	10 (18.2)	16 (21.3)	0.0456
Number (%) of patients censored	83 (88.3)	75 (97.4)	45 (81.8)	59 (78.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.1622 to NC)	29.0103 (14.9158 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd		0.0137		0.7580	
Stratified[a] Hazard ratio (95% CI) vs Pd		0.1768 (0.0381 to 0.8195)		1.1330 (0.5117 to 2.5086)	
P-value		0.0268		0.7582	
probability (95% CI)[c]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_region2_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.31 Subgroup analysis by regulatory region
16.2.7.1.31.1 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[d]**
2 Months	0.9144 (0.8361 to 0.9562)	1.0000 (1.0000 to 1.0000)	0.9091 (0.7953 to 0.9611)	0.9867 (0.9091 to 0.9981)	
4 Months	0.9032 (0.8222 to 0.9485)	1.0000 (1.0000 to 1.0000)	0.9091 (0.7953 to 0.9611)	0.9461 (0.8628 to 0.9794)	
6 Months	0.8801 (0.7938 to 0.9318)	0.9857 (0.9029 to 0.9980)	0.8902 (0.7716 to 0.9491)	0.9187 (0.8279 to 0.9626)	
8 Months	0.8801 (0.7938 to 0.9318)	0.9857 (0.9029 to 0.9980)	0.8684 (0.7431 to 0.9352)	0.9041 (0.8092 to 0.9531)	
10 Months	0.8801 (0.7938 to 0.9318)	0.9857 (0.9029 to 0.9980)	0.8684 (0.7431 to 0.9352)	0.8888 (0.7896 to 0.9429)	
12 Months	0.8801 (0.7938 to 0.9318)	0.9857 (0.9029 to 0.9980)	0.8684 (0.7431 to 0.9352)	0.8729 (0.7695 to 0.9319)	
14 Months	0.8801 (0.7938 to 0.9318)	0.9857 (0.9029 to 0.9980)	0.8188 (0.6779 to 0.9023)	0.8729 (0.7695 to 0.9319)	
16 Months	0.8801 (0.7938 to 0.9318)	0.9857 (0.9029 to 0.9980)	0.8188 (0.6779 to 0.9023)	0.8195 (0.7022 to 0.8940)	
18 Months	0.8801 (0.7938 to 0.9318)	0.9857 (0.9029 to 0.9980)	0.8188 (0.6779 to 0.9023)	0.8195 (0.7022 to 0.8940)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_region2_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.31 Subgroup analysis by regulatory region
16.2.7.1.31.1 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[d]**
20 Months	0.8801 (0.7938 to 0.9318)	0.9633 (0.8564 to 0.9910)	0.8188 (0.6779 to 0.9023)	0.8000 (0.6781 to 0.8797)	
22 Months	0.8801 (0.7938 to 0.9318)	0.9633 (0.8564 to 0.9910)	0.8188 (0.6779 to 0.9023)	0.7795 (0.6529 to 0.8645)	
24 Months	0.8801 (0.7938 to 0.9318)	0.9633 (0.8564 to 0.9910)	0.8188 (0.6779 to 0.9023)	0.7795 (0.6529 to 0.8645)	
26 Months	0.8801 (0.7938 to 0.9318)	0.9633 (0.8564 to 0.9910)	0.8188 (0.6779 to 0.9023)	0.7795 (0.6529 to 0.8645)	
Number of patients at risk[c]					
2 Months	83	75	50	73	
4 Months	78	70	49	69	
6 Months	72	61	41	65	
8 Months	63	59	40	61	
10 Months	61	56	38	57	
12 Months	56	52	35	53	
14 Months	53	52	31	52	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_region2_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.31 Subgroup analysis by regulatory region
16.2.7.1.31.1 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to regulatory region - Safety population

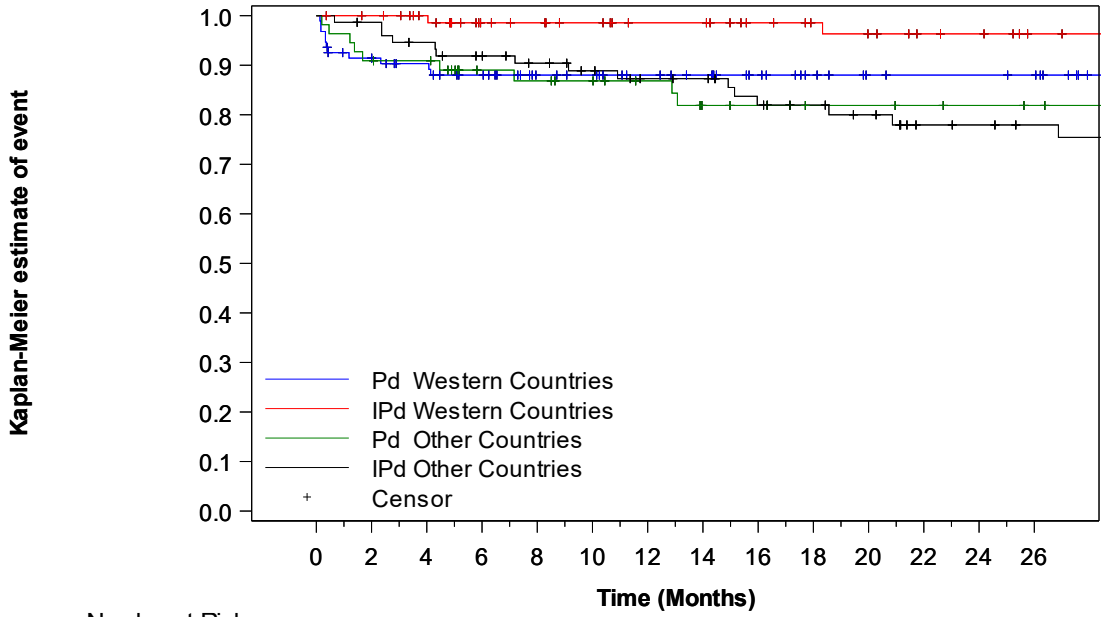
	Western countries		Other countries		
	Pd (N=94)	**IPd (N=77)**	**Pd (N=55)**	**IPd (N=75)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	47	47	30	46	
18 Months	42	44	27	43	
20 Months	38	42	27	40	
22 Months	37	39	26	34	
24 Months	37	38	25	33	
26 Months	36	34	24	31	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_region2_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints

16.2.7.1.31 Subgroup analysis by regulatory region

16.2.7.1.31.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment by treatment group according to regulatory region - Safety population



Number at Risk														
Pd Western Countries	94	83	78	72	63	61	56	53	47	42	38	37	37	36
IPd Western Countries	77	75	70	61	59	56	52	52	47	44	42	39	38	34
Pd Other Countries	55	50	49	41	40	38	35	31	30	27	27	26	25	24
IPd Other Countries	75	73	69	65	61	57	53	52	46	43	40	34	33	31

16.2.7.1 Safety endpoints
16.2.7.1.32 Subgroup analysis by baseline ECOG PS
16.2.7.1.32.1 Treatment emergent serious adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	81 (60.0)	95 (69.9)	9 (64.3)	16 (100.0)	0.0012
Number (%) of patients censored	54 (40.0)	41 (30.1)	5 (35.7)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.3142 (0.5914 to 1.9384)	1.3799 (0.5585 to 2.2669)	1.7741 (0.4271 to 6.5708)	0.1314 (0.0657 to 0.4271)	
Median (95% CI)	6.0452 (3.6140 to 22.3737)	8.3450 (4.1725 to 11.3018)	6.5708 (0.7556 to NC)	0.4271 (0.1314 to 1.0185)	
75% quantile (95% CI)	NC (NC to NC)	35.7782 (20.1068 to NC)	31.3758 (6.5708 to NC)	1.1499 (0.4271 to 8.6078)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd		0.4188		0.0102	
Stratified[a] Hazard ratio (95% CI) vs Pd		1.1309 (0.8386 to 1.5253)		3.7376 (1.2943 to 10.7936)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_ecog_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.32 Subgroup analysis by baseline ECOG PS
16.2.7.1.32.1 Treatment emergent serious adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[d]**
P-value		0.4201		0.0148	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.2675 (0.0926 to 0.7726)		
probability (95% CI)[c]					
2 Months	0.6741 (0.5880 to 0.7461)	0.7059 (0.6215 to 0.7748)	0.7143 (0.4063 to 0.8819)	0.1333 (0.0219 to 0.3457)	
4 Months	0.5767 (0.4887 to 0.6550)	0.6019 (0.5144 to 0.6787)	0.6429 (0.3433 to 0.8331)	0.1333 (0.0219 to 0.3457)	
6 Months	0.5076 (0.4200 to 0.5887)	0.5415 (0.4538 to 0.6212)	0.5625 (0.2718 to 0.7756)	0.0667 (0.0043 to 0.2603)	
8 Months	0.4918 (0.4043 to 0.5733)	0.5110 (0.4236 to 0.5917)	0.3750 (0.1254 to 0.6292)	0.0667 (0.0043 to 0.2603)	
10 Months	0.4918 (0.4043 to 0.5733)	0.4576 (0.3716 to 0.5394)	0.3750 (0.1254 to 0.6292)	0.0667 (0.0043 to 0.2603)	
12 Months	0.4745 (0.3872 to 0.5567)	0.4024 (0.3186 to 0.4845)	0.3750 (0.1254 to 0.6292)	0.0667 (0.0043 to 0.2603)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.32 Subgroup analysis by baseline ECOG PS
16.2.7.1.32.1 Treatment emergent serious adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.4383 (0.3514 to 0.5218)	0.3943 (0.3110 to 0.4764)	0.3750 (0.1254 to 0.6292)	0.0667 (0.0043 to 0.2603)	
16 Months	0.4201 (0.3335 to 0.5040)	0.3777 (0.2952 to 0.4598)	0.3750 (0.1254 to 0.6292)	0.0667 (0.0043 to 0.2603)	
18 Months	0.4201 (0.3335 to 0.5040)	0.3687 (0.2865 to 0.4509)	0.3750 (0.1254 to 0.6292)	0.0667 (0.0043 to 0.2603)	
20 Months	0.4201 (0.3335 to 0.5040)	0.3311 (0.2506 to 0.4136)	0.3750 (0.1254 to 0.6292)	0.0667 (0.0043 to 0.2603)	
22 Months	0.4201 (0.3335 to 0.5040)	0.3119 (0.2326 to 0.3943)	0.3750 (0.1254 to 0.6292)	0.0667 (0.0043 to 0.2603)	
24 Months	0.4087 (0.3219 to 0.4934)	0.3015 (0.2227 to 0.3840)	0.3750 (0.1254 to 0.6292)	0.0667 (0.0043 to 0.2603)	
26 Months	0.3970 (0.3101 to 0.4825)	0.2803 (0.2028 to 0.3628)	0.3750 (0.1254 to 0.6292)	0.0667 (0.0043 to 0.2603)	
Number of patients at risk[c]					
2 Months	90	96	10	2	
4 Months	77	80	9	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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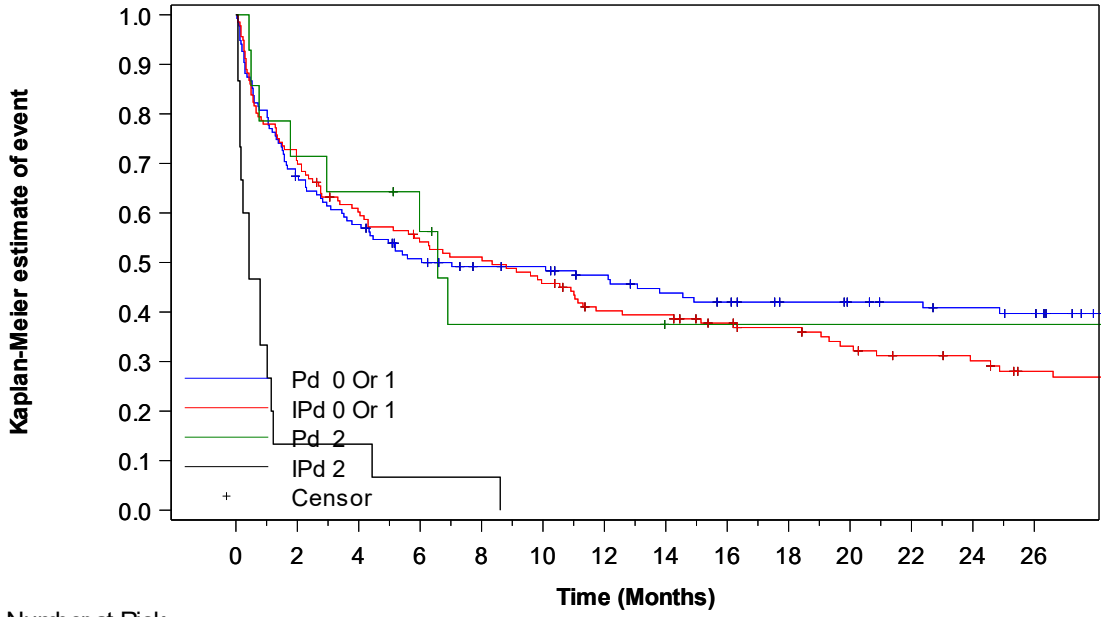
16.2.7.1 Safety endpoints
16.2.7.1.32 Subgroup analysis by baseline ECOG PS
16.2.7.1.32.1 Treatment emergent serious adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[d]**
6 Months	65	71	7	1	
8 Months	59	67	4	1	
10 Months	58	60	4	0	
12 Months	53	50	4	0	
14 Months	48	49	3	0	
16 Months	45	43	3	0	
18 Months	41	40	3	0	
20 Months	39	35	3	0	
22 Months	37	31	3	0	
24 Months	35	29	3	0	
26 Months	33	24	3	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_ecog_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.32 Subgroup analysis by baseline ECOG PS
16.2.7.1.32.2 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event by treatment group according to baseline ECOG PS - Safety population



Number at Risk

Pd 0 Or 1	135	90	77	65	59	58	53	48	45	41	39	37	35	33
IPd 0 Or 1	136	96	80	71	67	60	50	49	43	40	35	31	29	24
Pd 2	14	10	9	7	4	4	4	3	3	3	3	3	3	3
IPd 2	15	2	2	1	1	0	0	0	0	0	0	0	0	0

16.2.7.1 Safety endpoints
16.2.7.1.33 Subgroup analysis by R-ISS staging
16.2.7.1.33.1 Treatment emergent severe adverse event by treatment group according to R-ISS staging - Safety population

	I		II		III		
	Pd (N=38)	**IPd (N=43)**	**Pd (N=83)**	**IPd (N=86)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	24 (63.2)	33 (76.7)	60 (72.3)	82 (95.3)	21 (100.0)	12 (80.0)	0.0111
Number (%) of patients censored	14 (36.8)	10 (23.3)	23 (27.7)	4 (4.7)	0 (0.0)	3 (20.0)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	0.7885 (0.5257 to 3.4497)	0.5585 (0.2957 to 0.8542)	0.5914 (0.2957 to 0.7885)	0.5257 (0.2957 to 0.5914)	0.2300 (0.0657 to 0.3285)	0.4600 (0.1314 to 0.5257)	
Median (95% CI)	6.8337 (2.2669 to NC)	1.4456 (0.7556 to 2.7926)	1.6756 (0.9528 to 3.5154)	0.8214 (0.6899 to 1.0185)	0.5585 (0.2300 to 1.1170)	0.5257 (0.2957 to 3.9754)	
75% quantile (95% CI)	NC (24.8706 to NC)	20.8624 (2.6940 to NC)	27.8275 (4.6653 to NC)	2.1355 (1.3142 to 4.2053)	1.2813 (0.6242 to 3.7454)	3.9754 (0.5257 to NC)	
Comparison vs. Pd							
Stratified[a] Log-Rank test p-value[b] vs Pd		0.0553		0.0013		0.2993	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_riss_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.33 Subgroup analysis by R-ISS staging
16.2.7.1.33.1 Treatment emergent severe adverse event by treatment group according to R-ISS staging - Safety population

	I		II		III		
	Pd (N=38)	**IPd (N=43)**	**Pd (N=83)**	**IPd (N=86)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd		1.7092 (0.9818 to 2.9756)		1.7463 (1.2395 to 2.4603)		0.6530 (0.2904 to 1.4683)	
P-value		0.0581		0.0014		0.3026	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.5726 (0.4065 to 0.8068)				
probability (95% CI)[c]							
2 Months	0.7105 (0.5385 to 0.8280)	0.4419 (0.2916 to 0.5820)	0.4703 (0.3589 to 0.5739)	0.2706 (0.1814 to 0.3676)	0.0952 (0.0163 to 0.2612)	0.3636 (0.1339 to 0.6012)	
4 Months	0.5789 (0.4075 to 0.7169)	0.3023 (0.1740 to 0.4411)	0.3713 (0.2674 to 0.4751)	0.1757 (0.1035 to 0.2635)	0.0476 (0.0033 to 0.1970)	0.1818 (0.0318 to 0.4306)	
6 Months	0.5263 (0.3581 to 0.6695)	0.3023 (0.1740 to 0.4411)	0.3183 (0.2196 to 0.4212)	0.1232 (0.0631 to 0.2045)	0.0476 (0.0033 to 0.1970)	0.1818 (0.0318 to 0.4306)	
8 Months	0.4737 (0.3103 to 0.6206)	0.2558 (0.1379 to 0.3914)	0.3038 (0.2066 to 0.4065)	0.1232 (0.0631 to 0.2045)	0.0476 (0.0033 to 0.1970)	0.0909 (0.0058 to 0.3276)	
10 Months	0.4737 (0.3103 to 0.6206)	0.2558 (0.1379 to 0.3914)	0.3038 (0.2066 to 0.4065)	0.1095 (0.0532 to 0.1887)	0.0476 (0.0033 to 0.1970)	0.0909 (0.0058 to 0.3276)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_riss_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.33 Subgroup analysis by R-ISS staging
16.2.7.1.33.1 Treatment emergent severe adverse event by treatment group according to R-ISS staging - Safety population

	I		II		III		
	Pd (N=38)	**IPd (N=43)**	**Pd (N=83)**	**IPd (N=86)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	0.4737 (0.3103 to 0.6206)	0.2558 (0.1379 to 0.3914)	0.3038 (0.2066 to 0.4065)	0.1095 (0.0532 to 0.1887)	0.0476 (0.0033 to 0.1970)	0.0909 (0.0058 to 0.3276)	
14 Months	0.4161 (0.2584 to 0.5666)	0.2558 (0.1379 to 0.3914)	0.3038 (0.2066 to 0.4065)	0.0958 (0.0437 to 0.1726)	0.0476 (0.0033 to 0.1970)	0.0909 (0.0058 to 0.3276)	
16 Months	0.4161 (0.2584 to 0.5666)	0.2558 (0.1379 to 0.3914)	0.2859 (0.1898 to 0.3893)	0.0684 (0.0261 to 0.1391)	0.0476 (0.0033 to 0.1970)	0.0909 (0.0058 to 0.3276)	
18 Months	0.4161 (0.2584 to 0.5666)	0.2558 (0.1379 to 0.3914)	0.2859 (0.1898 to 0.3893)	0.0684 (0.0261 to 0.1391)	0.0476 (0.0033 to 0.1970)	0.0909 (0.0058 to 0.3276)	
20 Months	0.4161 (0.2584 to 0.5666)	0.2558 (0.1379 to 0.3914)	0.2859 (0.1898 to 0.3893)	0.0411 (0.0112 to 0.1035)	0.0476 (0.0033 to 0.1970)	0.0909 (0.0058 to 0.3276)	
22 Months	0.4161 (0.2584 to 0.5666)	0.2193 (0.1062 to 0.3582)	0.2859 (0.1898 to 0.3893)	0.0411 (0.0112 to 0.1035)	0.0476 (0.0033 to 0.1970)	0.0909 (0.0058 to 0.3276)	
24 Months	0.4161 (0.2584 to 0.5666)	0.2193 (0.1062 to 0.3582)	0.2859 (0.1898 to 0.3893)	0.0411 (0.0112 to 0.1035)	0.0476 (0.0033 to 0.1970)	0.0909 (0.0058 to 0.3276)	
26 Months	0.3841 (0.2297 to 0.5367)	0.2193 (0.1062 to 0.3582)	0.2542 (0.1548 to 0.3658)	0.0411 (0.0112 to 0.1035)	0.0476 (0.0033 to 0.1970)	0.0909 (0.0058 to 0.3276)	

Number of patients at risk[c]

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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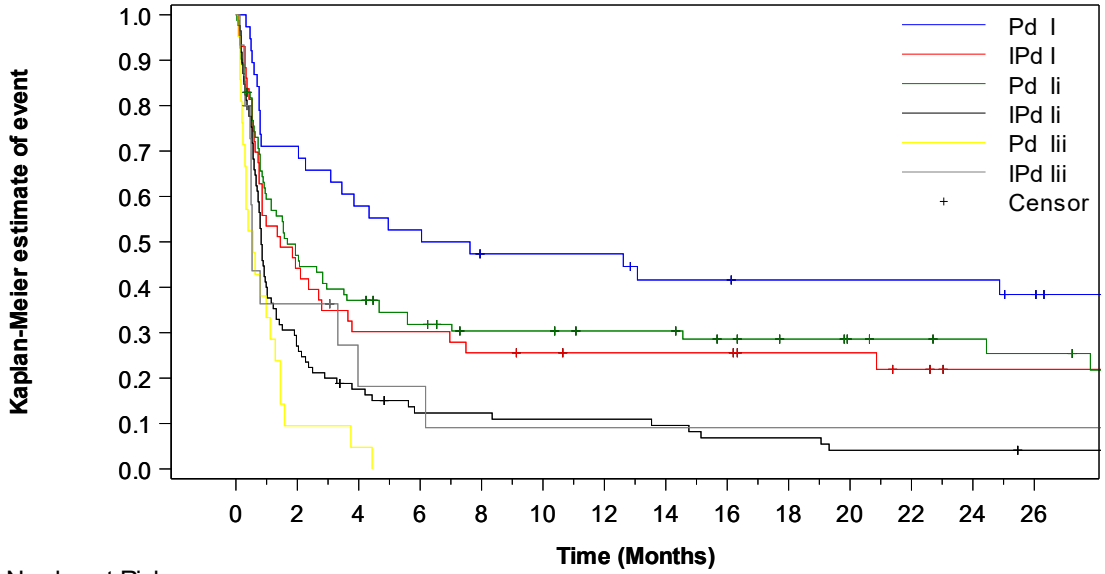
16.2.7.1 Safety endpoints
16.2.7.1.33 Subgroup analysis by R-ISS staging
16.2.7.1.33.1 Treatment emergent severe adverse event by treatment group according to R-ISS staging - Safety population

	I		II		III		
	Pd (N=38)	**IPd (N=43)**	**Pd (N=83)**	**IPd (N=86)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[d]**
2 Months	27	19	38	23	2	5	
4 Months	22	13	30	14	1	2	
6 Months	20	13	24	9	0	2	
8 Months	17	11	20	9	0	1	
10 Months	17	10	20	8	0	1	
12 Months	17	9	18	8	0	1	
14 Months	14	9	18	7	0	1	
16 Months	14	9	15	5	0	1	
18 Months	13	7	13	5	0	1	
20 Months	13	7	11	3	0	1	
22 Months	13	5	10	3	0	1	
24 Months	13	3	9	3	0	1	
26 Months	11	3	8	2	0	1	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_riss_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.33 Subgroup analysis by R-ISS staging
16.2.7.1.33.2 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event by treatment group according to R-ISS staging - Safety population



Number at Risk

Pd I	38	27	22	20	17	17	17	14	14	13	13	13	13	11
IPd I	43	19	13	13	11	10	9	9	9	7	7	5	3	3
Pd Ii	82	38	30	24	20	20	18	18	15	13	11	10	9	8
IPd Ii	85	23	14	9	9	8	8	7	5	5	3	3	3	2
Pd Iii	21	2	1	0	0	0	0	0	0	0	0	0	0	0
IPd Iii	15	5	2	2	1	1	1	1	1	1	1	1	1	1

16.2.7.1 Safety endpoints
16.2.7.1.33 Subgroup analysis by R-ISS staging
16.2.7.1.33.3 Treatment emergent severe adverse event including death by treatment group according to R-ISS staging - Safety population

	I		II		III		
	Pd (N=38)	**IPd (N=43)**	**Pd (N=83)**	**IPd (N=86)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	24 (63.2)	34 (79.1)	62 (74.7)	83 (96.5)	21 (100.0)	13 (86.7)	0.0164
Number (%) of patients censored	14 (36.8)	9 (20.9)	21 (25.3)	3 (3.5)	0 (0.0)	2 (13.3)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	0.7885 (0.5257 to 3.4497)	0.5585 (0.2957 to 0.8542)	0.5585 (0.2957 to 0.7885)	0.5257 (0.2957 to 0.5914)	0.2300 (0.0657 to 0.3285)	0.2957 (0.1314 to 0.4928)	
Median (95% CI)	6.8337 (2.2669 to NC)	1.4456 (0.7556 to 2.7926)	1.6263 (0.9199 to 2.9569)	0.8214 (0.6899 to 1.0185)	0.5585 (0.2300 to 1.1170)	0.5257 (0.2628 to 3.3183)	
75% quantile (95% CI)	NC (24.8706 to NC)	9.1335 (2.6940 to NC)	24.4435 (4.6653 to NC)	2.0370 (1.3142 to 4.2053)	1.2813 (0.6242 to 3.7454)	3.6468 (0.5257 to NC)	
Comparison vs. Pd							
Stratified[a] Log-Rank test p-value[b] vs Pd		0.0389		0.0015		0.3952	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_riss_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.33 Subgroup analysis by R-ISS staging
16.2.7.1.33.3 Treatment emergent severe adverse event including death by treatment group according to R-ISS staging - Safety population

	I		II		III		
	Pd (N=38)	**IPd (N=43)**	**Pd (N=83)**	**IPd (N=86)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd		1.7737 (1.0226 to 3.0765)		1.7225 (1.2274 to 2.4173)		0.7133 (0.3263 to 1.5593)	
P-value		0.0414		0.0017		0.3972	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.5638 (0.3250 to 0.9779)		0.5806 (0.4137 to 0.8147)				
probability (95% CI)[c]							
2 Months	0.7105 (0.5385 to 0.8280)	0.4419 (0.2916 to 0.5820)	0.4634 (0.3531 to 0.5666)	0.2588 (0.1714 to 0.3550)	0.0952 (0.0163 to 0.2612)	0.3333 (0.1215 to 0.5640)	
4 Months	0.5789 (0.4075 to 0.7169)	0.3023 (0.1740 to 0.4411)	0.3659 (0.2632 to 0.4689)	0.1647 (0.0952 to 0.2508)	0.0476 (0.0033 to 0.1970)	0.1667 (0.0294 to 0.4024)	
6 Months	0.5263 (0.3581 to 0.6695)	0.3023 (0.1740 to 0.4411)	0.3028 (0.2071 to 0.4039)	0.1155 (0.0583 to 0.1941)	0.0476 (0.0033 to 0.1970)	0.1667 (0.0294 to 0.4024)	
8 Months	0.4737 (0.3103 to 0.6206)	0.2558 (0.1379 to 0.3914)	0.2890 (0.1949 to 0.3898)	0.1155 (0.0583 to 0.1941)	0.0476 (0.0033 to 0.1970)	0.0833 (0.0054 to 0.3060)	
10 Months	0.4737 (0.3103 to 0.6206)	0.2326 (0.1205 to 0.3660)	0.2890 (0.1949 to 0.3898)	0.1027 (0.0492 to 0.1790)	0.0476 (0.0033 to 0.1970)	0.0833 (0.0054 to 0.3060)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_riss_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.33 Subgroup analysis by R-ISS staging
16.2.7.1.33.3 Treatment emergent severe adverse event including death by treatment group according to R-ISS staging - Safety population

	I		II		III		
	Pd (N=38)	**IPd (N=43)**	**Pd (N=83)**	**IPd (N=86)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	0.4737 (0.3103 to 0.6206)	0.2326 (0.1205 to 0.3660)	0.2890 (0.1949 to 0.3898)	0.1027 (0.0492 to 0.1790)	0.0476 (0.0033 to 0.1970)	0.0833 (0.0054 to 0.3060)	
14 Months	0.4161 (0.2584 to 0.5666)	0.2326 (0.1205 to 0.3660)	0.2890 (0.1949 to 0.3898)	0.0898 (0.0405 to 0.1636)	0.0476 (0.0033 to 0.1970)	0.0833 (0.0054 to 0.3060)	
16 Months	0.4161 (0.2584 to 0.5666)	0.2326 (0.1205 to 0.3660)	0.2720 (0.1791 to 0.3732)	0.0642 (0.0242 to 0.1316)	0.0476 (0.0033 to 0.1970)	0.0833 (0.0054 to 0.3060)	
18 Months	0.4161 (0.2584 to 0.5666)	0.2326 (0.1205 to 0.3660)	0.2720 (0.1791 to 0.3732)	0.0642 (0.0242 to 0.1316)	0.0476 (0.0033 to 0.1970)	0.0833 (0.0054 to 0.3060)	
20 Months	0.4161 (0.2584 to 0.5666)	0.2326 (0.1205 to 0.3660)	0.2720 (0.1791 to 0.3732)	0.0385 (0.0104 to 0.0978)	0.0476 (0.0033 to 0.1970)	0.0833 (0.0054 to 0.3060)	
22 Months	0.4161 (0.2584 to 0.5666)	0.1993 (0.0934 to 0.3339)	0.2720 (0.1791 to 0.3732)	0.0385 (0.0104 to 0.0978)	0.0476 (0.0033 to 0.1970)	0.0833 (0.0054 to 0.3060)	
24 Months	0.4161 (0.2584 to 0.5666)	0.1993 (0.0934 to 0.3339)	0.2720 (0.1791 to 0.3732)	0.0385 (0.0104 to 0.0978)	0.0476 (0.0033 to 0.1970)	0.0833 (0.0054 to 0.3060)	
26 Months	0.3841 (0.2297 to 0.5367)	0.1993 (0.0934 to 0.3339)	0.2418 (0.1464 to 0.3503)	0.0385 (0.0104 to 0.0978)	0.0476 (0.0033 to 0.1970)	0.0833 (0.0054 to 0.3060)	

Number of patients at risk[c]

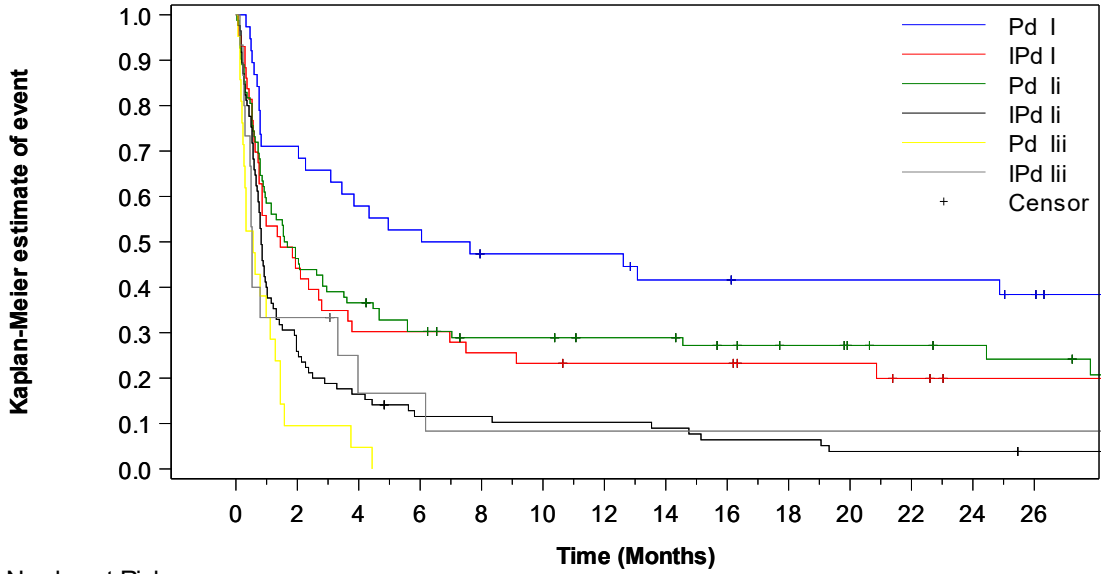
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_riss_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.33 Subgroup analysis by R-ISS staging
16.2.7.1.33.3 Treatment emergent severe adverse event including death by treatment group according to R-ISS staging - Safety population

	I		II		III		
	Pd (N=38)	**IPd (N=43)**	**Pd (N=83)**	**IPd (N=86)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[d]**
2 Months	27	19	38	22	2	5	
4 Months	22	13	30	14	1	2	
6 Months	20	13	24	9	0	2	
8 Months	17	11	20	9	0	1	
10 Months	17	10	20	8	0	1	
12 Months	17	9	18	8	0	1	
14 Months	14	9	18	7	0	1	
16 Months	14	9	15	5	0	1	
18 Months	13	7	13	5	0	1	
20 Months	13	7	11	3	0	1	
22 Months	13	5	10	3	0	1	
24 Months	13	3	9	3	0	1	
26 Months	11	3	8	2	0	1	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_riss_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.33 Subgroup analysis by R-ISS staging
16.2.7.1.33.4 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death by treatment group according to R-ISS staging - Safety population



Number at Risk

Pd I	38	27	22	20	17	17	17	14	14	13	13	13	13	11
IPd I	43	19	13	13	11	10	9	9	9	7	7	5	3	3
Pd Ii	82	38	30	24	20	20	18	18	15	13	11	10	9	8
IPd Ii	85	22	14	9	9	8	8	7	5	5	3	3	3	2
Pd Iii	21	2	1	0	0	0	0	0	0	0	0	0	0	0
IPd Iii	15	5	2	2	1	1	1	1	1	1	1	1	1	1

16.2.7.1 Safety endpoints
16.2.7.1.34 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.34.1 Treatment emergent severe adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	23 (67.6)	20 (87.0)	60 (78.9)	92 (89.3)	0.0330
Number (%) of patients censored	11 (32.4)	3 (13.0)	16 (21.1)	11 (10.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.3285 (0.1314 to 0.7885)	0.2957 (0.0657 to 0.4928)	0.6242 (0.5257 to 0.7885)	0.5914 (0.4271 to 0.7556)	
Median (95% CI)	2.0370 (0.6242 to 7.0308)	0.5585 (0.2957 to 0.7885)	1.5770 (0.9199 to 3.5154)	1.0185 (0.8214 to 1.9055)	
75% quantile (95% CI)	NC (4.4353 to NC)	0.8214 (0.5585 to NC)	7.6222 (3.8439 to NC)	3.7782 (2.3655 to 7.4251)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd		0.0083		0.0982	
Stratified[a] Hazard ratio (95% CI) vs Pd		2.4295 (1.2352 to 4.7784)		1.3277 (0.9479 to 1.8596)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_care_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.34 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.34.1 Treatment emergent severe adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
P-value		0.0101		0.0992	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.4116 (0.2093 to 0.8096)				
probability (95% CI)[c]					
2 Months	0.5152 (0.3354 to 0.6685)	0.1391 (0.0349 to 0.3136)	0.4809 (0.3644 to 0.5880)	0.3725 (0.2796 to 0.4653)	
4 Months	0.4242 (0.2559 to 0.5831)	0.0928 (0.0159 to 0.2552)	0.3473 (0.2421 to 0.4545)	0.2323 (0.1554 to 0.3185)	
6 Months	0.3590 (0.2008 to 0.5200)	0.0928 (0.0159 to 0.2552)	0.2783 (0.1821 to 0.3827)	0.1901 (0.1200 to 0.2726)	
8 Months	0.3263 (0.1747 to 0.4874)	0.0928 (0.0159 to 0.2552)	0.2488 (0.1569 to 0.3517)	0.1584 (0.0944 to 0.2372)	
10 Months	0.3263 (0.1747 to 0.4874)	0.0928 (0.0159 to 0.2552)	0.2488 (0.1569 to 0.3517)	0.1478 (0.0862 to 0.2252)	
12 Months	0.3263 (0.1747 to 0.4874)	0.0928 (0.0159 to 0.2552)	0.2488 (0.1569 to 0.3517)	0.1478 (0.0862 to 0.2252)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_care_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.34 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.34.1 Treatment emergent severe adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.3263 (0.1747 to 0.4874)	0.0928 (0.0159 to 0.2552)	0.2488 (0.1569 to 0.3517)	0.1478 (0.0862 to 0.2252)	
16 Months	0.3263 (0.1747 to 0.4874)	0.0928 (0.0159 to 0.2552)	0.2297 (0.1398 to 0.3329)	0.1251 (0.0685 to 0.1996)	
18 Months	0.3263 (0.1747 to 0.4874)	0.0928 (0.0159 to 0.2552)	0.2297 (0.1398 to 0.3329)	0.1251 (0.0685 to 0.1996)	
20 Months	0.3263 (0.1747 to 0.4874)	0.0928 (0.0159 to 0.2552)	0.2297 (0.1398 to 0.3329)	0.0973 (0.0470 to 0.1695)	
22 Months	0.3263 (0.1747 to 0.4874)	0.0928 (0.0159 to 0.2552)	0.2297 (0.1398 to 0.3329)	0.0834 (0.0370 to 0.1538)	
24 Months	0.3263 (0.1747 to 0.4874)	0.0928 (0.0159 to 0.2552)	0.2297 (0.1398 to 0.3329)	0.0834 (0.0370 to 0.1538)	
26 Months	0.3263 (0.1747 to 0.4874)	0.0928 (0.0159 to 0.2552)	0.1837 (0.0988 to 0.2893)	0.0834 (0.0370 to 0.1538)	
Number of patients at risk[c]					
2 Months	17	3	36	38	
4 Months	14	2	26	22	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.34 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.34.1 Treatment emergent severe adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

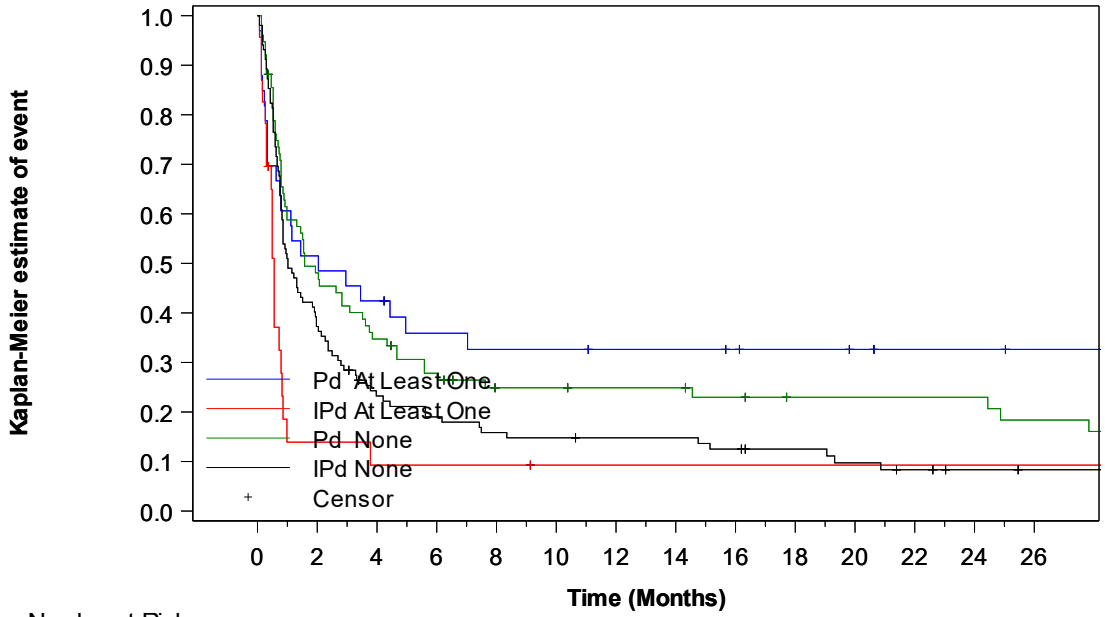
	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
6 Months	11	2	20	18	
8 Months	10	2	15	15	
10 Months	10	1	15	14	
12 Months	9	1	14	13	
14 Months	9	1	14	13	
16 Months	8	1	12	11	
18 Months	7	1	10	9	
20 Months	6	1	10	7	
22 Months	5	1	10	5	
24 Months	5	1	10	3	
26 Months	4	1	8	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_care_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints

16.2.7.1.34 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))

16.2.7.1.34.2 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population



Number at Risk														
Pd At Least One	33	17	14	11	10	10	9	9	8	7	6	5	5	4
IPd At Least One	23	3	2	2	2	1	1	1	1	1	1	1	1	1
Pd None	76	36	26	20	15	15	14	14	12	10	10	10	10	8
IPd None	102	38	22	18	15	14	13	13	11	9	7	5	3	2

16.2.7.1 Safety endpoints
16.2.7.1.34 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.34.3 Treatment emergent severe adverse event including death by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	23 (67.6)	22 (95.7)	62 (81.6)	93 (90.3)	0.0111
Number (%) of patients censored	11 (32.4)	1 (4.3)	14 (18.4)	10 (9.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.3285 (0.1314 to 0.7885)	0.2628 (0.0657 to 0.4928)	0.6078 (0.4600 to 0.7885)	0.5914 (0.4271 to 0.7556)	
Median (95% CI)	2.0370 (0.6242 to 7.0308)	0.4928 (0.2957 to 0.7228)	1.5770 (0.8871 to 3.5154)	1.0185 (0.8214 to 1.9055)	
75% quantile (95% CI)	NC (4.4353 to NC)	0.8214 (0.5585 to 3.7782)	6.8337 (3.7454 to NC)	3.6468 (2.2669 to 7.4251)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd		0.0019		0.1158	
Stratified[a] Hazard ratio (95% CI) vs Pd		2.7472 (1.4185 to 5.3205)		1.3057 (0.9356 to 1.8220)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.34 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.34.3 Treatment emergent severe adverse event including death by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
P-value		0.0027		0.1167	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.3640 (0.1880 to 0.7050)				
probability (95% CI)[c]					
2 Months	0.5152 (0.3354 to 0.6685)	0.1304 (0.0327 to 0.2972)	0.4737 (0.3584 to 0.5803)	0.3627 (0.2707 to 0.4553)	
4 Months	0.4242 (0.2559 to 0.5831)	0.0870 (0.0150 to 0.2417)	0.3421 (0.2382 to 0.4484)	0.2237 (0.1483 to 0.3088)	
6 Months	0.3590 (0.2008 to 0.5200)	0.0870 (0.0150 to 0.2417)	0.2632 (0.1704 to 0.3653)	0.1830 (0.1146 to 0.2641)	
8 Months	0.3263 (0.1747 to 0.4874)	0.0870 (0.0150 to 0.2417)	0.2353 (0.1470 to 0.3355)	0.1525 (0.0903 to 0.2297)	
10 Months	0.3263 (0.1747 to 0.4874)	0.0435 (0.0031 to 0.1824)	0.2353 (0.1470 to 0.3355)	0.1423 (0.0825 to 0.2180)	
12 Months	0.3263 (0.1747 to 0.4874)	0.0435 (0.0031 to 0.1824)	0.2353 (0.1470 to 0.3355)	0.1423 (0.0825 to 0.2180)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_care_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.34 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.34.3 Treatment emergent severe adverse event including death by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.3263 (0.1747 to 0.4874)	0.0435 (0.0031 to 0.1824)	0.2353 (0.1470 to 0.3355)	0.1423 (0.0825 to 0.2180)	
16 Months	0.3263 (0.1747 to 0.4874)	0.0435 (0.0031 to 0.1824)	0.2172 (0.1311 to 0.3174)	0.1204 (0.0656 to 0.1931)	
18 Months	0.3263 (0.1747 to 0.4874)	0.0435 (0.0031 to 0.1824)	0.2172 (0.1311 to 0.3174)	0.1204 (0.0656 to 0.1931)	
20 Months	0.3263 (0.1747 to 0.4874)	0.0435 (0.0031 to 0.1824)	0.2172 (0.1311 to 0.3174)	0.0937 (0.0450 to 0.1639)	
22 Months	0.3263 (0.1747 to 0.4874)	0.0435 (0.0031 to 0.1824)	0.2172 (0.1311 to 0.3174)	0.0803 (0.0355 to 0.1487)	
24 Months	0.3263 (0.1747 to 0.4874)	0.0435 (0.0031 to 0.1824)	0.2172 (0.1311 to 0.3174)	0.0803 (0.0355 to 0.1487)	
26 Months	0.3263 (0.1747 to 0.4874)	0.0435 (0.0031 to 0.1824)	0.1738 (0.0929 to 0.2755)	0.0803 (0.0355 to 0.1487)	
Number of patients at risk[c]					
2 Months	17	3	36	37	
4 Months	14	2	26	22	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.34 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.34.3 Treatment emergent severe adverse event including death by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

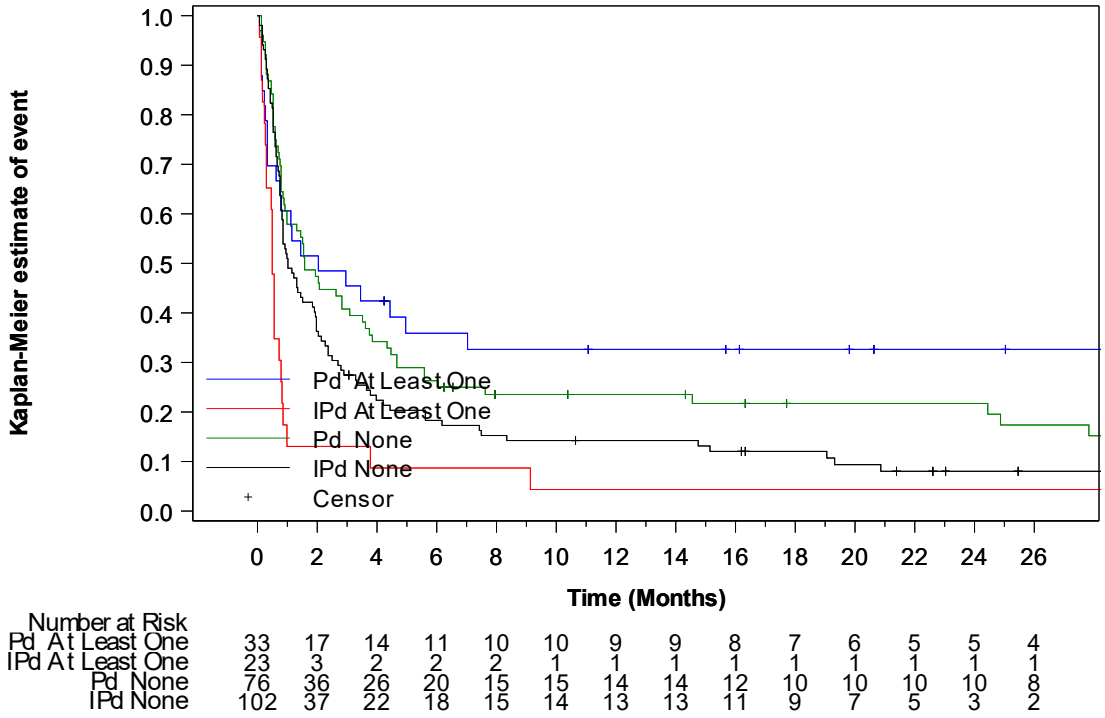
	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
6 Months	11	2	20	18	
8 Months	10	2	15	15	
10 Months	10	1	15	14	
12 Months	9	1	14	13	
14 Months	9	1	14	13	
16 Months	8	1	12	11	
18 Months	7	1	10	9	
20 Months	6	1	10	7	
22 Months	5	1	10	5	
24 Months	5	1	10	3	
26 Months	4	1	8	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_care_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints

16.2.7.1.34 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))

16.2.7.1.34.4 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.35 Subgroup analysis by MM type
16.2.7.1.35.1 Treatment emergent adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	95 (97.9)	100 (99.0)	50 (98.0)	50 (100.0)	0.0124
Number (%) of patients censored	2 (2.1)	1 (1.0)	1 (2.0)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0657 to 0.1314)	0.1314 (0.0657 to 0.1643)	0.1971 (0.1314 to 0.3285)	0.0657 (0.0657 to 0.0986)	
Median (95% CI)	0.2957 (0.1971 to 0.3943)	0.2300 (0.1643 to 0.3285)	0.4928 (0.3285 to 0.7885)	0.1314 (0.0986 to 0.1643)	
75% quantile (95% CI)	0.8214 (0.5585 to 1.0513)	0.6078 (0.4600 to 0.7885)	1.0185 (0.7885 to 2.4312)	0.3285 (0.1643 to 0.7228)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd		0.3834		0.0005	
Stratified[a] Hazard ratio (95% CI) vs Pd		1.1367 (0.8521 to 1.5164)		2.1566 (1.3912 to 3.3430)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.35 Subgroup analysis by MM type
16.2.7.1.35.1 Treatment emergent adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
P-value		0.3835		0.0006	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.4637 (0.2991 to 0.7188)		
probability (95% CI)[c]					
2 Months	0.0851 (0.0398 to 0.1522)	0.0800 (0.0374 to 0.1435)	0.1633 (0.0764 to 0.2787)	0.0204 (0.0017 to 0.0940)	
4 Months	0.0426 (0.0139 to 0.0973)	0.0300 (0.0081 to 0.0779)	0.0612 (0.0160 to 0.1516)	0.0204 (0.0017 to 0.0940)	
6 Months	0.0319 (0.0086 to 0.0826)	0.0200 (0.0039 to 0.0636)	0.0612 (0.0160 to 0.1516)	0.0204 (0.0017 to 0.0940)	
8 Months	0.0319 (0.0086 to 0.0826)	0.0100 (0.0009 to 0.0490)	0.0306 (0.0031 to 0.1224)	0.0204 (0.0017 to 0.0940)	
10 Months	0.0213 (0.0041 to 0.0674)	0.0100 (0.0009 to 0.0490)	0.0306 (0.0031 to 0.1224)	0.0204 (0.0017 to 0.0940)	
12 Months	0.0213 (0.0041 to 0.0674)	0.0100 (0.0009 to 0.0490)	0.0306 (0.0031 to 0.1224)	0.0204 (0.0017 to 0.0940)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.35 Subgroup analysis by MM type
16.2.7.1.35.1 Treatment emergent adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.0213 (0.0041 to 0.0674)	0.0100 (0.0009 to 0.0490)	0.0306 (0.0031 to 0.1224)	0.0204 (0.0017 to 0.0940)	
16 Months	0.0213 (0.0041 to 0.0674)	0.0100 (0.0009 to 0.0490)	0.0306 (0.0031 to 0.1224)	0.0204 (0.0017 to 0.0940)	
18 Months	0.0213 (0.0041 to 0.0674)	0.0100 (0.0009 to 0.0490)	0.0306 (0.0031 to 0.1224)	0.0204 (0.0017 to 0.0940)	
20 Months	0.0213 (0.0041 to 0.0674)	0.0100 (0.0009 to 0.0490)	0.0306 (0.0031 to 0.1224)	0.0204 (0.0017 to 0.0940)	
22 Months	0.0213 (0.0041 to 0.0674)	0.0100 (0.0009 to 0.0490)	0.0306 (0.0031 to 0.1224)	0.0204 (0.0017 to 0.0940)	
24 Months	0.0213 (0.0041 to 0.0674)	0.0100 (0.0009 to 0.0490)	0.0306 (0.0031 to 0.1224)	0.0204 (0.0017 to 0.0940)	
26 Months	0.0213 (0.0041 to 0.0674)	0.0100 (0.0009 to 0.0490)	0.0306 (0.0031 to 0.1224)	0.0204 (0.0017 to 0.0940)	
Number of patients at risk[c]					
2 Months	8	8	8	1	
4 Months	4	3	3	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.35 Subgroup analysis by MM type
16.2.7.1.35.1 Treatment emergent adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
6 Months	3	2	2	0	
8 Months	3	1	1	0	
10 Months	2	1	1	0	
12 Months	2	1	0	0	
14 Months	2	1	0	0	
16 Months	2	1	0	0	
18 Months	2	1	0	0	
20 Months	1	1	0	0	
22 Months	1	1	0	0	
24 Months	1	1	0	0	
26 Months	1	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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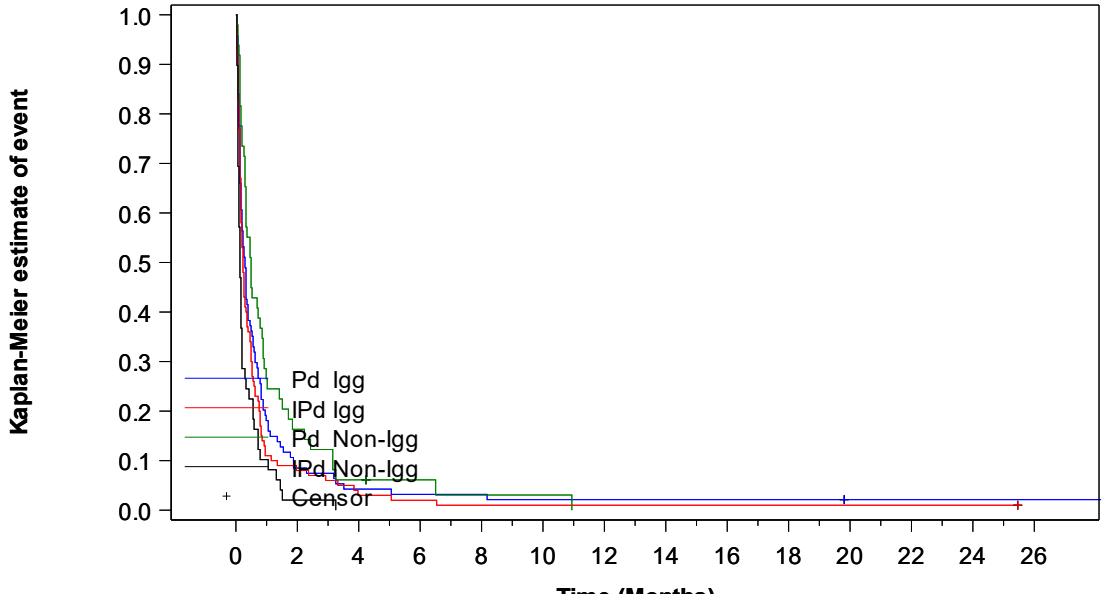
16.2.7.1 Safety endpoints
16.2.7.1.35 Subgroup analysis by MM type
16.2.7.1.35.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event by treatment group according to MM type - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.35 Subgroup analysis by MM type
16.2.7.1.35.3 Treatment emergent mild adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	89 (91.8)	94 (93.1)	48 (94.1)	47 (94.0)	0.0132
Number (%) of patients censored	8 (8.2)	7 (6.9)	3 (5.9)	3 (6.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0986 to 0.2300)	0.1314 (0.0657 to 0.1643)	0.2957 (0.1314 to 0.3943)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.3943 (0.2957 to 0.6242)	0.2628 (0.1971 to 0.4928)	0.7228 (0.3614 to 1.1170)	0.1643 (0.0986 to 0.1971)	
75% quantile (95% CI)	0.9856 (0.7885 to 1.6756)	1.0513 (0.7556 to 2.9240)	2.0370 (1.1170 to 3.1540)	0.5585 (0.1971 to 1.0513)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd		0.9558		0.0045	
Stratified[a] Hazard ratio (95% CI) vs Pd		1.0084 (0.7491 to 1.3576)		1.8987 (1.2124 to 2.9734)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.35 Subgroup analysis by MM type
16.2.7.1.35.3 Treatment emergent mild adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
P-value		0.9558		0.0051	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.5267 (0.3363 to 0.8248)		
probability (95% CI)[c]					
2 Months	0.1271 (0.0683 to 0.2048)	0.2277 (0.1517 to 0.3133)	0.2653 (0.1518 to 0.3930)	0.1020 (0.0375 to 0.2047)	
4 Months	0.0924 (0.0437 to 0.1636)	0.1373 (0.0786 to 0.2122)	0.0884 (0.0286 to 0.1909)	0.0680 (0.0161 to 0.1738)	
6 Months	0.0809 (0.0360 to 0.1494)	0.0929 (0.0454 to 0.1611)	0.0884 (0.0286 to 0.1909)	0.0680 (0.0161 to 0.1738)	
8 Months	0.0809 (0.0360 to 0.1494)	0.0697 (0.0296 to 0.1332)	0.0590 (0.0128 to 0.1592)	0.0680 (0.0161 to 0.1738)	
10 Months	0.0647 (0.0246 to 0.1323)	0.0697 (0.0296 to 0.1332)	0.0590 (0.0128 to 0.1592)	0.0680 (0.0161 to 0.1738)	
12 Months	0.0647 (0.0246 to 0.1323)	0.0697 (0.0296 to 0.1332)	0.0295 (0.0026 to 0.1243)	0.0680 (0.0161 to 0.1738)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_type_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.35 Subgroup analysis by MM type
16.2.7.1.35.3 Treatment emergent mild adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.0431 (0.0107 to 0.1132)	0.0697 (0.0296 to 0.1332)	0.0295 (0.0026 to 0.1243)	0.0680 (0.0161 to 0.1738)	
16 Months	0.0431 (0.0107 to 0.1132)	0.0581 (0.0223 to 0.1188)	0.0295 (0.0026 to 0.1243)	0.0680 (0.0161 to 0.1738)	
18 Months	0.0431 (0.0107 to 0.1132)	0.0581 (0.0223 to 0.1188)	0.0295 (0.0026 to 0.1243)	0.0680 (0.0161 to 0.1738)	
20 Months	0.0431 (0.0107 to 0.1132)	0.0581 (0.0223 to 0.1188)	0.0295 (0.0026 to 0.1243)	0.0680 (0.0161 to 0.1738)	
22 Months	0.0431 (0.0107 to 0.1132)	0.0581 (0.0223 to 0.1188)	0.0295 (0.0026 to 0.1243)	0.0680 (0.0161 to 0.1738)	
24 Months	0.0431 (0.0107 to 0.1132)	0.0581 (0.0223 to 0.1188)	0.0295 (0.0026 to 0.1243)	0.0680 (0.0161 to 0.1738)	
26 Months	0.0431 (0.0107 to 0.1132)	0.0581 (0.0223 to 0.1188)	0.0295 (0.0026 to 0.1243)	0.0680 (0.0161 to 0.1738)	
Number of patients at risk[c]					
2 Months	11	23	12	4	
4 Months	8	13	4	2	

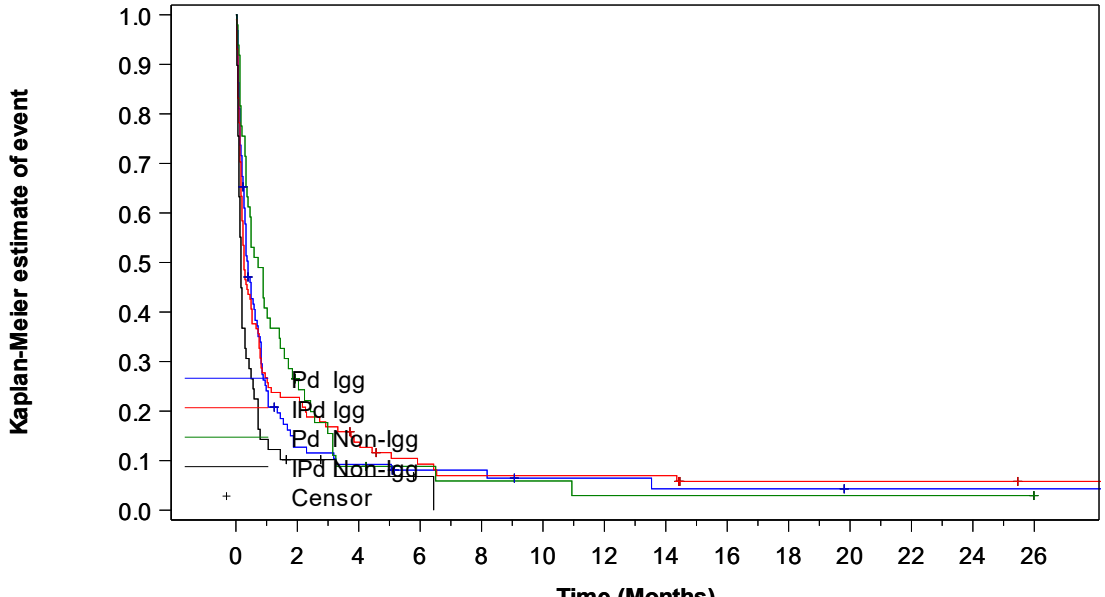
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_type_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.35 Subgroup analysis by MM type
16.2.7.1.35.3 Treatment emergent mild adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
6 Months	5	8	3	1	
8 Months	5	6	2	0	
10 Months	3	6	2	0	
12 Months	3	6	1	0	
14 Months	2	6	1	0	
16 Months	2	3	1	0	
18 Months	2	3	1	0	
20 Months	1	3	1	0	
22 Months	1	3	1	0	
24 Months	1	3	1	0	
26 Months	1	2	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_type_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.35 Subgroup analysis by MM type
16.2.7.1.35.4 Kaplan-Meier cumulative incidence curve of treatment emergent mild adverse event by treatment group according to MM type - Safety population



Number at Risk

Pd Igg	95	11	8	5	5	3	3	2	2	2	1	1	1	1
IPd Igg	101	23	13	8	6	6	6	6	3	3	3	3	3	2
Pd Non-Igg	49	12	4	3	2	2	1	1	1	1	1	1	1	0
IPd Non-Igg	49	4	2	1	0	0	0	0	0	0	0	0	0	0

16.2.7.1 Safety endpoints
16.2.7.1.36 Subgroup analysis by previous therapy with anti-CD38 mAB
16.2.7.1.36.1 Treatment emergent severe adverse event by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	2 (100.0)	1 (50.0)	108 (73.5)	134 (89.3)	0.0036
Number (%) of patients censored	0 (0.0)	1 (50.0)	39 (26.5)	16 (10.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1643 (0.1643 to 0.3285)	5.8152 (5.8152 to NC)	0.5914 (0.4600 to 0.7556)	0.5257 (0.3614 to 0.5585)	
Median (95% CI)	0.2464 (0.1643 to 0.3285)	NC (5.8152 to NC)	1.6756 (1.1170 to 2.9569)	0.8542 (0.7556 to 1.0185)	
75% quantile (95% CI)	0.3285 (0.1643 to 0.3285)	NC (5.8152 to NC)	27.8275 (6.0452 to NC)	3.6468 (2.1027 to 6.1766)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd		0.3173		0.0007	
Stratified[a] Hazard ratio (95% CI) vs Pd		NC (NC to NC)		1.5564 (1.2026 to 2.0144)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_prmabfl_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.36 Subgroup analysis by previous therapy with anti-CD38 mAB
16.2.7.1.36.1 Treatment emergent severe adverse event by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[d]**
P-value		1.0000		0.0008	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.6425 (0.4964 to 0.8316)		
probability (95% CI)[c]					
2 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.4765 (0.3933 to 0.5549)	0.3316 (0.2572 to 0.4077)	
4 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.3798 (0.3012 to 0.4580)	0.2215 (0.1582 to 0.2916)	
6 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3299 (0.2546 to 0.4070)	0.1850 (0.1265 to 0.2522)	
8 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3075 (0.2339 to 0.3840)	0.1554 (0.1016 to 0.2196)	
10 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3075 (0.2339 to 0.3840)	0.1480 (0.0955 to 0.2114)	
12 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3075 (0.2339 to 0.3840)	0.1398 (0.0886 to 0.2024)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_prmabfl_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.36 Subgroup analysis by previous therapy with anti-CD38 mAB
16.2.7.1.36.1 Treatment emergent severe adverse event by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2902 (0.2176 to 0.3665)	0.1315 (0.0818 to 0.1933)	
16 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2811 (0.2091 to 0.3574)	0.1151 (0.0685 to 0.1750)	
18 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2811 (0.2091 to 0.3574)	0.1151 (0.0685 to 0.1750)	
20 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2811 (0.2091 to 0.3574)	0.0959 (0.0529 to 0.1541)	
22 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2811 (0.2091 to 0.3574)	0.0863 (0.0455 to 0.1434)	
24 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2811 (0.2091 to 0.3574)	0.0863 (0.0455 to 0.1434)	
26 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2567 (0.1847 to 0.3345)	0.0863 (0.0455 to 0.1434)	
Number of patients at risk[c]					
2 Months	0	2	69	49	
4 Months	0	2	55	31	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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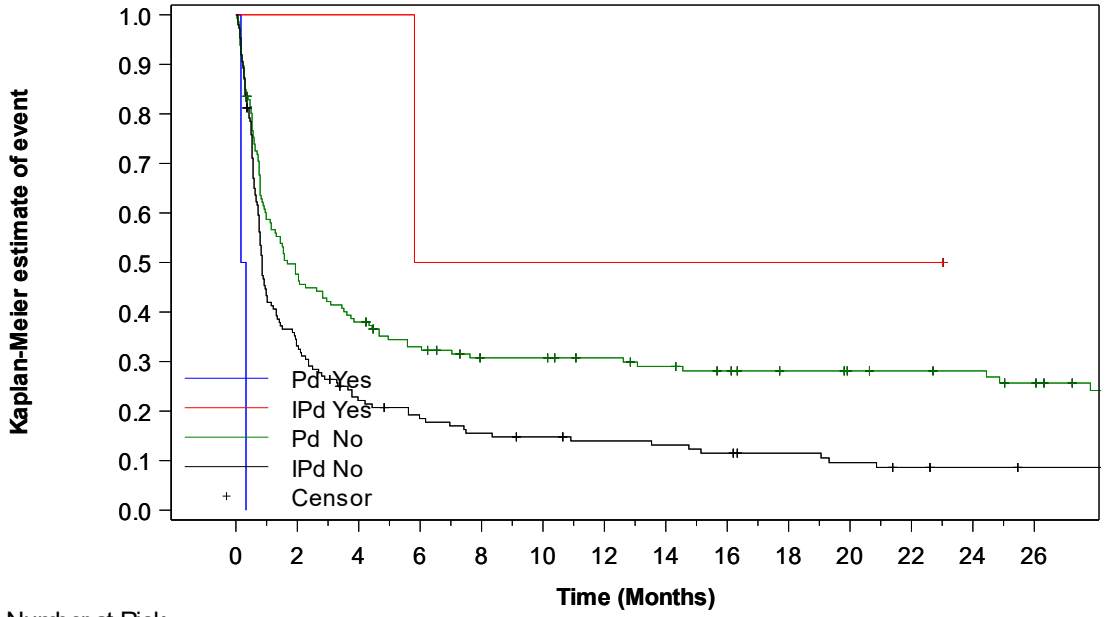
16.2.7.1 Safety endpoints
16.2.7.1.36 Subgroup analysis by previous therapy with anti-CD38 mAB
16.2.7.1.36.1 Treatment emergent severe adverse event by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[d]**
6 Months	0	1	46	25	
8 Months	0	1	39	21	
10 Months	0	1	39	19	
12 Months	0	1	36	17	
14 Months	0	1	33	16	
16 Months	0	1	30	14	
18 Months	0	1	27	12	
20 Months	0	1	25	10	
22 Months	0	1	24	8	
24 Months	0	0	23	7	
26 Months	0	0	20	6	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_prmabfl_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.36 Subgroup analysis by previous therapy with anti-CD38 mAB
16.2.7.1.36.2 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event by treatment group according to previous therapy with anti-CD38 mAB - Safety population



Number at Risk

Pd Yes	2	0	0	0	0	0	0	0	0	0	0	0	0	0
IPd Yes	2	2	2	1	1	1	1	1	1	1	1	1	0	0
Pd No	146	69	55	46	39	39	36	33	30	27	25	24	23	20
IPd No	149	49	31	25	21	19	17	16	14	12	10	8	7	6

16.2.7.1 Safety endpoints
16.2.7.1.36 Subgroup analysis by previous therapy with anti-CD38 mAB
16.2.7.1.36.3 Treatment emergent severe adverse event including death by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	2 (100.0)	1 (50.0)	110 (74.8)	137 (91.3)	0.0035
Number (%) of patients censored	0 (0.0)	1 (50.0)	37 (25.2)	13 (8.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1643 (0.1643 to 0.3285)	5.8152 (5.8152 to NC)	0.5585 (0.3614 to 0.7556)	0.5257 (0.3285 to 0.5585)	
Median (95% CI)	0.2464 (0.1643 to 0.3285)	NC (5.8152 to NC)	1.6263 (0.9856 to 2.9569)	0.8542 (0.7556 to 1.0185)	
75% quantile (95% CI)	0.3285 (0.1643 to 0.3285)	NC (5.8152 to NC)	24.8706 (5.5852 to NC)	3.2854 (1.9713 to 5.9795)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd		0.3173		0.0005	
Stratified[a] Hazard ratio (95% CI) vs Pd		NC (NC to NC)		1.5661 (1.2131 to 2.0218)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.36 Subgroup analysis by previous therapy with anti-CD38 mAB
16.2.7.1.36.3 Treatment emergent severe adverse event including death by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[d]**
P-value		1.0000		0.0006	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.6385 (0.4946 to 0.8243)		
probability (95% CI)[c]					
2 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.4726 (0.3898 to 0.5508)	0.3221 (0.2487 to 0.3976)	
4 Months	0.5000 (0.0060 to 0.9104)	1.0000 (1.0000 to 1.0000)	0.3767 (0.2985 to 0.4546)	0.2137 (0.1518 to 0.2827)	
6 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.3209 (0.2467 to 0.3973)	0.1785 (0.1215 to 0.2444)	
8 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2991 (0.2267 to 0.3748)	0.1499 (0.0976 to 0.2127)	
10 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2991 (0.2267 to 0.3748)	0.1356 (0.0859 to 0.1967)	
12 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2991 (0.2267 to 0.3748)	0.1281 (0.0798 to 0.1882)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.36 Subgroup analysis by previous therapy with anti-CD38 mAB
16.2.7.1.36.3 Treatment emergent severe adverse event including death by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2823 (0.2110 to 0.3577)	0.1206 (0.0737 to 0.1797)	
16 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2735 (0.2027 to 0.3488)	0.1055 (0.0618 to 0.1625)	
18 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2735 (0.2027 to 0.3488)	0.1055 (0.0618 to 0.1625)	
20 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2735 (0.2027 to 0.3488)	0.0879 (0.0479 to 0.1429)	
22 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2735 (0.2027 to 0.3488)	0.0791 (0.0412 to 0.1329)	
24 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2735 (0.2027 to 0.3488)	0.0791 (0.0412 to 0.1329)	
26 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.2497 (0.1792 to 0.3263)	0.0791 (0.0412 to 0.1329)	
Number of patients at risk[c]					
2 Months	0	2	69	48	
4 Months	0	2	55	31	

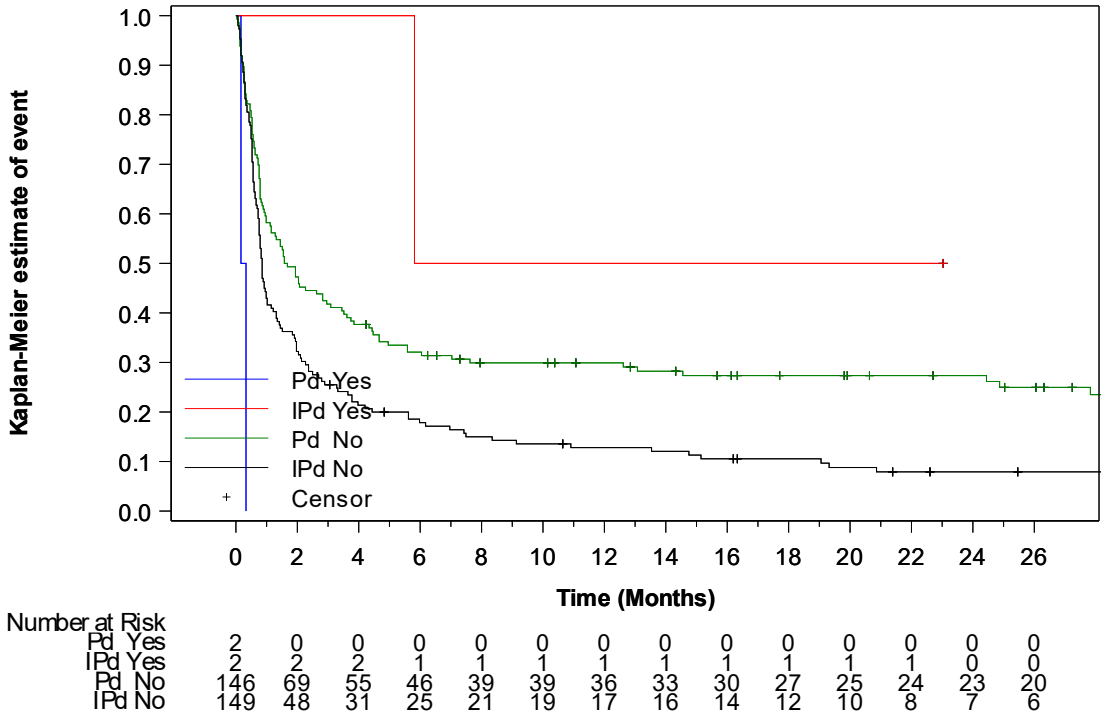
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_prmabfl_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.36 Subgroup analysis by previous therapy with anti-CD38 mAB
16.2.7.1.36.3 Treatment emergent severe adverse event including death by treatment group according to previous therapy with anti-CD38 mAB - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[d]**
6 Months	0	1	46	25	
8 Months	0	1	39	21	
10 Months	0	1	39	19	
12 Months	0	1	36	17	
14 Months	0	1	33	16	
16 Months	0	1	30	14	
18 Months	0	1	27	12	
20 Months	0	1	25	10	
22 Months	0	1	24	8	
24 Months	0	0	23	7	
26 Months	0	0	20	6	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_prmabfl_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.36 Subgroup analysis by previous therapy with anti-CD38 mAB
16.2.7.1.36.4 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death by treatment group according to previous therapy with anti-CD38 mAB - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.37 Subgroup analysis by refractory to PI
16.2.7.1.37.1 Treatment emergent serious adverse event by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	73 (65.8)	81 (69.2)	17 (44.7)	30 (85.7)	0.0107
Number (%) of patients censored	38 (34.2)	36 (30.8)	21 (55.3)	5 (14.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.2813 (0.5914 to 1.7741)	0.7885 (0.3614 to 1.5770)	2.2998 (0.1971 to 5.1910)	1.2813 (0.4600 to 1.9713)	
Median (95% CI)	5.5852 (2.9569 to 12.1889)	6.3080 (2.7926 to 11.0390)	NC (3.4497 to NC)	4.1725 (1.4127 to 9.9548)	
75% quantile (95% CI)	NC (24.8706 to NC)	NC (19.3183 to NC)	NC (NC to NC)	14.2587 (8.6078 to 35.7782)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd		0.8812		0.0047	
Stratified[a] Hazard ratio (95% CI) vs Pd		1.0246 (0.7448 to 1.4096)		2.3567 (1.2801 to 4.3389)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.37 Subgroup analysis by refractory to PI
16.2.7.1.37.1 Treatment emergent serious adverse event by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
P-value		0.8813		0.0059	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.4243 (0.2305 to 0.7812)		
probability (95% CI)[c]					
2 Months	0.6486 (0.5522 to 0.7294)	0.6638 (0.5700 to 0.7417)	0.7632 (0.5942 to 0.8690)	0.6000 (0.4200 to 0.7402)	
4 Months	0.5573 (0.4598 to 0.6440)	0.5686 (0.4734 to 0.6529)	0.6579 (0.4848 to 0.7849)	0.5113 (0.3362 to 0.6618)	
6 Months	0.4817 (0.3855 to 0.5715)	0.5071 (0.4127 to 0.5939)	0.6041 (0.4313 to 0.7393)	0.4511 (0.2821 to 0.6061)	
8 Months	0.4415 (0.3464 to 0.5324)	0.4804 (0.3867 to 0.5679)	0.6041 (0.4313 to 0.7393)	0.4211 (0.2560 to 0.5775)	
10 Months	0.4415 (0.3464 to 0.5324)	0.4359 (0.3440 to 0.5241)	0.6041 (0.4313 to 0.7393)	0.3308 (0.1817 to 0.4880)	
12 Months	0.4197 (0.3251 to 0.5113)	0.3802 (0.2913 to 0.4685)	0.6041 (0.4313 to 0.7393)	0.3008 (0.1583 to 0.4569)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.37 Subgroup analysis by refractory to PI
16.2.7.1.37.1 Treatment emergent serious adverse event by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.3853 (0.2919 to 0.4778)	0.3802 (0.2913 to 0.4685)	0.5739 (0.4008 to 0.7137)	0.2707 (0.1358 to 0.4252)	
16 Months	0.3733 (0.2803 to 0.4661)	0.3802 (0.2913 to 0.4685)	0.5437 (0.3711 to 0.6876)	0.2105 (0.0933 to 0.3594)	
18 Months	0.3733 (0.2803 to 0.4661)	0.3696 (0.2812 to 0.4581)	0.5437 (0.3711 to 0.6876)	0.2105 (0.0933 to 0.3594)	
20 Months	0.3733 (0.2803 to 0.4661)	0.3363 (0.2494 to 0.4253)	0.5437 (0.3711 to 0.6876)	0.1754 (0.0691 to 0.3219)	
22 Months	0.3733 (0.2803 to 0.4661)	0.3135 (0.2279 to 0.4026)	0.5437 (0.3711 to 0.6876)	0.1754 (0.0691 to 0.3219)	
24 Months	0.3584 (0.2652 to 0.4523)	0.3135 (0.2279 to 0.4026)	0.5437 (0.3711 to 0.6876)	0.1316 (0.0400 to 0.2786)	
26 Months	0.3428 (0.2495 to 0.4379)	0.2889 (0.2048 to 0.3782)	0.5437 (0.3711 to 0.6876)	0.1316 (0.0400 to 0.2786)	
Number of patients at risk[c]					
2 Months	71	77	29	21	
4 Months	61	65	25	17	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.37 Subgroup analysis by refractory to PI
16.2.7.1.37.1 Treatment emergent serious adverse event by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
6 Months	50	57	22	15	
8 Months	42	54	21	14	
10 Months	41	49	21	11	
12 Months	37	40	20	10	
14 Months	32	40	19	9	
16 Months	30	36	18	7	
18 Months	26	34	18	6	
20 Months	25	30	17	5	
22 Months	25	27	15	4	
24 Months	23	26	15	3	
26 Months	21	21	15	3	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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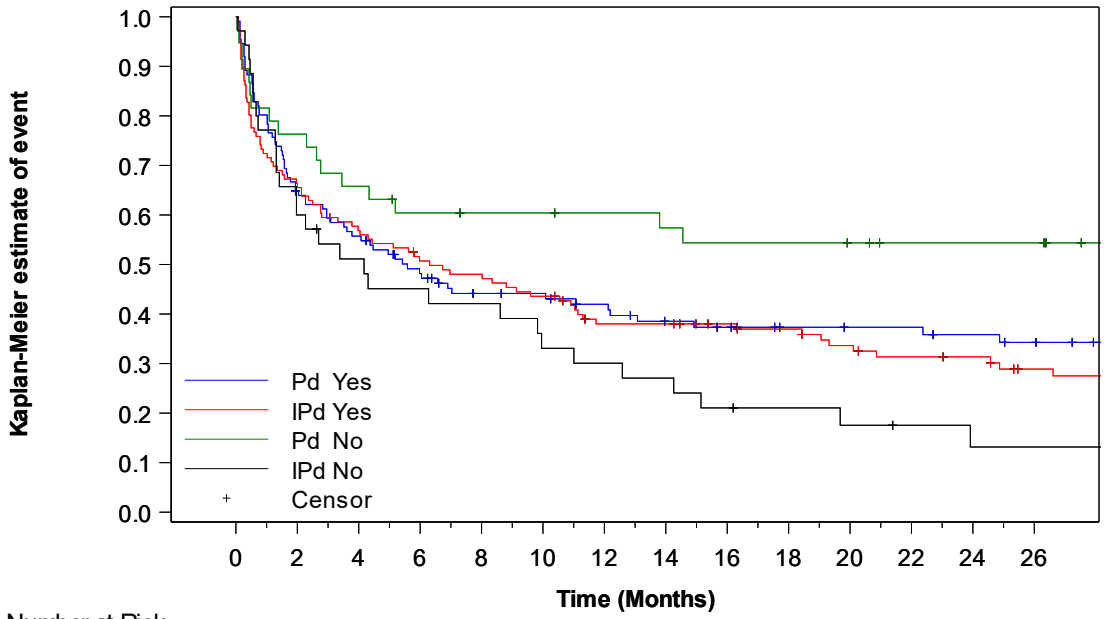
16.2.7.1 Safety endpoints
16.2.7.1.37 Subgroup analysis by refractory to PI
16.2.7.1.37.2 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event by treatment group according to refractory to PI - Safety population



Number at Risk

Pd Yes	111	71	61	50	42	41	37	32	30	26	25	25	23	21
IPd Yes	116	77	65	57	54	49	40	40	36	34	30	27	26	21
Pd No	38	29	25	22	21	21	20	19	18	18	17	15	15	15
IPd No	35	21	17	15	14	11	10	9	7	6	5	4	3	3

16.2.7.1 Safety endpoints
16.2.7.1.38 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.38.1 Treatment emergent adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	85 (97.7)	91 (100.0)	61 (98.4)	60 (98.4)	0.0494
Number (%) of patients censored	2 (2.3)	0 (0.0)	1 (1.6)	1 (1.6)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1314 (0.0986 to 0.1971)	0.0657 (0.0657 to 0.0986)	0.1314 (0.0986 to 0.1643)	0.1314 (0.0986 to 0.1971)	
Median (95% CI)	0.3943 (0.2957 to 0.5914)	0.1643 (0.0986 to 0.1971)	0.2957 (0.1643 to 0.3614)	0.2957 (0.1971 to 0.4928)	
75% quantile (95% CI)	0.8871 (0.6899 to 1.4784)	0.3943 (0.2300 to 0.6242)	0.8871 (0.4600 to 1.5113)	0.7228 (0.4928 to 0.8542)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd		0.0001		0.7292	
Stratified[a] Hazard ratio (95% CI) vs Pd		1.8410 (1.3434 to 2.5230)		1.0672 (0.7385 to 1.5424)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.38 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.38.1 Treatment emergent adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
P-value		0.0001		0.7290	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.5432 (0.3964 to 0.7444)				
probability (95% CI)[c]					
2 Months	0.1084 (0.0533 to 0.1858)	0.0337 (0.0090 to 0.0870)	0.1148 (0.0504 to 0.2082)	0.0984 (0.0400 to 0.1880)	
4 Months	0.0361 (0.0097 to 0.0929)	0.0112 (0.0010 to 0.0546)	0.0656 (0.0211 to 0.1460)	0.0328 (0.0061 to 0.1009)	
6 Months	0.0361 (0.0097 to 0.0929)	0.0112 (0.0010 to 0.0546)	0.0437 (0.0095 to 0.1217)	0.0328 (0.0061 to 0.1009)	
8 Months	0.0241 (0.0046 to 0.0758)	0.0112 (0.0010 to 0.0546)	0.0437 (0.0095 to 0.1217)	0.0164 (0.0014 to 0.0772)	
10 Months	0.0241 (0.0046 to 0.0758)	0.0112 (0.0010 to 0.0546)	0.0219 (0.0020 to 0.0953)	0.0164 (0.0014 to 0.0772)	
12 Months	0.0241 (0.0046 to 0.0758)	0.0112 (0.0010 to 0.0546)	0.0219 (0.0020 to 0.0953)	0.0164 (0.0014 to 0.0772)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.38 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.38.1 Treatment emergent adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.0241 (0.0046 to 0.0758)	0.0112 (0.0010 to 0.0546)	0.0219 (0.0020 to 0.0953)	0.0164 (0.0014 to 0.0772)	
16 Months	0.0241 (0.0046 to 0.0758)	0.0112 (0.0010 to 0.0546)	0.0219 (0.0020 to 0.0953)	0.0164 (0.0014 to 0.0772)	
18 Months	0.0241 (0.0046 to 0.0758)	0.0112 (0.0010 to 0.0546)	0.0219 (0.0020 to 0.0953)	0.0164 (0.0014 to 0.0772)	
20 Months	0.0241 (0.0046 to 0.0758)	0.0112 (0.0010 to 0.0546)	0.0219 (0.0020 to 0.0953)	0.0164 (0.0014 to 0.0772)	
22 Months	0.0241 (0.0046 to 0.0758)	0.0112 (0.0010 to 0.0546)	0.0219 (0.0020 to 0.0953)	0.0164 (0.0014 to 0.0772)	
24 Months	0.0241 (0.0046 to 0.0758)	0.0112 (0.0010 to 0.0546)	0.0219 (0.0020 to 0.0953)	0.0164 (0.0014 to 0.0772)	
26 Months	0.0241 (0.0046 to 0.0758)	0.0112 (0.0010 to 0.0546)	0.0219 (0.0020 to 0.0953)	0.0164 (0.0014 to 0.0772)	
Number of patients at risk[c]					
2 Months	9	3	7	6	
4 Months	3	1	4	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.38 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.38.1 Treatment emergent adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
6 Months	3	0	2	2	
8 Months	2	0	2	1	
10 Months	2	0	1	1	
12 Months	2	0	0	1	
14 Months	2	0	0	1	
16 Months	2	0	0	1	
18 Months	2	0	0	1	
20 Months	1	0	0	1	
22 Months	1	0	0	1	
24 Months	1	0	0	1	
26 Months	1	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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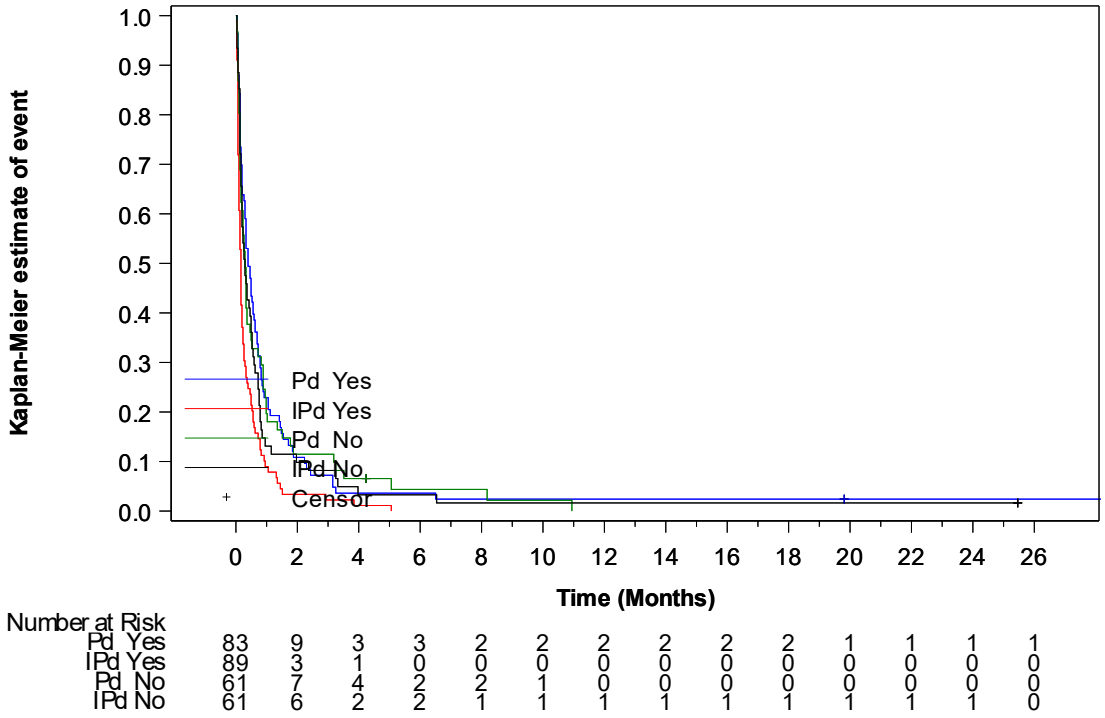
16.2.7.1 Safety endpoints
16.2.7.1.38 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.38.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.38 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.38.3 Treatment emergent mild adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	79 (90.8)	85 (93.4)	59 (95.2)	57 (93.4)	0.0352
Number (%) of patients censored	8 (9.2)	6 (6.6)	3 (4.8)	4 (6.6)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1807 (0.1314 to 0.2957)	0.0986 (0.0657 to 0.0986)	0.1643 (0.0986 to 0.2628)	0.1643 (0.1314 to 0.1971)	
Median (95% CI)	0.5585 (0.3285 to 0.8214)	0.1643 (0.1314 to 0.2300)	0.3614 (0.2628 to 0.8214)	0.4271 (0.2300 to 0.7228)	
75% quantile (95% CI)	1.6756 (1.0513 to 2.4312)	0.7228 (0.2957 to 2.1684)	0.9856 (0.8214 to 1.8727)	1.0513 (0.7228 to 3.3183)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd		0.0126		0.8798	
Stratified[a] Hazard ratio (95% CI) vs Pd		1.4910 (1.0873 to 2.0448)		0.9714 (0.6666 to 1.4154)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_llen_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.38 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.38.3 Treatment emergent mild adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
P-value		0.0132		0.8798	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6707 (0.4891 to 0.9197)				
probability (95% CI)[c]					
2 Months	0.2027 (0.1235 to 0.2959)	0.1667 (0.0984 to 0.2504)	0.1344 (0.0629 to 0.2332)	0.2131 (0.1210 to 0.3225)	
4 Months	0.0946 (0.0423 to 0.1723)	0.0884 (0.0392 to 0.1625)	0.0840 (0.0310 to 0.1711)	0.1475 (0.0726 to 0.2475)	
6 Months	0.0946 (0.0423 to 0.1723)	0.0707 (0.0268 to 0.1438)	0.0630 (0.0186 to 0.1470)	0.0984 (0.0400 to 0.1880)	
8 Months	0.0757 (0.0289 to 0.1527)	0.0236 (0.0023 to 0.0985)	0.0630 (0.0186 to 0.1470)	0.0820 (0.0302 to 0.1673)	
10 Months	0.0757 (0.0289 to 0.1527)	0.0236 (0.0023 to 0.0985)	0.0420 (0.0086 to 0.1212)	0.0820 (0.0302 to 0.1673)	
12 Months	0.0757 (0.0289 to 0.1527)	0.0236 (0.0023 to 0.0985)	0.0420 (0.0086 to 0.1212)	0.0820 (0.0302 to 0.1673)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_llen_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.38 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.38.3 Treatment emergent mild adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.0568 (0.0173 to 0.1316)	0.0236 (0.0023 to 0.0985)	0.0420 (0.0086 to 0.1212)	0.0820 (0.0302 to 0.1673)	
16 Months	0.0568 (0.0173 to 0.1316)	0.0236 (0.0023 to 0.0985)	0.0420 (0.0086 to 0.1212)	0.0656 (0.0211 to 0.1460)	
18 Months	0.0568 (0.0173 to 0.1316)	0.0236 (0.0023 to 0.0985)	0.0420 (0.0086 to 0.1212)	0.0656 (0.0211 to 0.1460)	
20 Months	0.0568 (0.0173 to 0.1316)	0.0236 (0.0023 to 0.0985)	0.0420 (0.0086 to 0.1212)	0.0656 (0.0211 to 0.1460)	
22 Months	0.0568 (0.0173 to 0.1316)	0.0236 (0.0023 to 0.0985)	0.0420 (0.0086 to 0.1212)	0.0656 (0.0211 to 0.1460)	
24 Months	0.0568 (0.0173 to 0.1316)	0.0236 (0.0023 to 0.0985)	0.0420 (0.0086 to 0.1212)	0.0656 (0.0211 to 0.1460)	
26 Months	0.0568 (0.0173 to 0.1316)	0.0236 (0.0023 to 0.0985)	0.0420 (0.0086 to 0.1212)	0.0656 (0.0211 to 0.1460)	
Number of patients at risk[c]					
2 Months	15	14	8	13	
4 Months	7	6	5	9	

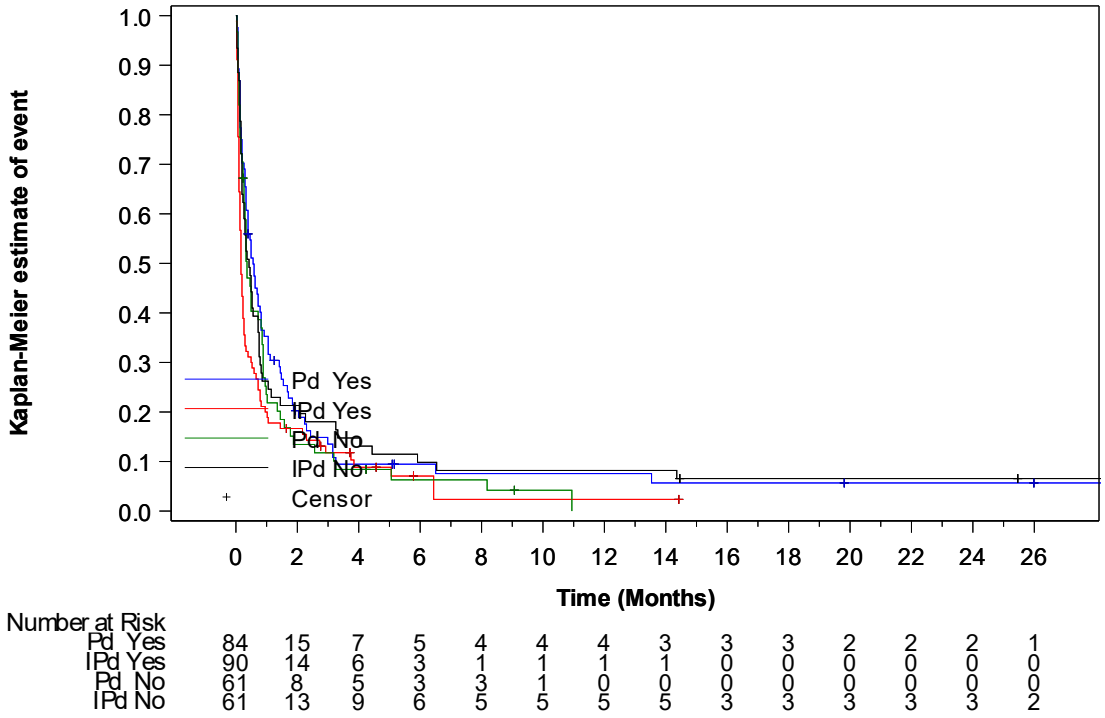
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_llen_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.38 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.38.3 Treatment emergent mild adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
6 Months	5	3	3	6	
8 Months	4	1	3	5	
10 Months	4	1	1	5	
12 Months	4	1	0	5	
14 Months	3	1	0	5	
16 Months	3	0	0	3	
18 Months	3	0	0	3	
20 Months	2	0	0	3	
22 Months	2	0	0	3	
24 Months	2	0	0	3	
26 Months	1	0	0	2	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_llen_s_t_x.rtf (17NOV2020 8:29)

16.2.7.1 Safety endpoints
16.2.7.1.38 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.38.4 Kaplan-Meier cumulative incidence curve of treatment emergent mild adverse event by treatment group according to refractory to lenalidomide in last previous regimen - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Blood and lymphatic system disorders (days)		
Number (%) of events	68 (45.6)	95 (62.5)
Number (%) of patients censored	81 (54.4)	57 (37.5)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	0.9528 (0.7556 to 1.8398)	0.6571 (0.5585 to 0.7885)
Median (95% CI)	31.4415 (4.6653 to NC)	2.3655 (0.9199 to 9.3306)
75% quantile (95% CI)	NC (NC to NC)	NC (36.1396 to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0039
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5788 (1.1552 to 2.1576)
P-value	-	0.0042
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6334 (0.4635 to 0.8656)	-
Events probability (95% CI)[c]		
2 Months	0.6714 (0.5888 to 0.7412)	0.5165 (0.4341 to 0.5928)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.6073 (0.5227 to 0.6815)	0.4554 (0.3744 to 0.5328)
6 Months	0.5616 (0.4761 to 0.6386)	0.4412 (0.3605 to 0.5187)
8 Months	0.5531 (0.4673 to 0.6307)	0.4325 (0.3519 to 0.5105)
10 Months	0.5445 (0.4584 to 0.6226)	0.4141 (0.3333 to 0.4930)
12 Months	0.5445 (0.4584 to 0.6226)	0.4049 (0.3241 to 0.4842)
14 Months	0.5445 (0.4584 to 0.6226)	0.3955 (0.3147 to 0.4751)
16 Months	0.5445 (0.4584 to 0.6226)	0.3955 (0.3147 to 0.4751)
18 Months	0.5321 (0.4446 to 0.6120)	0.3851 (0.3041 to 0.4653)
20 Months	0.5321 (0.4446 to 0.6120)	0.3851 (0.3041 to 0.4653)
22 Months	0.5181 (0.4287 to 0.6002)	0.3738 (0.2925 to 0.4548)
24 Months	0.5181 (0.4287 to 0.6002)	0.3504 (0.2687 to 0.4330)
26 Months	0.5181 (0.4287 to 0.6002)	0.3504 (0.2687 to 0.4330)
Number of patients at risk[c]		
2 Months	97	77
4 Months	84	64
6 Months	72	52
8 Months	64	49
10 Months	61	45
12 Months	57	43

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	51	42
16 Months	47	41
18 Months	42	37
20 Months	39	37
22 Months	37	33
24 Months	36	28
26 Months	34	26
Cardiac disorders (days)		
Number (%) of events	9 (6.0)	33 (21.7)
Number (%) of patients censored	140 (94.0)	119 (78.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	19.4497 (11.4004 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0005

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	3.4552 (1.6500 to 7.2352)
P-value	-	0.0010
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.2894 (0.1382 to 0.6061)	-
Events probability (95% CI)[c]		
2 Months	0.9931 (0.9521 to 0.9990)	0.9270 (0.8721 to 0.9589)
4 Months	0.9931 (0.9521 to 0.9990)	0.9067 (0.8476 to 0.9437)
6 Months	0.9778 (0.9327 to 0.9928)	0.8925 (0.8304 to 0.9327)
8 Months	0.9689 (0.9187 to 0.9883)	0.8766 (0.8110 to 0.9205)
10 Months	0.9591 (0.9037 to 0.9829)	0.8429 (0.7705 to 0.8940)
12 Months	0.9591 (0.9037 to 0.9829)	0.8250 (0.7492 to 0.8797)
14 Months	0.9371 (0.8711 to 0.9699)	0.8250 (0.7492 to 0.8797)
16 Months	0.9371 (0.8711 to 0.9699)	0.8148 (0.7369 to 0.8717)
18 Months	0.9239 (0.8511 to 0.9619)	0.7723 (0.6863 to 0.8375)
20 Months	0.9239 (0.8511 to 0.9619)	0.7496 (0.6598 to 0.8189)
22 Months	0.9239 (0.8511 to 0.9619)	0.7377 (0.6459 to 0.8091)
24 Months	0.9239 (0.8511 to 0.9619)	0.7377 (0.6459 to 0.8091)
26 Months	0.9239 (0.8511 to 0.9619)	0.7238 (0.6292 to 0.7981)
Number of patients at risk[c]		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	142	138
4 Months	134	129
6 Months	115	116
8 Months	103	109
10 Months	98	98
12 Months	89	90
14 Months	81	90
16 Months	74	80
18 Months	66	70
20 Months	62	65
22 Months	60	58
24 Months	59	55
26 Months	56	50
Eye disorders (days)		
Number (%) of events	20 (13.4)	23 (15.1)
Number (%) of patients censored	129 (86.6)	129 (84.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (18.0370 to NC)	NC (21.0924 to NC)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9559
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0171 (0.5582 to 1.8530)
P-value	-	0.9559
Events probability (95% CI)[c]		
2 Months	0.9727 (0.9290 to 0.9897)	0.9868 (0.9482 to 0.9967)
4 Months	0.9074 (0.8458 to 0.9452)	0.9800 (0.9394 to 0.9935)
6 Months	0.8912 (0.8258 to 0.9331)	0.9800 (0.9394 to 0.9935)
8 Months	0.8912 (0.8258 to 0.9331)	0.9318 (0.8727 to 0.9640)
10 Months	0.8912 (0.8258 to 0.9331)	0.9146 (0.8505 to 0.9519)
12 Months	0.8912 (0.8258 to 0.9331)	0.8966 (0.8280 to 0.9389)
14 Months	0.8582 (0.7822 to 0.9092)	0.8966 (0.8280 to 0.9389)
16 Months	0.8459 (0.7662 to 0.9002)	0.8665 (0.7901 to 0.9165)
18 Months	0.8459 (0.7662 to 0.9002)	0.8665 (0.7901 to 0.9165)
20 Months	0.8321 (0.7477 to 0.8902)	0.8434 (0.7609 to 0.8992)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
22 Months	0.8321 (0.7477 to 0.8902)	0.8311 (0.7456 to 0.8900)
24 Months	0.8321 (0.7477 to 0.8902)	0.8175 (0.7283 to 0.8798)
26 Months	0.8321 (0.7477 to 0.8902)	0.8175 (0.7283 to 0.8798)
Number of patients at risk[c]		
2 Months	139	147
4 Months	122	138
6 Months	104	125
8 Months	94	114
10 Months	91	105
12 Months	83	96
14 Months	75	95
16 Months	69	83
18 Months	61	76
20 Months	56	72
22 Months	54	64
24 Months	53	60
26 Months	51	54
Gastrointestinal disorders (days)		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of events	80 (53.7)	85 (55.9)
Number (%) of patients censored	69 (46.3)	67 (44.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	0.8214 (0.5585 to 1.9713)	0.6899 (0.4271 to 1.1828)
Median (95% CI)	7.2608 (3.8439 to 24.4107)	7.1951 (3.2197 to 15.2115)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9443
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0110 (0.7429 to 1.3759)
P-value	-	0.9443
Events probability (95% CI)[c]		
2 Months	0.6768 (0.5941 to 0.7463)	0.6429 (0.5609 to 0.7135)
4 Months	0.5653 (0.4793 to 0.6424)	0.5532 (0.4698 to 0.6288)
6 Months	0.5133 (0.4262 to 0.5938)	0.5457 (0.4622 to 0.6217)
8 Months	0.4844 (0.3965 to 0.5667)	0.4994 (0.4155 to 0.5775)
10 Months	0.4741 (0.3859 to 0.5571)	0.4832 (0.3994 to 0.5620)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	0.4634 (0.3748 to 0.5471)	0.4386 (0.3545 to 0.5195)
14 Months	0.4526 (0.3638 to 0.5371)	0.4203 (0.3364 to 0.5019)
16 Months	0.4407 (0.3514 to 0.5262)	0.4106 (0.3266 to 0.4926)
18 Months	0.4265 (0.3361 to 0.5137)	0.4106 (0.3266 to 0.4926)
20 Months	0.4112 (0.3197 to 0.5004)	0.4106 (0.3266 to 0.4926)
22 Months	0.4112 (0.3197 to 0.5004)	0.3981 (0.3135 to 0.4813)
24 Months	0.4112 (0.3197 to 0.5004)	0.3981 (0.3135 to 0.4813)
26 Months	0.3934 (0.2999 to 0.4854)	0.3981 (0.3135 to 0.4813)
Number of patients at risk[c]		
2 Months	95	95
4 Months	74	78
6 Months	57	71
8 Months	47	63
10 Months	45	55
12 Months	43	48
14 Months	41	46
16 Months	35	40
18 Months	28	38
20 Months	24	37

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
22 Months	23	31
24 Months	23	30
26 Months	21	27
General disorders and administration site conditions (days)		
Number (%) of events	91 (61.1)	89 (58.6)
Number (%) of patients censored	58 (38.9)	63 (41.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	0.8214 (0.3943 to 1.3799)	1.5606 (0.8214 to 2.3326)
Median (95% CI)	4.3696 (2.9897 to 7.1951)	8.5092 (4.4025 to 17.5441)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1933
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.8222 (0.6119 to 1.1048)
P-value	-	0.1940
Events probability (95% CI)[c]		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	0.6241 (0.5402 to 0.6970)	0.7235 (0.6450 to 0.7875)
4 Months	0.5168 (0.4322 to 0.5948)	0.6037 (0.5211 to 0.6766)
6 Months	0.4636 (0.3796 to 0.5432)	0.5493 (0.4662 to 0.6247)
8 Months	0.4160 (0.3333 to 0.4965)	0.5053 (0.4222 to 0.5825)
10 Months	0.3898 (0.3077 to 0.4708)	0.4653 (0.3821 to 0.5441)
12 Months	0.3707 (0.2891 to 0.4523)	0.4565 (0.3733 to 0.5358)
14 Months	0.3610 (0.2796 to 0.4428)	0.4477 (0.3645 to 0.5274)
16 Months	0.3610 (0.2796 to 0.4428)	0.4274 (0.3436 to 0.5084)
18 Months	0.3610 (0.2796 to 0.4428)	0.4167 (0.3327 to 0.4984)
20 Months	0.3610 (0.2796 to 0.4428)	0.4057 (0.3215 to 0.4882)
22 Months	0.3610 (0.2796 to 0.4428)	0.4057 (0.3215 to 0.4882)
24 Months	0.3610 (0.2796 to 0.4428)	0.3822 (0.2973 to 0.4664)
26 Months	0.3610 (0.2796 to 0.4428)	0.3694 (0.2842 to 0.4546)
Number of patients at risk[c]		
2 Months	90	109
4 Months	71	90
6 Months	59	76
8 Months	50	68
10 Months	43	57

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	39	52
14 Months	36	51
16 Months	34	43
18 Months	32	38
20 Months	30	37
22 Months	29	35
24 Months	29	31
26 Months	28	27
Infections and infestations (days)		
Number (%) of events	101 (67.8)	126 (82.9)
Number (%) of patients censored	48 (32.2)	26 (17.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	1.2813 (0.8542 to 1.5113)	0.6899 (0.4928 to 0.7885)
Median (95% CI)	2.3984 (1.9055 to 4.9610)	2.2669 (1.7741 to 3.0883)
75% quantile (95% CI)	29.5688 (9.3306 to NC)	5.9138 (4.1725 to 11.2690)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0165

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.3806 (1.0596 to 1.7989)
P-value	-	0.0169
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.7243 (0.5559 to 0.9437)	-
Events probability (95% CI)[c]		
2 Months	0.5609 (0.4763 to 0.6371)	0.5399 (0.4568 to 0.6157)
4 Months	0.4235 (0.3415 to 0.5029)	0.3422 (0.2669 to 0.4188)
6 Months	0.3998 (0.3187 to 0.4795)	0.2498 (0.1827 to 0.3225)
8 Months	0.3483 (0.2691 to 0.4286)	0.2044 (0.1425 to 0.2742)
10 Months	0.3208 (0.2429 to 0.4012)	0.1880 (0.1282 to 0.2568)
12 Months	0.3111 (0.2336 to 0.3915)	0.1709 (0.1134 to 0.2385)
14 Months	0.3014 (0.2244 to 0.3818)	0.1538 (0.0989 to 0.2200)
16 Months	0.3014 (0.2244 to 0.3818)	0.1453 (0.0917 to 0.2107)
18 Months	0.2898 (0.2131 to 0.3707)	0.1356 (0.0835 to 0.2003)
20 Months	0.2777 (0.2013 to 0.3591)	0.1356 (0.0835 to 0.2003)
22 Months	0.2777 (0.2013 to 0.3591)	0.1356 (0.0835 to 0.2003)
24 Months	0.2777 (0.2013 to 0.3591)	0.1356 (0.0835 to 0.2003)
26 Months	0.2777 (0.2013 to 0.3591)	0.1356 (0.0835 to 0.2003)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	80	80
4 Months	57	49
6 Months	49	33
8 Months	39	27
10 Months	35	23
12 Months	32	20
14 Months	29	18
16 Months	26	16
18 Months	24	13
20 Months	21	12
22 Months	19	11
24 Months	18	11
26 Months	16	9
Injury, poisoning and procedural complications (days)		
Number (%) of events	18 (12.1)	75 (49.3)
Number (%) of patients censored	131 (87.9)	77 (50.7)
Kaplan-Meier estimates of Events in months		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	IPd (N=152)
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0986 to 0.1643)
Median (95% CI)	NC (NC to NC)	18.0370 (5.2238 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	<.0001
Stratified[a] Hazard ratio (95% CI) vs Pd	-	5.5710 (3.2834 to 9.4525)
P-value	-	<.0001
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.1795 (0.1058 to 0.3046)	-
Events probability (95% CI)[c]		
2 Months	0.9583 (0.9095 to 0.9811)	0.6051 (0.5226 to 0.6777)
4 Months	0.9365 (0.8815 to 0.9665)	0.5915 (0.5088 to 0.6648)
6 Months	0.9290 (0.8719 to 0.9612)	0.5769 (0.4940 to 0.6512)
8 Months	0.8942 (0.8273 to 0.9362)	0.5458 (0.4621 to 0.6220)
10 Months	0.8753 (0.8035 to 0.9221)	0.5374 (0.4535 to 0.6142)
12 Months	0.8753 (0.8035 to 0.9221)	0.5280 (0.4435 to 0.6055)
14 Months	0.8753 (0.8035 to 0.9221)	0.5280 (0.4435 to 0.6055)
16 Months	0.8753 (0.8035 to 0.9221)	0.5069 (0.4209 to 0.5865)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	0.8753 (0.8035 to 0.9221)	0.5069 (0.4209 to 0.5865)
20 Months	0.8753 (0.8035 to 0.9221)	0.4951 (0.4082 to 0.5761)
22 Months	0.8753 (0.8035 to 0.9221)	0.4951 (0.4082 to 0.5761)
24 Months	0.8753 (0.8035 to 0.9221)	0.4951 (0.4082 to 0.5761)
26 Months	0.8753 (0.8035 to 0.9221)	0.4951 (0.4082 to 0.5761)
Number of patients at risk[c]		
2 Months	135	91
4 Months	127	85
6 Months	111	75
8 Months	96	67
10 Months	91	61
12 Months	82	55
14 Months	76	54
16 Months	71	46
18 Months	63	43
20 Months	59	39
22 Months	57	35
24 Months	56	34
26 Months	53	31

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Investigations (days)		
Number (%) of events	14 (9.4)	21 (13.8)
Number (%) of patients censored	135 (90.6)	131 (86.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2998
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.4406 (0.7198 to 2.8831)
P-value	-	0.3025
Events probability (95% CI)[c]		
2 Months	0.9723 (0.9278 to 0.9895)	0.9473 (0.8973 to 0.9733)
4 Months	0.9580 (0.9088 to 0.9809)	0.9064 (0.8470 to 0.9435)
6 Months	0.9416 (0.8863 to 0.9704)	0.8991 (0.8382 to 0.9380)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.9416 (0.8863 to 0.9704)	0.8991 (0.8382 to 0.9380)
10 Months	0.9416 (0.8863 to 0.9704)	0.8908 (0.8277 to 0.9318)
12 Months	0.9416 (0.8863 to 0.9704)	0.8818 (0.8162 to 0.9251)
14 Months	0.9081 (0.8377 to 0.9489)	0.8726 (0.8046 to 0.9182)
16 Months	0.9081 (0.8377 to 0.9489)	0.8726 (0.8046 to 0.9182)
18 Months	0.9081 (0.8377 to 0.9489)	0.8726 (0.8046 to 0.9182)
20 Months	0.9081 (0.8377 to 0.9489)	0.8614 (0.7897 to 0.9101)
22 Months	0.9081 (0.8377 to 0.9489)	0.8491 (0.7732 to 0.9013)
24 Months	0.8924 (0.8134 to 0.9392)	0.8491 (0.7732 to 0.9013)
26 Months	0.8765 (0.7902 to 0.9289)	0.8354 (0.7546 to 0.8915)
Number of patients at risk[c]		
2 Months	137	142
4 Months	127	128
6 Months	109	115
8 Months	98	111
10 Months	95	103
12 Months	86	96
14 Months	78	94
16 Months	71	85

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	63	78
20 Months	59	73
22 Months	58	65
24 Months	56	64
26 Months	53	57
Metabolism and nutrition disorders (days)		
Number (%) of events	22 (14.8)	34 (22.4)
Number (%) of patients censored	127 (85.2)	118 (77.6)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	18.9569 (9.5934 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1283
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5126 (0.8840 to 2.5883)
P-value	-	0.1310

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[c]		
2 Months	0.9112 (0.8519 to 0.9474)	0.9008 (0.8409 to 0.9390)
4 Months	0.8751 (0.8089 to 0.9194)	0.8397 (0.7703 to 0.8896)
6 Months	0.8518 (0.7815 to 0.9009)	0.8322 (0.7618 to 0.8834)
8 Months	0.8518 (0.7815 to 0.9009)	0.8322 (0.7618 to 0.8834)
10 Months	0.8518 (0.7815 to 0.9009)	0.8157 (0.7424 to 0.8699)
12 Months	0.8518 (0.7815 to 0.9009)	0.8071 (0.7324 to 0.8629)
14 Months	0.8518 (0.7815 to 0.9009)	0.7892 (0.7115 to 0.8481)
16 Months	0.8518 (0.7815 to 0.9009)	0.7892 (0.7115 to 0.8481)
18 Months	0.8518 (0.7815 to 0.9009)	0.7577 (0.6742 to 0.8226)
20 Months	0.8518 (0.7815 to 0.9009)	0.7466 (0.6610 to 0.8136)
22 Months	0.8518 (0.7815 to 0.9009)	0.7466 (0.6610 to 0.8136)
24 Months	0.8518 (0.7815 to 0.9009)	0.7466 (0.6610 to 0.8136)
26 Months	0.8376 (0.7613 to 0.8912)	0.7466 (0.6610 to 0.8136)
Number of patients at risk[c]		
2 Months	130	135
4 Months	120	120
6 Months	102	109

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	93	105
10 Months	90	97
12 Months	82	90
14 Months	78	87
16 Months	73	78
18 Months	67	69
20 Months	63	66
22 Months	61	60
24 Months	60	58
26 Months	57	52
Musculoskeletal and connective tissue disorders (days)		
Number (%) of events	78 (52.3)	92 (60.5)
Number (%) of patients censored	71 (47.7)	60 (39.5)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	1.9713 (0.9856 to 3.0554)	2.0370 (1.2156 to 2.8912)
Median (95% CI)	9.1335 (4.8624 to 21.7823)	7.9179 (6.3409 to 13.6345)
75% quantile (95% CI)	NC (NC to NC)	NC (26.8090 to NC)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6819
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0655 (0.7861 to 1.4441)
P-value	-	0.6825
Events probability (95% CI)[c]		
2 Months	0.7453 (0.6661 to 0.8085)	0.7553 (0.6786 to 0.8162)
4 Months	0.6350 (0.5498 to 0.7084)	0.6127 (0.5296 to 0.6856)
6 Months	0.5434 (0.4551 to 0.6234)	0.5913 (0.5077 to 0.6655)
8 Months	0.5060 (0.4168 to 0.5884)	0.4993 (0.4146 to 0.5781)
10 Months	0.4840 (0.3939 to 0.5683)	0.4524 (0.3685 to 0.5325)
12 Months	0.4486 (0.3571 to 0.5358)	0.4282 (0.3448 to 0.5088)
14 Months	0.4365 (0.3447 to 0.5245)	0.4115 (0.3286 to 0.4925)
16 Months	0.4232 (0.3309 to 0.5125)	0.3845 (0.3022 to 0.4661)
18 Months	0.4232 (0.3309 to 0.5125)	0.3845 (0.3022 to 0.4661)
20 Months	0.4232 (0.3309 to 0.5125)	0.3746 (0.2925 to 0.4565)
22 Months	0.4081 (0.3149 to 0.4991)	0.3746 (0.2925 to 0.4565)
24 Months	0.4081 (0.3149 to 0.4991)	0.3636 (0.2814 to 0.4461)
26 Months	0.4081 (0.3149 to 0.4991)	0.3636 (0.2814 to 0.4461)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	106	113
4 Months	84	88
6 Months	60	78
8 Months	48	65
10 Months	44	57
12 Months	37	52
14 Months	33	49
16 Months	32	42
18 Months	31	39
20 Months	28	38
22 Months	27	34
24 Months	26	33
26 Months	25	30
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (days)		
Number (%) of events	4 (2.7)	11 (7.2)
Number (%) of patients censored	145 (97.3)	141 (92.8)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1509
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.2696 (0.7192 to 7.1623)
P-value	-	0.1622
Events probability (95% CI)[c]		
2 Months	0.9931 (0.9521 to 0.9990)	0.9934 (0.9539 to 0.9991)
4 Months	0.9931 (0.9521 to 0.9990)	0.9865 (0.9470 to 0.9966)
6 Months	0.9931 (0.9521 to 0.9990)	0.9641 (0.9157 to 0.9849)
8 Months	0.9931 (0.9521 to 0.9990)	0.9560 (0.9046 to 0.9801)
10 Months	0.9931 (0.9521 to 0.9990)	0.9560 (0.9046 to 0.9801)
12 Months	0.9931 (0.9521 to 0.9990)	0.9473 (0.8922 to 0.9746)
14 Months	0.9707 (0.9096 to 0.9907)	0.9473 (0.8922 to 0.9746)
16 Months	0.9707 (0.9096 to 0.9907)	0.9473 (0.8922 to 0.9746)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	0.9575 (0.8883 to 0.9842)	0.9370 (0.8769 to 0.9682)
20 Months	0.9575 (0.8883 to 0.9842)	0.9260 (0.8609 to 0.9612)
22 Months	0.9575 (0.8883 to 0.9842)	0.9142 (0.8442 to 0.9536)
24 Months	0.9575 (0.8883 to 0.9842)	0.9142 (0.8442 to 0.9536)
26 Months	0.9575 (0.8883 to 0.9842)	0.9002 (0.8234 to 0.9447)
Number of patients at risk[c]		
2 Months	141	148
4 Months	133	139
6 Months	116	124
8 Months	105	118
10 Months	101	111
12 Months	92	103
14 Months	84	102
16 Months	77	93
18 Months	68	85
20 Months	64	81
22 Months	62	73
24 Months	61	70
26 Months	58	63

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Nervous system disorders (days)		
Number (%) of events	48 (32.2)	65 (42.8)
Number (%) of patients censored	101 (67.8)	87 (57.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	5.3881 (3.4497 to 19.5483)	2.8255 (1.9055 to 5.8480)
Median (95% CI)	NC (NC to NC)	NC (9.3963 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0914
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.3840 (0.9474 to 2.0217)
P-value	-	0.0928
Events probability (95% CI)[c]		
2 Months	0.8408 (0.7702 to 0.8913)	0.8079 (0.7355 to 0.8623)
4 Months	0.7955 (0.7190 to 0.8533)	0.7263 (0.6472 to 0.7905)
6 Months	0.7376 (0.6546 to 0.8037)	0.6661 (0.5830 to 0.7365)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.7197 (0.6348 to 0.7882)	0.6178 (0.5320 to 0.6924)
10 Months	0.7103 (0.6243 to 0.7800)	0.5835 (0.4963 to 0.6609)
12 Months	0.6998 (0.6125 to 0.7711)	0.5656 (0.4776 to 0.6444)
14 Months	0.6998 (0.6125 to 0.7711)	0.5561 (0.4677 to 0.6357)
16 Months	0.6998 (0.6125 to 0.7711)	0.5561 (0.4677 to 0.6357)
18 Months	0.6882 (0.5990 to 0.7614)	0.5561 (0.4677 to 0.6357)
20 Months	0.6471 (0.5509 to 0.7278)	0.5452 (0.4560 to 0.6259)
22 Months	0.6324 (0.5338 to 0.7157)	0.5336 (0.4435 to 0.6156)
24 Months	0.6324 (0.5338 to 0.7157)	0.5336 (0.4435 to 0.6156)
26 Months	0.6170 (0.5160 to 0.7030)	0.5336 (0.4435 to 0.6156)
Number of patients at risk[c]		
2 Months	118	120
4 Months	105	103
6 Months	86	85
8 Months	77	75
10 Months	72	66
12 Months	67	60
14 Months	64	59
16 Months	61	54

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	53	51
20 Months	46	50
22 Months	43	44
24 Months	42	42
26 Months	38	37
Psychiatric disorders (days)		
Number (%) of events	32 (21.5)	31 (20.4)
Number (%) of patients censored	117 (78.5)	121 (79.6)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	28.6817 (5.6181 to NC)	NC (9.7906 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6111
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.8795 (0.5364 to 1.4420)
P-value	-	0.6108

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	IPd (N=152)
Events probability (95% CI)[c]		
2 Months	0.8909 (0.8281 to 0.9317)	0.9009 (0.8410 to 0.9390)
4 Months	0.8546 (0.7856 to 0.9027)	0.8735 (0.8088 to 0.9174)
6 Months	0.8213 (0.7465 to 0.8758)	0.8296 (0.7580 to 0.8816)
8 Months	0.8032 (0.7253 to 0.8611)	0.8296 (0.7580 to 0.8816)
10 Months	0.8032 (0.7253 to 0.8611)	0.8209 (0.7478 to 0.8746)
12 Months	0.7926 (0.7125 to 0.8527)	0.8209 (0.7478 to 0.8746)
14 Months	0.7818 (0.6995 to 0.8440)	0.8118 (0.7370 to 0.8673)
16 Months	0.7697 (0.6848 to 0.8345)	0.8020 (0.7252 to 0.8594)
18 Months	0.7697 (0.6848 to 0.8345)	0.7917 (0.7128 to 0.8512)
20 Months	0.7697 (0.6848 to 0.8345)	0.7917 (0.7128 to 0.8512)
22 Months	0.7697 (0.6848 to 0.8345)	0.7917 (0.7128 to 0.8512)
24 Months	0.7537 (0.6636 to 0.8229)	0.7917 (0.7128 to 0.8512)
26 Months	0.7537 (0.6636 to 0.8229)	0.7783 (0.6955 to 0.8412)
Number of patients at risk[c]		
2 Months	126	134
4 Months	114	124
6 Months	95	108

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	85	103
10 Months	82	95
12 Months	73	90
14 Months	68	88
16 Months	61	78
18 Months	54	73
20 Months	50	69
22 Months	48	62
24 Months	46	59
26 Months	43	53
Renal and urinary disorders (days)		
Number (%) of events	23 (15.4)	21 (13.8)
Number (%) of patients censored	126 (84.6)	131 (86.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4886
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.8110 (0.4479 to 1.4687)
P-value	-	0.4894
Events probability (95% CI)[c]		
2 Months	0.8832 (0.8188 to 0.9257)	0.9272 (0.8725 to 0.9590)
4 Months	0.8690 (0.8023 to 0.9144)	0.9072 (0.8484 to 0.9440)
6 Months	0.8609 (0.7925 to 0.9080)	0.8998 (0.8392 to 0.9384)
8 Months	0.8349 (0.7614 to 0.8874)	0.8843 (0.8203 to 0.9266)
10 Months	0.8349 (0.7614 to 0.8874)	0.8761 (0.8101 to 0.9202)
12 Months	0.8349 (0.7614 to 0.8874)	0.8761 (0.8101 to 0.9202)
14 Months	0.8349 (0.7614 to 0.8874)	0.8671 (0.7990 to 0.9134)
16 Months	0.8349 (0.7614 to 0.8874)	0.8671 (0.7990 to 0.9134)
18 Months	0.8349 (0.7614 to 0.8874)	0.8572 (0.7863 to 0.9059)
20 Months	0.8349 (0.7614 to 0.8874)	0.8572 (0.7863 to 0.9059)
22 Months	0.8349 (0.7614 to 0.8874)	0.8572 (0.7863 to 0.9059)
24 Months	0.8349 (0.7614 to 0.8874)	0.8451 (0.7701 to 0.8972)
26 Months	0.8349 (0.7614 to 0.8874)	0.8451 (0.7701 to 0.8972)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	126	139
4 Months	119	130
6 Months	105	118
8 Months	92	112
10 Months	89	105
12 Months	84	99
14 Months	79	97
16 Months	72	87
18 Months	65	81
20 Months	62	78
22 Months	60	71
24 Months	59	67
26 Months	56	61
Reproductive system and breast disorders (days)		
Number (%) of events	4 (2.7)	11 (7.2)
Number (%) of patients censored	145 (97.3)	141 (92.8)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0990
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.5377 (0.8065 to 7.9848)
P-value	-	0.1113
Events probability (95% CI)[c]		
2 Months	0.9863 (0.9462 to 0.9965)	0.9934 (0.9539 to 0.9991)
4 Months	0.9863 (0.9462 to 0.9965)	0.9800 (0.9391 to 0.9935)
6 Months	0.9781 (0.9334 to 0.9929)	0.9729 (0.9293 to 0.9897)
8 Months	0.9690 (0.9188 to 0.9883)	0.9648 (0.9173 to 0.9852)
10 Months	0.9690 (0.9188 to 0.9883)	0.9563 (0.9048 to 0.9802)
12 Months	0.9690 (0.9188 to 0.9883)	0.9474 (0.8922 to 0.9747)
14 Months	0.9690 (0.9188 to 0.9883)	0.9292 (0.8675 to 0.9628)
16 Months	0.9690 (0.9188 to 0.9883)	0.9194 (0.8543 to 0.9562)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	0.9690 (0.9188 to 0.9883)	0.9194 (0.8543 to 0.9562)
20 Months	0.9690 (0.9188 to 0.9883)	0.9083 (0.8390 to 0.9487)
22 Months	0.9690 (0.9188 to 0.9883)	0.9083 (0.8390 to 0.9487)
24 Months	0.9690 (0.9188 to 0.9883)	0.9083 (0.8390 to 0.9487)
26 Months	0.9690 (0.9188 to 0.9883)	0.9083 (0.8390 to 0.9487)
Number of patients at risk[c]		
2 Months	140	148
4 Months	132	138
6 Months	114	125
8 Months	103	119
10 Months	99	112
12 Months	91	104
14 Months	85	101
16 Months	78	90
18 Months	70	84
20 Months	66	80
22 Months	64	73
24 Months	63	70
26 Months	60	64

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Respiratory, thoracic and mediastinal disorders (days)		
Number (%) of events	51 (34.2)	68 (44.7)
Number (%) of patients censored	98 (65.8)	84 (55.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	3.8111 (1.2813 to 9.0021)	3.7454 (1.8398 to 4.5667)
Median (95% CI)	NC (NC to NC)	27.3676 (9.1335 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1861
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.2780 (0.8876 to 1.8400)
P-value	-	0.1872
Events probability (95% CI)[c]		
2 Months	0.7806 (0.7041 to 0.8395)	0.7943 (0.7205 to 0.8506)
4 Months	0.7442 (0.6646 to 0.8076)	0.7318 (0.6528 to 0.7957)
6 Months	0.7197 (0.6377 to 0.7862)	0.6591 (0.5758 to 0.7299)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.7023 (0.6187 to 0.7711)	0.6100 (0.5241 to 0.6852)
10 Months	0.6661 (0.5791 to 0.7391)	0.5660 (0.4781 to 0.6447)
12 Months	0.6567 (0.5690 to 0.7308)	0.5471 (0.4584 to 0.6273)
14 Months	0.6264 (0.5360 to 0.7041)	0.5173 (0.4274 to 0.5998)
16 Months	0.6264 (0.5360 to 0.7041)	0.5173 (0.4274 to 0.5998)
18 Months	0.6264 (0.5360 to 0.7041)	0.5173 (0.4274 to 0.5998)
20 Months	0.6264 (0.5360 to 0.7041)	0.5173 (0.4274 to 0.5998)
22 Months	0.6264 (0.5360 to 0.7041)	0.5173 (0.4274 to 0.5998)
24 Months	0.6122 (0.5193 to 0.6924)	0.5173 (0.4274 to 0.5998)
26 Months	0.6122 (0.5193 to 0.6924)	0.5021 (0.4100 to 0.5871)
Number of patients at risk[c]		
2 Months	111	118
4 Months	99	103
6 Months	85	83
8 Months	79	73
10 Months	72	62
12 Months	65	56
14 Months	59	52
16 Months	54	47

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	49	42
20 Months	46	41
22 Months	44	36
24 Months	42	34
26 Months	40	31
Skin and subcutaneous tissue disorders (days)		
Number (%) of events	37 (24.8)	47 (30.9)
Number (%) of patients censored	112 (75.2)	105 (69.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	9.1992 (3.6140 to NC)	9.2320 (2.8255 to 17.7741)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4290
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.1905 (0.7724 to 1.8348)
P-value	-	0.4296

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[c]		
2 Months	0.8505 (0.7819 to 0.8990)	0.8481 (0.7803 to 0.8964)
4 Months	0.8137 (0.7399 to 0.8683)	0.8074 (0.7349 to 0.8620)
6 Months	0.7792 (0.7003 to 0.8397)	0.8001 (0.7266 to 0.8558)
8 Months	0.7521 (0.6695 to 0.8168)	0.7758 (0.6989 to 0.8353)
10 Months	0.7418 (0.6576 to 0.8083)	0.7323 (0.6500 to 0.7983)
12 Months	0.7418 (0.6576 to 0.8083)	0.7141 (0.6297 to 0.7826)
14 Months	0.7304 (0.6441 to 0.7989)	0.7047 (0.6193 to 0.7744)
16 Months	0.7304 (0.6441 to 0.7989)	0.6848 (0.5972 to 0.7573)
18 Months	0.7304 (0.6441 to 0.7989)	0.6736 (0.5845 to 0.7478)
20 Months	0.7304 (0.6441 to 0.7989)	0.6736 (0.5845 to 0.7478)
22 Months	0.7304 (0.6441 to 0.7989)	0.6736 (0.5845 to 0.7478)
24 Months	0.7304 (0.6441 to 0.7989)	0.6607 (0.5694 to 0.7371)
26 Months	0.7304 (0.6441 to 0.7989)	0.6607 (0.5694 to 0.7371)
Number of patients at risk[c]		
2 Months	120	126
4 Months	108	114
6 Months	87	101

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	76	93
10 Months	72	81
12 Months	66	76
14 Months	62	74
16 Months	56	66
18 Months	50	59
20 Months	46	57
22 Months	44	52
24 Months	43	48
26 Months	40	43
Vascular disorders (days)		
Number (%) of events	20 (13.4)	29 (19.1)
Number (%) of patients censored	129 (86.6)	123 (80.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (12.2875 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2642
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.3824 (0.7810 to 2.4468)
P-value	-	0.2663
Events probability (95% CI)[c]		
2 Months	0.9589 (0.9109 to 0.9813)	0.9469 (0.8967 to 0.9731)
4 Months	0.9301 (0.8740 to 0.9618)	0.8919 (0.8295 to 0.9323)
6 Months	0.8988 (0.8349 to 0.9389)	0.8775 (0.8126 to 0.9211)
8 Months	0.8723 (0.8019 to 0.9189)	0.8696 (0.8029 to 0.9148)
10 Months	0.8723 (0.8019 to 0.9189)	0.8613 (0.7929 to 0.9084)
12 Months	0.8615 (0.7880 to 0.9110)	0.8337 (0.7593 to 0.8868)
14 Months	0.8615 (0.7880 to 0.9110)	0.8148 (0.7369 to 0.8717)
16 Months	0.8615 (0.7880 to 0.9110)	0.8048 (0.7249 to 0.8636)
18 Months	0.8358 (0.7538 to 0.8924)	0.8048 (0.7249 to 0.8636)
20 Months	0.8358 (0.7538 to 0.8924)	0.7934 (0.7110 to 0.8547)
22 Months	0.8358 (0.7538 to 0.8924)	0.7934 (0.7110 to 0.8547)
24 Months	0.8358 (0.7538 to 0.8924)	0.7934 (0.7110 to 0.8547)
26 Months	0.8358 (0.7538 to 0.8924)	0.7790 (0.6922 to 0.8441)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.1 Treatment emergent adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	136	141
4 Months	126	125
6 Months	106	111
8 Months	92	105
10 Months	88	97
12 Months	80	89
14 Months	75	86
16 Months	70	78
18 Months	61	72
20 Months	57	67
22 Months	55	60
24 Months	54	57
26 Months	51	50

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Arthralgia (days)		
Number (%) of events	15 (10.1)	17 (11.2)
Number (%) of patients censored	134 (89.9)	135 (88.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9320
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0307 (0.5141 to 2.0664)
P-value	-	0.9321
Events probability (95% CI)[c]		
2 Months	0.9658 (0.9197 to 0.9856)	0.9538 (0.9056 to 0.9777)
4 Months	0.9367 (0.8818 to 0.9666)	0.9256 (0.8697 to 0.9581)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	0.9286 (0.8711 to 0.9610)	0.9256 (0.8697 to 0.9581)
8 Months	0.9012 (0.8350 to 0.9417)	0.9095 (0.8489 to 0.9465)
10 Months	0.9012 (0.8350 to 0.9417)	0.9095 (0.8489 to 0.9465)
12 Months	0.9012 (0.8350 to 0.9417)	0.8916 (0.8259 to 0.9335)
14 Months	0.8896 (0.8190 to 0.9338)	0.8824 (0.8143 to 0.9267)
16 Months	0.8896 (0.8190 to 0.9338)	0.8824 (0.8143 to 0.9267)
18 Months	0.8767 (0.8010 to 0.9250)	0.8824 (0.8143 to 0.9267)
20 Months	0.8767 (0.8010 to 0.9250)	0.8824 (0.8143 to 0.9267)
22 Months	0.8767 (0.8010 to 0.9250)	0.8824 (0.8143 to 0.9267)
24 Months	0.8767 (0.8010 to 0.9250)	0.8824 (0.8143 to 0.9267)
26 Months	0.8767 (0.8010 to 0.9250)	0.8824 (0.8143 to 0.9267)
Number of patients at risk[c]		
2 Months	137	142
4 Months	125	130
6 Months	107	119
8 Months	94	112
10 Months	91	105
12 Months	82	97
14 Months	75	95

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	69	86
18 Months	61	80
20 Months	58	78
22 Months	57	70
24 Months	56	67
26 Months	53	61
Asthenia (days)		
Number (%) of events	28 (18.8)	24 (15.8)
Number (%) of patients censored	121 (81.2)	128 (84.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (9.3306 to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4530
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.8101 (0.4671 to 1.4049)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
P-value	-	0.4533
Events probability (95% CI)[c]		
2 Months	0.9037 (0.8428 to 0.9418)	0.9274 (0.8727 to 0.9591)
4 Months	0.8813 (0.8159 to 0.9246)	0.8730 (0.8081 to 0.9171)
6 Months	0.8563 (0.7857 to 0.9050)	0.8584 (0.7910 to 0.9054)
8 Months	0.8387 (0.7647 to 0.8911)	0.8427 (0.7724 to 0.8927)
10 Months	0.8098 (0.7301 to 0.8680)	0.8427 (0.7724 to 0.8927)
12 Months	0.7993 (0.7175 to 0.8596)	0.8334 (0.7611 to 0.8854)
14 Months	0.7885 (0.7047 to 0.8510)	0.8334 (0.7611 to 0.8854)
16 Months	0.7885 (0.7047 to 0.8510)	0.8334 (0.7611 to 0.8854)
18 Months	0.7885 (0.7047 to 0.8510)	0.8334 (0.7611 to 0.8854)
20 Months	0.7885 (0.7047 to 0.8510)	0.8334 (0.7611 to 0.8854)
22 Months	0.7885 (0.7047 to 0.8510)	0.8334 (0.7611 to 0.8854)
24 Months	0.7885 (0.7047 to 0.8510)	0.8334 (0.7611 to 0.8854)
26 Months	0.7885 (0.7047 to 0.8510)	0.8334 (0.7611 to 0.8854)
Number of patients at risk[c]		
2 Months	128	139
4 Months	118	123

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	101	111
8 Months	90	105
10 Months	83	98
12 Months	76	90
14 Months	70	90
16 Months	66	83
18 Months	60	78
20 Months	56	74
22 Months	54	66
24 Months	53	63
26 Months	51	57
Atrial fibrillation (days)		
Number (%) of events	3 (2.0)	10 (6.6)
Number (%) of patients censored	146 (98.0)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	IPd (N=152)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1111
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.7539 (0.7517 to 10.0898)
P-value	-	0.1262
Events probability (95% CI)[c]		
2 Months	0.9931 (0.9521 to 0.9990)	0.9802 (0.9398 to 0.9936)
4 Months	0.9931 (0.9521 to 0.9990)	0.9802 (0.9398 to 0.9936)
6 Months	0.9931 (0.9521 to 0.9990)	0.9658 (0.9196 to 0.9856)
8 Months	0.9931 (0.9521 to 0.9990)	0.9658 (0.9196 to 0.9856)
10 Months	0.9834 (0.9338 to 0.9959)	0.9489 (0.8952 to 0.9754)
12 Months	0.9834 (0.9338 to 0.9959)	0.9489 (0.8952 to 0.9754)
14 Months	0.9723 (0.9149 to 0.9912)	0.9489 (0.8952 to 0.9754)
16 Months	0.9723 (0.9149 to 0.9912)	0.9489 (0.8952 to 0.9754)
18 Months	0.9723 (0.9149 to 0.9912)	0.9277 (0.8638 to 0.9622)
20 Months	0.9723 (0.9149 to 0.9912)	0.9277 (0.8638 to 0.9622)
22 Months	0.9723 (0.9149 to 0.9912)	0.9277 (0.8638 to 0.9622)
24 Months	0.9723 (0.9149 to 0.9912)	0.9277 (0.8638 to 0.9622)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
26 Months	0.9723 (0.9149 to 0.9912)	0.9140 (0.8426 to 0.9539)
Number of patients at risk[c]		
2 Months	142	146
4 Months	134	138
6 Months	117	124
8 Months	106	119
10 Months	101	110
12 Months	92	103
14 Months	85	103
16 Months	78	93
18 Months	71	85
20 Months	67	81
22 Months	65	73
24 Months	64	70
26 Months	61	63
Back pain (days)		
Number (%) of events	26 (17.4)	28 (18.4)
Number (%) of patients censored	123 (82.6)	124 (81.6)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (12.0575 to NC)	NC (11.7947 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9461
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.9817 (0.5753 to 1.6754)
P-value	-	0.9461
Events probability (95% CI)[c]		
2 Months	0.9312 (0.8759 to 0.9624)	0.9537 (0.9054 to 0.9777)
4 Months	0.8797 (0.8135 to 0.9235)	0.8920 (0.8297 to 0.9324)
6 Months	0.8641 (0.7950 to 0.9112)	0.8700 (0.8036 to 0.9151)
8 Months	0.8556 (0.7848 to 0.9045)	0.8384 (0.7665 to 0.8898)
10 Months	0.8556 (0.7848 to 0.9045)	0.8303 (0.7570 to 0.8831)
12 Months	0.8350 (0.7590 to 0.8888)	0.8215 (0.7467 to 0.8761)
14 Months	0.8244 (0.7460 to 0.8806)	0.8128 (0.7366 to 0.8689)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	0.8244 (0.7460 to 0.8806)	0.8128 (0.7366 to 0.8689)
18 Months	0.8244 (0.7460 to 0.8806)	0.8128 (0.7366 to 0.8689)
20 Months	0.8244 (0.7460 to 0.8806)	0.8128 (0.7366 to 0.8689)
22 Months	0.8244 (0.7460 to 0.8806)	0.8128 (0.7366 to 0.8689)
24 Months	0.8244 (0.7460 to 0.8806)	0.8128 (0.7366 to 0.8689)
26 Months	0.8244 (0.7460 to 0.8806)	0.7993 (0.7186 to 0.8590)
Number of patients at risk[c]		
2 Months	132	142
4 Months	117	126
6 Months	102	111
8 Months	92	106
10 Months	88	101
12 Months	79	94
14 Months	75	92
16 Months	69	84
18 Months	62	78
20 Months	58	74
22 Months	56	67
24 Months	55	65

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
26 Months	53	58
Bone pain (days)		
Number (%) of events	10 (6.7)	12 (7.9)
Number (%) of patients censored	139 (93.3)	140 (92.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.7808
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.1261 (0.4863 to 2.6081)
P-value	-	0.7816
Events probability (95% CI)[c]		
2 Months	0.9658 (0.9197 to 0.9856)	0.9735 (0.9309 to 0.9900)
4 Months	0.9658 (0.9197 to 0.9856)	0.9463 (0.8955 to 0.9728)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	0.9573 (0.9071 to 0.9807)	0.9463 (0.8955 to 0.9728)
8 Months	0.9573 (0.9071 to 0.9807)	0.9463 (0.8955 to 0.9728)
10 Months	0.9379 (0.8784 to 0.9688)	0.9463 (0.8955 to 0.9728)
12 Months	0.9273 (0.8633 to 0.9620)	0.9289 (0.8712 to 0.9613)
14 Months	0.9273 (0.8633 to 0.9620)	0.9289 (0.8712 to 0.9613)
16 Months	0.9273 (0.8633 to 0.9620)	0.9089 (0.8436 to 0.9478)
18 Months	0.9273 (0.8633 to 0.9620)	0.9089 (0.8436 to 0.9478)
20 Months	0.9273 (0.8633 to 0.9620)	0.9089 (0.8436 to 0.9478)
22 Months	0.9273 (0.8633 to 0.9620)	0.9089 (0.8436 to 0.9478)
24 Months	0.9273 (0.8633 to 0.9620)	0.9089 (0.8436 to 0.9478)
26 Months	0.9273 (0.8633 to 0.9620)	0.9089 (0.8436 to 0.9478)
Number of patients at risk[c]		
2 Months	138	145
4 Months	131	133
6 Months	113	120
8 Months	102	115
10 Months	96	112
12 Months	87	103
14 Months	81	102

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	77	91
18 Months	70	85
20 Months	66	81
22 Months	64	72
24 Months	63	70
26 Months	61	65
Bronchitis (days)		
Number (%) of events	17 (11.4)	41 (27.0)
Number (%) of patients censored	132 (88.6)	111 (73.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (27.1704 to NC)	12.4846 (4.5010 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0015
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.4288 (1.3791 to 4.2776)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
P-value	-	0.0021
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.4117 (0.2338 to 0.7251)	-
Events probability (95% CI)[c]		
2 Months	0.9725 (0.9284 to 0.9896)	0.9006 (0.8405 to 0.9388)
4 Months	0.9576 (0.9081 to 0.9808)	0.8383 (0.7684 to 0.8886)
6 Months	0.9339 (0.8766 to 0.9651)	0.7867 (0.7104 to 0.8451)
8 Months	0.9159 (0.8527 to 0.9527)	0.7627 (0.6836 to 0.8246)
10 Months	0.9159 (0.8527 to 0.9527)	0.7627 (0.6836 to 0.8246)
12 Months	0.9051 (0.8378 to 0.9454)	0.7537 (0.6734 to 0.8170)
14 Months	0.8942 (0.8232 to 0.9378)	0.7444 (0.6628 to 0.8091)
16 Months	0.8816 (0.8058 to 0.9292)	0.7253 (0.6412 to 0.7929)
18 Months	0.8687 (0.7883 to 0.9201)	0.7253 (0.6412 to 0.7929)
20 Months	0.8687 (0.7883 to 0.9201)	0.7142 (0.6282 to 0.7837)
22 Months	0.8687 (0.7883 to 0.9201)	0.7142 (0.6282 to 0.7837)
24 Months	0.8532 (0.7665 to 0.9095)	0.7142 (0.6282 to 0.7837)
26 Months	0.8532 (0.7665 to 0.9095)	0.7002 (0.6110 to 0.7727)
Number of patients at risk[c]		
2 Months	138	134

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	128	117
6 Months	110	100
8 Months	97	93
10 Months	93	87
12 Months	83	81
14 Months	76	80
16 Months	69	71
18 Months	63	67
20 Months	59	62
22 Months	57	54
24 Months	55	53
26 Months	52	47
Cataract (days)		
Number (%) of events	10 (6.7)	14 (9.2)
Number (%) of patients censored	139 (93.3)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6128
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.2329 (0.5472 to 2.7781)
P-value	-	0.6134
Events probability (95% CI)[c]		
2 Months	0.9930 (0.9514 to 0.9990)	1.0000 (1.0000 to 1.0000)
4 Months	0.9709 (0.9244 to 0.9890)	0.9932 (0.9530 to 0.9990)
6 Months	0.9465 (0.8909 to 0.9742)	0.9932 (0.9530 to 0.9990)
8 Months	0.9465 (0.8909 to 0.9742)	0.9612 (0.9091 to 0.9837)
10 Months	0.9465 (0.8909 to 0.9742)	0.9440 (0.8859 to 0.9730)
12 Months	0.9465 (0.8909 to 0.9742)	0.9352 (0.8743 to 0.9671)
14 Months	0.9242 (0.8577 to 0.9604)	0.9352 (0.8743 to 0.9671)
16 Months	0.9242 (0.8577 to 0.9604)	0.9150 (0.8469 to 0.9536)
18 Months	0.9242 (0.8577 to 0.9604)	0.9150 (0.8469 to 0.9536)
20 Months	0.9102 (0.8362 to 0.9518)	0.9150 (0.8469 to 0.9536)
22 Months	0.9102 (0.8362 to 0.9518)	0.9150 (0.8469 to 0.9536)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
24 Months	0.9102 (0.8362 to 0.9518)	0.9150 (0.8469 to 0.9536)
26 Months	0.9102 (0.8362 to 0.9518)	0.9013 (0.8266 to 0.9449)
Number of patients at risk[c]		
2 Months	141	149
4 Months	130	140
6 Months	110	127
8 Months	99	118
10 Months	95	109
12 Months	87	101
14 Months	79	100
16 Months	74	88
18 Months	66	81
20 Months	61	78
22 Months	59	70
24 Months	58	67
26 Months	56	60
Constipation (days)		
Number (%) of events	30 (20.1)	25 (16.4)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	119 (79.9)	127 (83.6)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (5.5852 to NC)	NC (26.4476 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2993
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.7550 (0.4434 to 1.2857)
P-value	-	0.3008
Events probability (95% CI)[c]		
2 Months	0.8632 (0.7959 to 0.9095)	0.8942 (0.8331 to 0.9338)
4 Months	0.8338 (0.7622 to 0.8854)	0.8669 (0.8013 to 0.9120)
6 Months	0.8176 (0.7435 to 0.8721)	0.8595 (0.7927 to 0.9061)
8 Months	0.8084 (0.7326 to 0.8647)	0.8430 (0.7729 to 0.8930)
10 Months	0.8084 (0.7326 to 0.8647)	0.8430 (0.7729 to 0.8930)
12 Months	0.8084 (0.7326 to 0.8647)	0.8430 (0.7729 to 0.8930)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.8084 (0.7326 to 0.8647)	0.8335 (0.7612 to 0.8856)
16 Months	0.8084 (0.7326 to 0.8647)	0.8335 (0.7612 to 0.8856)
18 Months	0.8084 (0.7326 to 0.8647)	0.8335 (0.7612 to 0.8856)
20 Months	0.8084 (0.7326 to 0.8647)	0.8335 (0.7612 to 0.8856)
22 Months	0.7611 (0.6688 to 0.8309)	0.8335 (0.7612 to 0.8856)
24 Months	0.7611 (0.6688 to 0.8309)	0.8335 (0.7612 to 0.8856)
26 Months	0.7611 (0.6688 to 0.8309)	0.8335 (0.7612 to 0.8856)
Number of patients at risk[c]		
2 Months	122	133
4 Months	112	122
6 Months	97	108
8 Months	85	101
10 Months	81	95
12 Months	74	89
14 Months	70	88
16 Months	63	79
18 Months	56	73
20 Months	52	72
22 Months	47	63

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
24 Months	46	61
26 Months	45	55
Cough (days)		
Number (%) of events	12 (8.1)	14 (9.2)
Number (%) of patients censored	137 (91.9)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8778
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0623 (0.4909 to 2.2988)
P-value	-	0.8780
Events probability (95% CI)[c]		
2 Months	0.9588 (0.9107 to 0.9813)	0.9732 (0.9303 to 0.9899)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.9444 (0.8918 to 0.9718)	0.9524 (0.9028 to 0.9770)
6 Months	0.9285 (0.8710 to 0.9610)	0.9382 (0.8846 to 0.9674)
8 Months	0.9285 (0.8710 to 0.9610)	0.9059 (0.8431 to 0.9444)
10 Months	0.9191 (0.8580 to 0.9546)	0.8974 (0.8323 to 0.9381)
12 Months	0.9191 (0.8580 to 0.9546)	0.8974 (0.8323 to 0.9381)
14 Months	0.9085 (0.8432 to 0.9474)	0.8974 (0.8323 to 0.9381)
16 Months	0.9085 (0.8432 to 0.9474)	0.8974 (0.8323 to 0.9381)
18 Months	0.9085 (0.8432 to 0.9474)	0.8974 (0.8323 to 0.9381)
20 Months	0.9085 (0.8432 to 0.9474)	0.8974 (0.8323 to 0.9381)
22 Months	0.9085 (0.8432 to 0.9474)	0.8974 (0.8323 to 0.9381)
24 Months	0.9085 (0.8432 to 0.9474)	0.8974 (0.8323 to 0.9381)
26 Months	0.9085 (0.8432 to 0.9474)	0.8974 (0.8323 to 0.9381)
Number of patients at risk[c]		
2 Months	136	145
4 Months	127	134
6 Months	110	120
8 Months	101	111
10 Months	96	103
12 Months	87	97

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	80	96
16 Months	74	88
18 Months	68	81
20 Months	64	78
22 Months	62	70
24 Months	61	67
26 Months	58	61
Decreased appetite (days)		
Number (%) of events	8 (5.4)	17 (11.2)
Number (%) of patients censored	141 (94.6)	135 (88.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1001

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	IPd (N=152)
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.9988 (0.8611 to 4.6396)
P-value	-	0.1070
Events probability (95% CI)[c]		
2 Months	0.9793 (0.9371 to 0.9933)	0.9469 (0.8967 to 0.9731)
4 Months	0.9574 (0.9076 to 0.9807)	0.9128 (0.8545 to 0.9484)
6 Months	0.9490 (0.8958 to 0.9754)	0.9128 (0.8545 to 0.9484)
8 Months	0.9490 (0.8958 to 0.9754)	0.9049 (0.8446 to 0.9426)
10 Months	0.9490 (0.8958 to 0.9754)	0.8965 (0.8339 to 0.9364)
12 Months	0.9490 (0.8958 to 0.9754)	0.8965 (0.8339 to 0.9364)
14 Months	0.9490 (0.8958 to 0.9754)	0.8965 (0.8339 to 0.9364)
16 Months	0.9490 (0.8958 to 0.9754)	0.8965 (0.8339 to 0.9364)
18 Months	0.9490 (0.8958 to 0.9754)	0.8763 (0.8071 to 0.9218)
20 Months	0.9490 (0.8958 to 0.9754)	0.8763 (0.8071 to 0.9218)
22 Months	0.9490 (0.8958 to 0.9754)	0.8763 (0.8071 to 0.9218)
24 Months	0.9490 (0.8958 to 0.9754)	0.8763 (0.8071 to 0.9218)
26 Months	0.9337 (0.8670 to 0.9676)	0.8763 (0.8071 to 0.9218)
Number of patients at risk[c]		
2 Months	139	141

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	129	130
6 Months	112	119
8 Months	101	114
10 Months	97	107
12 Months	88	101
14 Months	82	100
16 Months	76	91
18 Months	69	82
20 Months	65	79
22 Months	63	71
24 Months	62	68
26 Months	59	62
Diarrhoea (days)		
Number (%) of events	33 (22.1)	46 (30.3)
Number (%) of patients censored	116 (77.9)	106 (69.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	26.9076 (5.6181 to NC)	10.1191 (4.1725 to 19.5154)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	IPd (N=152)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2630
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.2908 (0.8246 to 2.0206)
P-value	-	0.2643
Events probability (95% CI)[c]		
2 Months	0.8970 (0.8349 to 0.9366)	0.8678 (0.8026 to 0.9126)
4 Months	0.8386 (0.7670 to 0.8898)	0.8265 (0.7556 to 0.8784)
6 Months	0.8217 (0.7472 to 0.8760)	0.8121 (0.7394 to 0.8663)
8 Months	0.8126 (0.7365 to 0.8687)	0.7731 (0.6955 to 0.8333)
10 Months	0.8028 (0.7248 to 0.8608)	0.7570 (0.6776 to 0.8194)
12 Months	0.7928 (0.7129 to 0.8527)	0.7217 (0.6381 to 0.7891)
14 Months	0.7818 (0.6996 to 0.8440)	0.7126 (0.6282 to 0.7813)
16 Months	0.7703 (0.6858 to 0.8348)	0.6934 (0.6068 to 0.7646)
18 Months	0.7703 (0.6858 to 0.8348)	0.6830 (0.5952 to 0.7557)
20 Months	0.7565 (0.6685 to 0.8243)	0.6718 (0.5825 to 0.7462)
22 Months	0.7565 (0.6685 to 0.8243)	0.6596 (0.5685 to 0.7360)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
24 Months	0.7565 (0.6685 to 0.8243)	0.6596 (0.5685 to 0.7360)
26 Months	0.7565 (0.6685 to 0.8243)	0.6596 (0.5685 to 0.7360)
Number of patients at risk[c]		
2 Months	127	129
4 Months	113	118
6 Months	96	106
8 Months	85	97
10 Months	82	88
12 Months	76	80
14 Months	71	78
16 Months	64	69
18 Months	56	63
20 Months	51	59
22 Months	50	53
24 Months	49	52
26 Months	46	47
Disease progression (days)		
Number (%) of events	9 (6.0)	9 (5.9)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	140 (94.0)	143 (94.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8052
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.8898 (0.3523 to 2.2476)
P-value	-	0.8049
Events probability (95% CI)[c]		
2 Months	0.9794 (0.9375 to 0.9933)	0.9735 (0.9308 to 0.9900)
4 Months	0.9505 (0.8990 to 0.9761)	0.9668 (0.9221 to 0.9860)
6 Months	0.9431 (0.8894 to 0.9712)	0.9528 (0.9035 to 0.9772)
8 Months	0.9431 (0.8894 to 0.9712)	0.9452 (0.8932 to 0.9722)
10 Months	0.9431 (0.8894 to 0.9712)	0.9452 (0.8932 to 0.9722)
12 Months	0.9431 (0.8894 to 0.9712)	0.9452 (0.8932 to 0.9722)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.9431 (0.8894 to 0.9712)	0.9452 (0.8932 to 0.9722)
16 Months	0.9431 (0.8894 to 0.9712)	0.9452 (0.8932 to 0.9722)
18 Months	0.9431 (0.8894 to 0.9712)	0.9452 (0.8932 to 0.9722)
20 Months	0.9431 (0.8894 to 0.9712)	0.9345 (0.8767 to 0.9658)
22 Months	0.9431 (0.8894 to 0.9712)	0.9345 (0.8767 to 0.9658)
24 Months	0.9431 (0.8894 to 0.9712)	0.9345 (0.8767 to 0.9658)
26 Months	0.9286 (0.8633 to 0.9633)	0.9345 (0.8767 to 0.9658)
Number of patients at risk[c]		
2 Months	140	146
4 Months	129	140
6 Months	115	127
8 Months	104	123
10 Months	100	116
12 Months	91	109
14 Months	87	108
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
24 Months	65	75
26 Months	61	69
Dyspnoea (days)		
Number (%) of events	15 (10.1)	25 (16.4)
Number (%) of patients censored	134 (89.9)	127 (83.6)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (19.4168 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1485
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5969 (0.8414 to 3.0308)
P-value	-	0.1522
Events probability (95% CI)[c]		
2 Months	0.9448 (0.8926 to 0.9720)	0.9339 (0.8806 to 0.9639)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.9302 (0.8741 to 0.9618)	0.9136 (0.8559 to 0.9489)
6 Months	0.9218 (0.8630 to 0.9560)	0.8623 (0.7945 to 0.9090)
8 Months	0.9132 (0.8518 to 0.9499)	0.8543 (0.7850 to 0.9026)
10 Months	0.8945 (0.8274 to 0.9365)	0.8371 (0.7645 to 0.8890)
12 Months	0.8945 (0.8274 to 0.9365)	0.8371 (0.7645 to 0.8890)
14 Months	0.8841 (0.8137 to 0.9290)	0.8278 (0.7533 to 0.8816)
16 Months	0.8841 (0.8137 to 0.9290)	0.8278 (0.7533 to 0.8816)
18 Months	0.8841 (0.8137 to 0.9290)	0.8278 (0.7533 to 0.8816)
20 Months	0.8841 (0.8137 to 0.9290)	0.8163 (0.7386 to 0.8729)
22 Months	0.8841 (0.8137 to 0.9290)	0.8163 (0.7386 to 0.8729)
24 Months	0.8841 (0.8137 to 0.9290)	0.8163 (0.7386 to 0.8729)
26 Months	0.8841 (0.8137 to 0.9290)	0.8163 (0.7386 to 0.8729)
Number of patients at risk[c]		
2 Months	134	139
4 Months	124	130
6 Months	109	112
8 Months	99	106
10 Months	93	97
12 Months	86	91

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	81	89
16 Months	74	79
18 Months	67	73
20 Months	64	69
22 Months	62	61
24 Months	61	59
26 Months	59	54
Fatigue (days)		
Number (%) of events	32 (21.5)	30 (19.7)
Number (%) of patients censored	117 (78.5)	122 (80.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (2.5298 to NC)	NC (8.3450 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5058

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	IPd (N=152)
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.8440 (0.5123 to 1.3905)
P-value	-	0.5055
Events probability (95% CI)[c]		
2 Months	0.8422 (0.7721 to 0.8922)	0.9073 (0.8486 to 0.9441)
4 Months	0.8058 (0.7311 to 0.8617)	0.8865 (0.8238 to 0.9279)
6 Months	0.8058 (0.7311 to 0.8617)	0.8717 (0.8062 to 0.9163)
8 Months	0.7798 (0.7012 to 0.8401)	0.8314 (0.7584 to 0.8840)
10 Months	0.7705 (0.6905 to 0.8323)	0.8142 (0.7384 to 0.8700)
12 Months	0.7705 (0.6905 to 0.8323)	0.8142 (0.7384 to 0.8700)
14 Months	0.7705 (0.6905 to 0.8323)	0.8049 (0.7274 to 0.8624)
16 Months	0.7705 (0.6905 to 0.8323)	0.8049 (0.7274 to 0.8624)
18 Months	0.7705 (0.6905 to 0.8323)	0.8049 (0.7274 to 0.8624)
20 Months	0.7705 (0.6905 to 0.8323)	0.7934 (0.7131 to 0.8535)
22 Months	0.7705 (0.6905 to 0.8323)	0.7934 (0.7131 to 0.8535)
24 Months	0.7705 (0.6905 to 0.8323)	0.7801 (0.6962 to 0.8435)
26 Months	0.7705 (0.6905 to 0.8323)	0.7801 (0.6962 to 0.8435)
Number of patients at risk[c]		
2 Months	119	135

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	107	124
6 Months	95	110
8 Months	84	101
10 Months	79	92
12 Months	73	88
14 Months	69	86
16 Months	64	76
18 Months	58	70
20 Months	55	67
22 Months	54	60
24 Months	53	57
26 Months	51	51
Febrile neutropenia (days)		
Number (%) of events	5 (3.4)	18 (11.8)
Number (%) of patients censored	144 (96.6)	134 (88.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0059
Stratified[a] Hazard ratio (95% CI) vs Pd	-	3.6697 (1.3622 to 9.8861)
P-value	-	0.0101
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.2725 (0.1012 to 0.7341)	-
Events probability (95% CI)[c]		
2 Months	0.9860 (0.9452 to 0.9965)	0.9073 (0.8485 to 0.9440)
4 Months	0.9860 (0.9452 to 0.9965)	0.9005 (0.8404 to 0.9388)
6 Months	0.9860 (0.9452 to 0.9965)	0.8865 (0.8238 to 0.9279)
8 Months	0.9860 (0.9452 to 0.9965)	0.8865 (0.8238 to 0.9279)
10 Months	0.9763 (0.9270 to 0.9924)	0.8865 (0.8238 to 0.9279)
12 Months	0.9763 (0.9270 to 0.9924)	0.8777 (0.8126 to 0.9213)
14 Months	0.9653 (0.9083 to 0.9871)	0.8777 (0.8126 to 0.9213)
16 Months	0.9653 (0.9083 to 0.9871)	0.8777 (0.8126 to 0.9213)
18 Months	0.9653 (0.9083 to 0.9871)	0.8777 (0.8126 to 0.9213)
20 Months	0.9511 (0.8826 to 0.9801)	0.8777 (0.8126 to 0.9213)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
22 Months	0.9511 (0.8826 to 0.9801)	0.8777 (0.8126 to 0.9213)
24 Months	0.9511 (0.8826 to 0.9801)	0.8777 (0.8126 to 0.9213)
26 Months	0.9511 (0.8826 to 0.9801)	0.8777 (0.8126 to 0.9213)
Number of patients at risk[c]		
2 Months	140	135
4 Months	132	129
6 Months	116	114
8 Months	105	110
10 Months	100	107
12 Months	92	99
14 Months	85	98
16 Months	78	89
18 Months	70	83
20 Months	66	79
22 Months	64	71
24 Months	63	68
26 Months	60	63
Headache (days)		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of events	9 (6.0)	16 (10.5)
Number (%) of patients censored	140 (94.0)	136 (89.5)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1683
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.8028 (0.7701 to 4.2204)
P-value	-	0.1745
Events probability (95% CI)[c]		
2 Months	0.9720 (0.9271 to 0.9894)	0.9734 (0.9306 to 0.9899)
4 Months	0.9720 (0.9271 to 0.9894)	0.9667 (0.9218 to 0.9860)
6 Months	0.9473 (0.8924 to 0.9746)	0.9297 (0.8730 to 0.9616)
8 Months	0.9473 (0.8924 to 0.9746)	0.9217 (0.8628 to 0.9560)
10 Months	0.9473 (0.8924 to 0.9746)	0.9053 (0.8421 to 0.9440)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	0.9473 (0.8924 to 0.9746)	0.8968 (0.8314 to 0.9377)
14 Months	0.9473 (0.8924 to 0.9746)	0.8877 (0.8200 to 0.9310)
16 Months	0.9473 (0.8924 to 0.9746)	0.8877 (0.8200 to 0.9310)
18 Months	0.9473 (0.8924 to 0.9746)	0.8877 (0.8200 to 0.9310)
20 Months	0.9473 (0.8924 to 0.9746)	0.8877 (0.8200 to 0.9310)
22 Months	0.9321 (0.8642 to 0.9667)	0.8877 (0.8200 to 0.9310)
24 Months	0.9321 (0.8642 to 0.9667)	0.8877 (0.8200 to 0.9310)
26 Months	0.9321 (0.8642 to 0.9667)	0.8877 (0.8200 to 0.9310)
Number of patients at risk[c]		
2 Months	137	145
4 Months	129	138
6 Months	111	121
8 Months	101	115
10 Months	97	107
12 Months	89	99
14 Months	83	97
16 Months	76	88
18 Months	68	82
20 Months	64	79

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
22 Months	61	70
24 Months	60	67
26 Months	57	61
Hypertension (days)		
Number (%) of events	9 (6.0)	12 (7.9)
Number (%) of patients censored	140 (94.0)	140 (92.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.7277
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.1664 (0.4899 to 2.7769)
P-value	-	0.7280
Events probability (95% CI)[c]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	0.9794 (0.9375 to 0.9933)	0.9868 (0.9481 to 0.9967)
4 Months	0.9575 (0.9077 to 0.9807)	0.9729 (0.9294 to 0.9897)
6 Months	0.9497 (0.8973 to 0.9757)	0.9657 (0.9196 to 0.9856)
8 Months	0.9408 (0.8847 to 0.9700)	0.9578 (0.9083 to 0.9809)
10 Months	0.9408 (0.8847 to 0.9700)	0.9578 (0.9083 to 0.9809)
12 Months	0.9301 (0.8687 to 0.9634)	0.9399 (0.8827 to 0.9697)
14 Months	0.9301 (0.8687 to 0.9634)	0.9399 (0.8827 to 0.9697)
16 Months	0.9301 (0.8687 to 0.9634)	0.9299 (0.8685 to 0.9632)
18 Months	0.9301 (0.8687 to 0.9634)	0.9299 (0.8685 to 0.9632)
20 Months	0.9301 (0.8687 to 0.9634)	0.9184 (0.8518 to 0.9559)
22 Months	0.9301 (0.8687 to 0.9634)	0.9184 (0.8518 to 0.9559)
24 Months	0.9301 (0.8687 to 0.9634)	0.9184 (0.8518 to 0.9559)
26 Months	0.9301 (0.8687 to 0.9634)	0.9041 (0.8296 to 0.9470)
Number of patients at risk[c]		
2 Months	139	147
4 Months	128	137
6 Months	111	123
8 Months	99	117
10 Months	95	110

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	86	101
14 Months	81	100
16 Months	75	89
18 Months	68	82
20 Months	64	77
22 Months	62	69
24 Months	61	66
26 Months	58	59
Influenza (days)		
Number (%) of events	8 (5.4)	12 (7.9)
Number (%) of patients censored	141 (94.6)	140 (92.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5067

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	IPd (N=152)
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.3534 (0.5520 to 3.3182)
P-value	-	0.5083
Events probability (95% CI)[c]		
2 Months	0.9931 (0.9517 to 0.9990)	0.9868 (0.9481 to 0.9967)
4 Months	0.9493 (0.8965 to 0.9755)	0.9729 (0.9295 to 0.9898)
6 Months	0.9412 (0.8858 to 0.9702)	0.9578 (0.9084 to 0.9809)
8 Months	0.9412 (0.8858 to 0.9702)	0.9416 (0.8863 to 0.9705)
10 Months	0.9412 (0.8858 to 0.9702)	0.9330 (0.8747 to 0.9647)
12 Months	0.9412 (0.8858 to 0.9702)	0.9330 (0.8747 to 0.9647)
14 Months	0.9412 (0.8858 to 0.9702)	0.9330 (0.8747 to 0.9647)
16 Months	0.9412 (0.8858 to 0.9702)	0.9234 (0.8616 to 0.9583)
18 Months	0.9412 (0.8858 to 0.9702)	0.9234 (0.8616 to 0.9583)
20 Months	0.9412 (0.8858 to 0.9702)	0.9234 (0.8616 to 0.9583)
22 Months	0.9412 (0.8858 to 0.9702)	0.9234 (0.8616 to 0.9583)
24 Months	0.9412 (0.8858 to 0.9702)	0.9234 (0.8616 to 0.9583)
26 Months	0.9412 (0.8858 to 0.9702)	0.9095 (0.8393 to 0.9499)
Number of patients at risk[c]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	141	147
4 Months	127	137
6 Months	110	122
8 Months	99	116
10 Months	96	108
12 Months	89	102
14 Months	83	101
16 Months	76	91
18 Months	68	85
20 Months	64	81
22 Months	62	73
24 Months	61	70
26 Months	59	63
Infusion related reaction (days)		
Number (%) of events	2 (1.3)	57 (37.5)
Number (%) of patients censored	147 (98.7)	95 (62.5)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0986 to 0.1643)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	<.0001
Stratified[a] Hazard ratio (95% CI) vs Pd	-	33.7688 (8.2392 to 138.4043)
P-value	-	<.0001
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.0296 (0.0072 to 0.1214)	-
Events probability (95% CI)[c]		
2 Months	0.9931 (0.9517 to 0.9990)	0.6316 (0.5496 to 0.7027)
4 Months	0.9931 (0.9517 to 0.9990)	0.6316 (0.5496 to 0.7027)
6 Months	0.9931 (0.9517 to 0.9990)	0.6316 (0.5496 to 0.7027)
8 Months	0.9845 (0.9390 to 0.9961)	0.6316 (0.5496 to 0.7027)
10 Months	0.9845 (0.9390 to 0.9961)	0.6316 (0.5496 to 0.7027)
12 Months	0.9845 (0.9390 to 0.9961)	0.6316 (0.5496 to 0.7027)
14 Months	0.9845 (0.9390 to 0.9961)	0.6316 (0.5496 to 0.7027)
16 Months	0.9845 (0.9390 to 0.9961)	0.6316 (0.5496 to 0.7027)
18 Months	0.9845 (0.9390 to 0.9961)	0.6316 (0.5496 to 0.7027)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
20 Months	0.9845 (0.9390 to 0.9961)	0.6203 (0.5367 to 0.6932)
22 Months	0.9845 (0.9390 to 0.9961)	0.6203 (0.5367 to 0.6932)
24 Months	0.9845 (0.9390 to 0.9961)	0.6203 (0.5367 to 0.6932)
26 Months	0.9845 (0.9390 to 0.9961)	0.6203 (0.5367 to 0.6932)
Number of patients at risk[c]		
2 Months	141	95
4 Months	134	90
6 Months	117	81
8 Months	105	77
10 Months	101	71
12 Months	92	66
14 Months	86	65
16 Months	80	59
18 Months	72	56
20 Months	68	52
22 Months	66	48
24 Months	65	47
26 Months	62	43

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Insomnia (days)		
Number (%) of events	14 (9.4)	15 (9.9)
Number (%) of patients censored	135 (90.6)	137 (90.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9702
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.9862 (0.4759 to 2.0438)
P-value	-	0.9702
Events probability (95% CI)[c]		
2 Months	0.9388 (0.8857 to 0.9677)	0.9603 (0.9139 to 0.9820)
4 Months	0.9314 (0.8762 to 0.9625)	0.9532 (0.9044 to 0.9774)
6 Months	0.9233 (0.8656 to 0.9569)	0.9233 (0.8656 to 0.9569)
8 Months	0.9233 (0.8656 to 0.9569)	0.9073 (0.8453 to 0.9452)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
10 Months	0.9233 (0.8656 to 0.9569)	0.8984 (0.8340 to 0.9388)
12 Months	0.9127 (0.8503 to 0.9499)	0.8984 (0.8340 to 0.9388)
14 Months	0.9127 (0.8503 to 0.9499)	0.8891 (0.8219 to 0.9319)
16 Months	0.9002 (0.8317 to 0.9418)	0.8891 (0.8219 to 0.9319)
18 Months	0.9002 (0.8317 to 0.9418)	0.8891 (0.8219 to 0.9319)
20 Months	0.9002 (0.8317 to 0.9418)	0.8891 (0.8219 to 0.9319)
22 Months	0.9002 (0.8317 to 0.9418)	0.8891 (0.8219 to 0.9319)
24 Months	0.9002 (0.8317 to 0.9418)	0.8891 (0.8219 to 0.9319)
26 Months	0.9002 (0.8317 to 0.9418)	0.8891 (0.8219 to 0.9319)
Number of patients at risk[c]		
2 Months	133	143
4 Months	124	134
6 Months	107	117
8 Months	97	110
10 Months	93	102
12 Months	83	96
14 Months	77	94
16 Months	69	85
18 Months	62	79

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
20 Months	58	75
22 Months	56	68
24 Months	55	65
26 Months	52	59
Lower respiratory tract infection (days)		
Number (%) of events	9 (6.0)	12 (7.9)
Number (%) of patients censored	140 (94.0)	140 (92.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9110
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0507 (0.4399 to 2.5098)
P-value	-	0.9113

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[c]		
2 Months	0.9932 (0.9530 to 0.9990)	0.9868 (0.9481 to 0.9967)
4 Months	0.9715 (0.9259 to 0.9892)	0.9728 (0.9290 to 0.9897)
6 Months	0.9550 (0.9023 to 0.9796)	0.9728 (0.9290 to 0.9897)
8 Months	0.9459 (0.8893 to 0.9740)	0.9728 (0.9290 to 0.9897)
10 Months	0.9361 (0.8756 to 0.9678)	0.9477 (0.8929 to 0.9749)
12 Months	0.9361 (0.8756 to 0.9678)	0.9477 (0.8929 to 0.9749)
14 Months	0.9361 (0.8756 to 0.9678)	0.9386 (0.8803 to 0.9690)
16 Months	0.9361 (0.8756 to 0.9678)	0.9386 (0.8803 to 0.9690)
18 Months	0.9361 (0.8756 to 0.9678)	0.9282 (0.8653 to 0.9623)
20 Months	0.9222 (0.8527 to 0.9596)	0.9057 (0.8339 to 0.9474)
22 Months	0.9222 (0.8527 to 0.9596)	0.9057 (0.8339 to 0.9474)
24 Months	0.9222 (0.8527 to 0.9596)	0.9057 (0.8339 to 0.9474)
26 Months	0.9222 (0.8527 to 0.9596)	0.8919 (0.8142 to 0.9384)
Number of patients at risk[c]		
2 Months	141	147
4 Months	130	137
6 Months	111	125
8 Months	100	120

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
10 Months	96	110
12 Months	87	104
14 Months	81	102
16 Months	75	92
18 Months	67	84
20 Months	63	79
22 Months	61	71
24 Months	60	68
26 Months	57	61
Muscle spasms (days)		
Number (%) of events	16 (10.7)	16 (10.5)
Number (%) of patients censored	133 (89.3)	136 (89.5)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8254
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.9248 (0.4620 to 1.8511)
P-value	-	0.8252
Events probability (95% CI)[c]		
2 Months	0.9513 (0.9006 to 0.9765)	0.9669 (0.9224 to 0.9861)
4 Months	0.9224 (0.8643 to 0.9563)	0.9392 (0.8863 to 0.9679)
6 Months	0.9061 (0.8434 to 0.9444)	0.9316 (0.8765 to 0.9626)
8 Months	0.9061 (0.8434 to 0.9444)	0.9074 (0.8454 to 0.9453)
10 Months	0.8857 (0.8163 to 0.9300)	0.8990 (0.8348 to 0.9391)
12 Months	0.8857 (0.8163 to 0.9300)	0.8990 (0.8348 to 0.9391)
14 Months	0.8857 (0.8163 to 0.9300)	0.8895 (0.8226 to 0.9322)
16 Months	0.8723 (0.7971 to 0.9209)	0.8895 (0.8226 to 0.9322)
18 Months	0.8723 (0.7971 to 0.9209)	0.8895 (0.8226 to 0.9322)
20 Months	0.8723 (0.7971 to 0.9209)	0.8895 (0.8226 to 0.9322)
22 Months	0.8723 (0.7971 to 0.9209)	0.8895 (0.8226 to 0.9322)
24 Months	0.8723 (0.7971 to 0.9209)	0.8762 (0.8033 to 0.9234)
26 Months	0.8723 (0.7971 to 0.9209)	0.8762 (0.8033 to 0.9234)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	135	144
4 Months	123	132
6 Months	104	118
8 Months	93	110
10 Months	87	102
12 Months	79	96
14 Months	73	94
16 Months	65	84
18 Months	57	77
20 Months	53	73
22 Months	51	67
24 Months	50	63
26 Months	47	57
Muscular weakness (days)		
Number (%) of events	7 (4.7)	13 (8.6)
Number (%) of patients censored	142 (95.3)	139 (91.4)
Kaplan-Meier estimates of Events in months		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	IPd (N=152)
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2721
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.6657 (0.6635 to 4.1814)
P-value	-	0.2773
Events probability (95% CI)[c]		
2 Months	0.9865 (0.9472 to 0.9966)	0.9867 (0.9477 to 0.9966)
4 Months	0.9646 (0.9169 to 0.9851)	0.9664 (0.9211 to 0.9859)
6 Months	0.9570 (0.9067 to 0.9805)	0.9517 (0.9012 to 0.9767)
8 Months	0.9570 (0.9067 to 0.9805)	0.9438 (0.8905 to 0.9715)
10 Months	0.9570 (0.9067 to 0.9805)	0.9438 (0.8905 to 0.9715)
12 Months	0.9466 (0.8902 to 0.9744)	0.9351 (0.8785 to 0.9658)
14 Months	0.9466 (0.8902 to 0.9744)	0.9351 (0.8785 to 0.9658)
16 Months	0.9466 (0.8902 to 0.9744)	0.9060 (0.8391 to 0.9460)
18 Months	0.9466 (0.8902 to 0.9744)	0.9060 (0.8391 to 0.9460)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
20 Months	0.9466 (0.8902 to 0.9744)	0.9060 (0.8391 to 0.9460)
22 Months	0.9466 (0.8902 to 0.9744)	0.9060 (0.8391 to 0.9460)
24 Months	0.9466 (0.8902 to 0.9744)	0.8933 (0.8207 to 0.9376)
26 Months	0.9466 (0.8902 to 0.9744)	0.8933 (0.8207 to 0.9376)
Number of patients at risk[c]		
2 Months	140	147
4 Months	129	137
6 Months	111	123
8 Months	100	118
10 Months	96	111
12 Months	86	103
14 Months	80	102
16 Months	73	91
18 Months	65	84
20 Months	61	80
22 Months	60	71
24 Months	59	68
26 Months	56	62

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Musculoskeletal chest pain (days)		
Number (%) of events	7 (4.7)	14 (9.2)
Number (%) of patients censored	142 (95.3)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1866
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.8299 (0.7363 to 4.5477)
P-value	-	0.1933
Events probability (95% CI)[c]		
2 Months	0.9930 (0.9514 to 0.9990)	0.9669 (0.9224 to 0.9861)
4 Months	0.9715 (0.9258 to 0.9892)	0.9321 (0.8773 to 0.9629)
6 Months	0.9634 (0.9141 to 0.9846)	0.9248 (0.8682 to 0.9577)
8 Months	0.9547 (0.9016 to 0.9795)	0.9248 (0.8682 to 0.9577)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
10 Months	0.9547 (0.9016 to 0.9795)	0.9080 (0.8465 to 0.9457)
12 Months	0.9443 (0.8858 to 0.9733)	0.9080 (0.8465 to 0.9457)
14 Months	0.9443 (0.8858 to 0.9733)	0.9080 (0.8465 to 0.9457)
16 Months	0.9443 (0.8858 to 0.9733)	0.9080 (0.8465 to 0.9457)
18 Months	0.9443 (0.8858 to 0.9733)	0.9080 (0.8465 to 0.9457)
20 Months	0.9443 (0.8858 to 0.9733)	0.8968 (0.8305 to 0.9381)
22 Months	0.9443 (0.8858 to 0.9733)	0.8968 (0.8305 to 0.9381)
24 Months	0.9443 (0.8858 to 0.9733)	0.8968 (0.8305 to 0.9381)
26 Months	0.9443 (0.8858 to 0.9733)	0.8968 (0.8305 to 0.9381)
Number of patients at risk[c]		
2 Months	141	144
4 Months	130	131
6 Months	112	119
8 Months	100	115
10 Months	98	106
12 Months	88	99
14 Months	82	98
16 Months	75	90
18 Months	67	84

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
20 Months	63	79
22 Months	61	70
24 Months	60	67
26 Months	58	61
Myalgia (days)		
Number (%) of events	5 (3.4)	11 (7.2)
Number (%) of patients censored	144 (96.6)	141 (92.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0968
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.5481 (0.8112 to 8.0042)
P-value	-	0.1092

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[c]		
2 Months	0.9862 (0.9459 to 0.9965)	0.9670 (0.9225 to 0.9861)
4 Months	0.9862 (0.9459 to 0.9965)	0.9532 (0.9044 to 0.9774)
6 Months	0.9776 (0.9318 to 0.9928)	0.9461 (0.8951 to 0.9727)
8 Months	0.9687 (0.9180 to 0.9882)	0.9461 (0.8951 to 0.9727)
10 Months	0.9687 (0.9180 to 0.9882)	0.9461 (0.8951 to 0.9727)
12 Months	0.9687 (0.9180 to 0.9882)	0.9461 (0.8951 to 0.9727)
14 Months	0.9687 (0.9180 to 0.9882)	0.9370 (0.8819 to 0.9669)
16 Months	0.9687 (0.9180 to 0.9882)	0.9278 (0.8690 to 0.9608)
18 Months	0.9687 (0.9180 to 0.9882)	0.9278 (0.8690 to 0.9608)
20 Months	0.9687 (0.9180 to 0.9882)	0.9278 (0.8690 to 0.9608)
22 Months	0.9687 (0.9180 to 0.9882)	0.9278 (0.8690 to 0.9608)
24 Months	0.9687 (0.9180 to 0.9882)	0.9278 (0.8690 to 0.9608)
26 Months	0.9687 (0.9180 to 0.9882)	0.9278 (0.8690 to 0.9608)
Number of patients at risk[c]		
2 Months	139	144
4 Months	131	134
6 Months	113	120
8 Months	102	117

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
10 Months	98	110
12 Months	89	104
14 Months	83	102
16 Months	76	92
18 Months	69	85
20 Months	65	82
22 Months	63	75
24 Months	62	72
26 Months	59	66
Nasopharyngitis (days)		
Number (%) of events	10 (6.7)	21 (13.8)
Number (%) of patients censored	139 (93.3)	131 (86.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (21.3224 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0919
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.8934 (0.8900 to 4.0280)
P-value	-	0.0974
Events probability (95% CI)[c]		
2 Months	0.9791 (0.9367 to 0.9932)	0.9734 (0.9306 to 0.9899)
4 Months	0.9648 (0.9175 to 0.9852)	0.9458 (0.8946 to 0.9726)
6 Months	0.9648 (0.9175 to 0.9852)	0.9313 (0.8759 to 0.9625)
8 Months	0.9561 (0.9046 to 0.9801)	0.9233 (0.8656 to 0.9569)
10 Months	0.9561 (0.9046 to 0.9801)	0.9064 (0.8437 to 0.9447)
12 Months	0.9351 (0.8727 to 0.9675)	0.9064 (0.8437 to 0.9447)
14 Months	0.9351 (0.8727 to 0.9675)	0.8878 (0.8198 to 0.9312)
16 Months	0.9228 (0.8542 to 0.9598)	0.8775 (0.8064 to 0.9237)
18 Months	0.9228 (0.8542 to 0.9598)	0.8668 (0.7926 to 0.9158)
20 Months	0.9228 (0.8542 to 0.9598)	0.8441 (0.7638 to 0.8989)
22 Months	0.9228 (0.8542 to 0.9598)	0.8185 (0.7312 to 0.8797)
24 Months	0.9074 (0.8299 to 0.9506)	0.8185 (0.7312 to 0.8797)
26 Months	0.9074 (0.8299 to 0.9506)	0.8185 (0.7312 to 0.8797)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	139	145
4 Months	129	134
6 Months	112	119
8 Months	100	114
10 Months	96	105
12 Months	85	98
14 Months	80	95
16 Months	74	85
18 Months	66	78
20 Months	62	73
22 Months	60	62
24 Months	58	60
26 Months	55	55
Nausea (days)		
Number (%) of events	14 (9.4)	23 (15.1)
Number (%) of patients censored	135 (90.6)	129 (84.9)
Kaplan-Meier estimates of Events in months		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1408
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.6396 (0.8435 to 3.1869)
P-value	-	0.1448
Events probability (95% CI)[c]		
2 Months	0.9520 (0.9019 to 0.9768)	0.8878 (0.8258 to 0.9287)
4 Months	0.9227 (0.8646 to 0.9565)	0.8739 (0.8094 to 0.9177)
6 Months	0.9144 (0.8540 to 0.9506)	0.8666 (0.8007 to 0.9118)
8 Months	0.9052 (0.8418 to 0.9440)	0.8587 (0.7913 to 0.9056)
10 Months	0.8954 (0.8288 to 0.9370)	0.8587 (0.7913 to 0.9056)
12 Months	0.8954 (0.8288 to 0.9370)	0.8409 (0.7696 to 0.8916)
14 Months	0.8954 (0.8288 to 0.9370)	0.8409 (0.7696 to 0.8916)
16 Months	0.8954 (0.8288 to 0.9370)	0.8409 (0.7696 to 0.8916)
18 Months	0.8954 (0.8288 to 0.9370)	0.8409 (0.7696 to 0.8916)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
20 Months	0.8954 (0.8288 to 0.9370)	0.8409 (0.7696 to 0.8916)
22 Months	0.8954 (0.8288 to 0.9370)	0.8409 (0.7696 to 0.8916)
24 Months	0.8954 (0.8288 to 0.9370)	0.8409 (0.7696 to 0.8916)
26 Months	0.8954 (0.8288 to 0.9370)	0.8409 (0.7696 to 0.8916)
Number of patients at risk[c]		
2 Months	135	132
4 Months	123	122
6 Months	105	111
8 Months	96	105
10 Months	91	98
12 Months	83	92
14 Months	78	91
16 Months	72	83
18 Months	65	76
20 Months	61	72
22 Months	59	65
24 Months	58	62
26 Months	56	56

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Neutropenia (days)		
Number (%) of events	54 (36.2)	77 (50.7)
Number (%) of patients censored	95 (63.8)	75 (49.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	1.9384 (0.9856 to 4.5010)	0.8542 (0.7556 to 0.9856)
Median (95% CI)	NC (31.4415 to NC)	21.9138 (2.8912 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0164
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5270 (1.0778 to 2.1636)
P-value	-	0.0173
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6549 (0.4622 to 0.9278)	-
Events probability (95% CI)[c]		
2 Months	0.7463 (0.6674 to 0.8092)	0.6157 (0.5331 to 0.6880)
4 Months	0.6958 (0.6136 to 0.7639)	0.5749 (0.4919 to 0.6494)
6 Months	0.6479 (0.5626 to 0.7207)	0.5678 (0.4847 to 0.6426)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.6389 (0.5529 to 0.7126)	0.5514 (0.4676 to 0.6273)
10 Months	0.6389 (0.5529 to 0.7126)	0.5330 (0.4483 to 0.6105)
12 Months	0.6389 (0.5529 to 0.7126)	0.5236 (0.4385 to 0.6019)
14 Months	0.6389 (0.5529 to 0.7126)	0.5139 (0.4284 to 0.5929)
16 Months	0.6389 (0.5529 to 0.7126)	0.5139 (0.4284 to 0.5929)
18 Months	0.6258 (0.5376 to 0.7019)	0.5032 (0.4170 to 0.5833)
20 Months	0.6258 (0.5376 to 0.7019)	0.5032 (0.4170 to 0.5833)
22 Months	0.6113 (0.5203 to 0.6902)	0.4907 (0.4032 to 0.5723)
24 Months	0.6113 (0.5203 to 0.6902)	0.4511 (0.3604 to 0.5375)
26 Months	0.6113 (0.5203 to 0.6902)	0.4511 (0.3604 to 0.5375)
Number of patients at risk[c]		
2 Months	108	92
4 Months	93	81
6 Months	78	70
8 Months	69	65
10 Months	67	57
12 Months	63	54
14 Months	57	53
16 Months	52	51

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	47	46
20 Months	44	46
22 Months	42	39
24 Months	41	33
26 Months	38	30
Oedema peripheral (days)		
Number (%) of events	18 (12.1)	29 (19.1)
Number (%) of patients censored	131 (87.9)	123 (80.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	24.9692 (13.5031 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2525
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.4090 (0.7809 to 2.5424)
P-value	-	0.2548

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[c]		
2 Months	0.9243 (0.8675 to 0.9574)	0.9868 (0.9481 to 0.9967)
4 Months	0.9099 (0.8499 to 0.9467)	0.9528 (0.9034 to 0.9772)
6 Months	0.8938 (0.8297 to 0.9347)	0.9385 (0.8850 to 0.9675)
8 Months	0.8938 (0.8297 to 0.9347)	0.9065 (0.8439 to 0.9447)
10 Months	0.8844 (0.8176 to 0.9278)	0.8642 (0.7925 to 0.9125)
12 Months	0.8844 (0.8176 to 0.9278)	0.8465 (0.7714 to 0.8986)
14 Months	0.8844 (0.8176 to 0.9278)	0.8278 (0.7492 to 0.8836)
16 Months	0.8844 (0.8176 to 0.9278)	0.8278 (0.7492 to 0.8836)
18 Months	0.8844 (0.8176 to 0.9278)	0.8053 (0.7216 to 0.8661)
20 Months	0.8844 (0.8176 to 0.9278)	0.7817 (0.6933 to 0.8475)
22 Months	0.8689 (0.7936 to 0.9181)	0.7573 (0.6644 to 0.8278)
24 Months	0.8689 (0.7936 to 0.9181)	0.7573 (0.6644 to 0.8278)
26 Months	0.8689 (0.7936 to 0.9181)	0.7430 (0.6470 to 0.8166)
Number of patients at risk[c]		
2 Months	132	147
4 Months	123	136
6 Months	104	121

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	95	112
10 Months	90	100
12 Months	82	91
14 Months	77	88
16 Months	71	78
18 Months	63	69
20 Months	59	66
22 Months	56	58
24 Months	55	55
26 Months	53	48
Oropharyngeal pain (days)		
Number (%) of events	4 (2.7)	11 (7.2)
Number (%) of patients censored	145 (97.3)	141 (92.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	IPd (N=152)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1306
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.3673 (0.7489 to 7.4831)
P-value	-	0.1422
Events probability (95% CI)[c]		
2 Months	0.9862 (0.9460 to 0.9965)	0.9801 (0.9397 to 0.9935)
4 Months	0.9862 (0.9460 to 0.9965)	0.9733 (0.9303 to 0.9899)
6 Months	0.9786 (0.9349 to 0.9930)	0.9662 (0.9206 to 0.9858)
8 Months	0.9694 (0.9200 to 0.9885)	0.9583 (0.9092 to 0.9811)
10 Months	0.9694 (0.9200 to 0.9885)	0.9497 (0.8969 to 0.9758)
12 Months	0.9694 (0.9200 to 0.9885)	0.9497 (0.8969 to 0.9758)
14 Months	0.9694 (0.9200 to 0.9885)	0.9311 (0.8707 to 0.9638)
16 Months	0.9694 (0.9200 to 0.9885)	0.9311 (0.8707 to 0.9638)
18 Months	0.9694 (0.9200 to 0.9885)	0.9311 (0.8707 to 0.9638)
20 Months	0.9694 (0.9200 to 0.9885)	0.9197 (0.8541 to 0.9566)
22 Months	0.9694 (0.9200 to 0.9885)	0.9197 (0.8541 to 0.9566)
24 Months	0.9694 (0.9200 to 0.9885)	0.9197 (0.8541 to 0.9566)
26 Months	0.9694 (0.9200 to 0.9885)	0.9060 (0.8332 to 0.9480)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	140	146
4 Months	132	137
6 Months	115	123
8 Months	103	117
10 Months	99	109
12 Months	90	103
14 Months	84	100
16 Months	77	90
18 Months	69	84
20 Months	65	80
22 Months	63	71
24 Months	62	68
26 Months	59	62
Pain in extremity (days)		
Number (%) of events	4 (2.7)	11 (7.2)
Number (%) of patients censored	145 (97.3)	141 (92.8)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1227
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.3973 (0.7624 to 7.5378)
P-value	-	0.1347
Events probability (95% CI)[c]		
2 Months	0.9798 (0.9387 to 0.9934)	0.9934 (0.9539 to 0.9991)
4 Months	0.9725 (0.9282 to 0.9896)	0.9934 (0.9539 to 0.9991)
6 Months	0.9725 (0.9282 to 0.9896)	0.9859 (0.9444 to 0.9965)
8 Months	0.9725 (0.9282 to 0.9896)	0.9620 (0.9109 to 0.9840)
10 Months	0.9725 (0.9282 to 0.9896)	0.9366 (0.8769 to 0.9679)
12 Months	0.9725 (0.9282 to 0.9896)	0.9274 (0.8647 to 0.9617)
14 Months	0.9725 (0.9282 to 0.9896)	0.9181 (0.8527 to 0.9553)
16 Months	0.9725 (0.9282 to 0.9896)	0.9181 (0.8527 to 0.9553)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	0.9725 (0.9282 to 0.9896)	0.9181 (0.8527 to 0.9553)
20 Months	0.9725 (0.9282 to 0.9896)	0.9181 (0.8527 to 0.9553)
22 Months	0.9725 (0.9282 to 0.9896)	0.9181 (0.8527 to 0.9553)
24 Months	0.9725 (0.9282 to 0.9896)	0.9181 (0.8527 to 0.9553)
26 Months	0.9725 (0.9282 to 0.9896)	0.9181 (0.8527 to 0.9553)
Number of patients at risk[c]		
2 Months	139	148
4 Months	130	140
6 Months	113	126
8 Months	103	118
10 Months	99	108
12 Months	90	101
14 Months	84	99
16 Months	77	90
18 Months	71	83
20 Months	67	80
22 Months	65	71
24 Months	64	68
26 Months	61	63

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Pathological fracture (days)		
Number (%) of events	8 (5.4)	12 (7.9)
Number (%) of patients censored	141 (94.6)	140 (92.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5214
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.3398 (0.5462 to 3.2866)
P-value	-	0.5229
Events probability (95% CI)[c]		
2 Months	0.9728 (0.9292 to 0.9897)	0.9668 (0.9222 to 0.9861)
4 Months	0.9728 (0.9292 to 0.9897)	0.9602 (0.9135 to 0.9819)
6 Months	0.9563 (0.9050 to 0.9802)	0.9602 (0.9135 to 0.9819)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.9473 (0.8920 to 0.9747)	0.9524 (0.9025 to 0.9770)
10 Months	0.9473 (0.8920 to 0.9747)	0.9440 (0.8908 to 0.9717)
12 Months	0.9370 (0.8768 to 0.9683)	0.9351 (0.8783 to 0.9659)
14 Months	0.9370 (0.8768 to 0.9683)	0.9351 (0.8783 to 0.9659)
16 Months	0.9370 (0.8768 to 0.9683)	0.9161 (0.8524 to 0.9531)
18 Months	0.9370 (0.8768 to 0.9683)	0.9161 (0.8524 to 0.9531)
20 Months	0.9370 (0.8768 to 0.9683)	0.9161 (0.8524 to 0.9531)
22 Months	0.9370 (0.8768 to 0.9683)	0.9161 (0.8524 to 0.9531)
24 Months	0.9370 (0.8768 to 0.9683)	0.9161 (0.8524 to 0.9531)
26 Months	0.9370 (0.8768 to 0.9683)	0.9020 (0.8304 to 0.9444)
Number of patients at risk[c]		
2 Months	139	145
4 Months	131	137
6 Months	112	125
8 Months	100	120
10 Months	97	113
12 Months	89	105
14 Months	83	104
16 Months	76	92

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	69	86
20 Months	66	82
22 Months	64	74
24 Months	63	71
26 Months	60	64
Peripheral sensory neuropathy (days)		
Number (%) of events	11 (7.4)	15 (9.9)
Number (%) of patients censored	138 (92.6)	137 (90.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4207
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.3884 (0.6224 to 3.0971)
P-value	-	0.4228

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	IPd (N=152)
Events probability (95% CI)[c]		
2 Months	0.9862 (0.9461 to 0.9965)	0.9604 (0.9140 to 0.9820)
4 Months	0.9715 (0.9258 to 0.9892)	0.9470 (0.8967 to 0.9731)
6 Months	0.9629 (0.9129 to 0.9845)	0.9243 (0.8673 to 0.9574)
8 Months	0.9536 (0.8989 to 0.9790)	0.9243 (0.8673 to 0.9574)
10 Months	0.9438 (0.8849 to 0.9731)	0.9156 (0.8557 to 0.9513)
12 Months	0.9330 (0.8690 to 0.9663)	0.9156 (0.8557 to 0.9513)
14 Months	0.9216 (0.8529 to 0.9590)	0.9156 (0.8557 to 0.9513)
16 Months	0.9216 (0.8529 to 0.9590)	0.9156 (0.8557 to 0.9513)
18 Months	0.9216 (0.8529 to 0.9590)	0.9156 (0.8557 to 0.9513)
20 Months	0.9216 (0.8529 to 0.9590)	0.8927 (0.8231 to 0.9360)
22 Months	0.9216 (0.8529 to 0.9590)	0.8796 (0.8044 to 0.9272)
24 Months	0.9216 (0.8529 to 0.9590)	0.8796 (0.8044 to 0.9272)
26 Months	0.9054 (0.8267 to 0.9495)	0.8796 (0.8044 to 0.9272)
Number of patients at risk[c]		
2 Months	139	143
4 Months	129	133
6 Months	111	117

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	99	112
10 Months	94	104
12 Months	86	98
14 Months	79	97
16 Months	72	88
18 Months	64	81
20 Months	60	76
22 Months	58	67
24 Months	57	64
26 Months	53	58
Pneumonia (days)		
Number (%) of events	38 (25.5)	42 (27.6)
Number (%) of patients censored	111 (74.5)	110 (72.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	19.5483 (4.3696 to NC)	12.0575 (6.2752 to 27.7618)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	IPd (N=152)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9471
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0150 (0.6538 to 1.5758)
P-value	-	0.9471
Events probability (95% CI)[c]		
2 Months	0.8903 (0.8272 to 0.9313)	0.9207 (0.8646 to 0.9542)
4 Months	0.8252 (0.7522 to 0.8784)	0.8593 (0.7923 to 0.9059)
6 Months	0.8014 (0.7251 to 0.8586)	0.8227 (0.7503 to 0.8757)
8 Months	0.7928 (0.7153 to 0.8514)	0.7996 (0.7242 to 0.8564)
10 Months	0.7836 (0.7046 to 0.8438)	0.7834 (0.7060 to 0.8428)
12 Months	0.7836 (0.7046 to 0.8438)	0.7664 (0.6867 to 0.8283)
14 Months	0.7731 (0.6921 to 0.8354)	0.7492 (0.6675 to 0.8136)
16 Months	0.7502 (0.6646 to 0.8170)	0.7399 (0.6570 to 0.8057)
18 Months	0.7502 (0.6646 to 0.8170)	0.7399 (0.6570 to 0.8057)
20 Months	0.7366 (0.6478 to 0.8063)	0.7294 (0.6448 to 0.7970)
22 Months	0.7219 (0.6294 to 0.7949)	0.7183 (0.6319 to 0.7878)
24 Months	0.7219 (0.6294 to 0.7949)	0.7183 (0.6319 to 0.7878)
26 Months	0.7068 (0.6110 to 0.7831)	0.6914 (0.5996 to 0.7663)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	127	137
4 Months	111	122
6 Months	98	108
8 Months	88	102
10 Months	85	96
12 Months	78	89
14 Months	72	86
16 Months	63	77
18 Months	57	71
20 Months	52	66
22 Months	49	58
24 Months	48	55
26 Months	45	48
Pruritus (days)		
Number (%) of events	11 (7.4)	9 (5.9)
Number (%) of patients censored	138 (92.6)	143 (94.1)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5964
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.7886 (0.3268 to 1.9033)
P-value	-	0.5973
Events probability (95% CI)[c]		
2 Months	0.9253 (0.8692 to 0.9579)	0.9474 (0.8975 to 0.9733)
4 Months	0.9253 (0.8692 to 0.9579)	0.9474 (0.8975 to 0.9733)
6 Months	0.9253 (0.8692 to 0.9579)	0.9474 (0.8975 to 0.9733)
8 Months	0.9253 (0.8692 to 0.9579)	0.9474 (0.8975 to 0.9733)
10 Months	0.9253 (0.8692 to 0.9579)	0.9474 (0.8975 to 0.9733)
12 Months	0.9253 (0.8692 to 0.9579)	0.9474 (0.8975 to 0.9733)
14 Months	0.9253 (0.8692 to 0.9579)	0.9382 (0.8839 to 0.9675)
16 Months	0.9253 (0.8692 to 0.9579)	0.9382 (0.8839 to 0.9675)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	0.9253 (0.8692 to 0.9579)	0.9382 (0.8839 to 0.9675)
20 Months	0.9253 (0.8692 to 0.9579)	0.9382 (0.8839 to 0.9675)
22 Months	0.9253 (0.8692 to 0.9579)	0.9382 (0.8839 to 0.9675)
24 Months	0.9253 (0.8692 to 0.9579)	0.9382 (0.8839 to 0.9675)
26 Months	0.9253 (0.8692 to 0.9579)	0.9382 (0.8839 to 0.9675)
Number of patients at risk[c]		
2 Months	131	141
4 Months	123	133
6 Months	106	120
8 Months	96	115
10 Months	92	108
12 Months	85	103
14 Months	80	101
16 Months	73	91
18 Months	65	85
20 Months	61	82
22 Months	59	74
24 Months	58	71
26 Months	55	66

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Pyrexia (days)		
Number (%) of events	21 (14.1)	25 (16.4)
Number (%) of patients censored	128 (85.9)	127 (83.6)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (34.9569 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8989
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0385 (0.5797 to 1.8604)
P-value	-	0.8990
Events probability (95% CI)[c]		
2 Months	0.9172 (0.8588 to 0.9521)	0.9408 (0.8893 to 0.9687)
4 Months	0.8951 (0.8320 to 0.9355)	0.9137 (0.8559 to 0.9489)
6 Months	0.8710 (0.8028 to 0.9169)	0.9063 (0.8469 to 0.9435)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.8625 (0.7924 to 0.9102)	0.8832 (0.8185 to 0.9258)
10 Months	0.8532 (0.7811 to 0.9030)	0.8665 (0.7981 to 0.9130)
12 Months	0.8432 (0.7686 to 0.8953)	0.8492 (0.7773 to 0.8994)
14 Months	0.8432 (0.7686 to 0.8953)	0.8402 (0.7666 to 0.8923)
16 Months	0.8432 (0.7686 to 0.8953)	0.8302 (0.7543 to 0.8845)
18 Months	0.8432 (0.7686 to 0.8953)	0.8302 (0.7543 to 0.8845)
20 Months	0.8432 (0.7686 to 0.8953)	0.8302 (0.7543 to 0.8845)
22 Months	0.8432 (0.7686 to 0.8953)	0.8302 (0.7543 to 0.8845)
24 Months	0.8432 (0.7686 to 0.8953)	0.8302 (0.7543 to 0.8845)
26 Months	0.8432 (0.7686 to 0.8953)	0.8302 (0.7543 to 0.8845)
Number of patients at risk[c]		
2 Months	130	141
4 Months	121	132
6 Months	104	119
8 Months	96	111
10 Months	91	102
12 Months	81	95
14 Months	76	94
16 Months	69	84

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	63	77
20 Months	60	74
22 Months	58	66
24 Months	57	63
26 Months	54	59
Rash (days)		
Number (%) of events	8 (5.4)	11 (7.2)
Number (%) of patients censored	141 (94.6)	141 (92.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6308
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.2500 (0.5022 to 3.1115)
P-value	-	0.6315

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	IPd (N=152)
Events probability (95% CI)[c]		
2 Months	0.9657 (0.9195 to 0.9856)	0.9802 (0.9398 to 0.9936)
4 Months	0.9513 (0.9005 to 0.9765)	0.9666 (0.9216 to 0.9860)
6 Months	0.9513 (0.9005 to 0.9765)	0.9596 (0.9121 to 0.9816)
8 Months	0.9513 (0.9005 to 0.9765)	0.9596 (0.9121 to 0.9816)
10 Months	0.9413 (0.8851 to 0.9704)	0.9512 (0.9001 to 0.9765)
12 Months	0.9413 (0.8851 to 0.9704)	0.9337 (0.8757 to 0.9651)
14 Months	0.9413 (0.8851 to 0.9704)	0.9337 (0.8757 to 0.9651)
16 Months	0.9413 (0.8851 to 0.9704)	0.9337 (0.8757 to 0.9651)
18 Months	0.9413 (0.8851 to 0.9704)	0.9337 (0.8757 to 0.9651)
20 Months	0.9413 (0.8851 to 0.9704)	0.9337 (0.8757 to 0.9651)
22 Months	0.9413 (0.8851 to 0.9704)	0.9337 (0.8757 to 0.9651)
24 Months	0.9413 (0.8851 to 0.9704)	0.9337 (0.8757 to 0.9651)
26 Months	0.9413 (0.8851 to 0.9704)	0.9337 (0.8757 to 0.9651)
Number of patients at risk[c]		
2 Months	137	146
4 Months	127	137
6 Months	110	123

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	99	118
10 Months	94	110
12 Months	85	102
14 Months	79	101
16 Months	72	91
18 Months	66	84
20 Months	62	81
22 Months	60	73
24 Months	59	70
26 Months	56	64
Stomatitis (days)		
Number (%) of events	4 (2.7)	10 (6.6)
Number (%) of patients censored	145 (97.3)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1273
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.3972 (0.7515 to 7.6468)
P-value	-	0.1396
Events probability (95% CI)[c]		
2 Months	0.9861 (0.9454 to 0.9965)	0.9601 (0.9134 to 0.9819)
4 Months	0.9861 (0.9454 to 0.9965)	0.9394 (0.8867 to 0.9680)
6 Months	0.9775 (0.9314 to 0.9927)	0.9394 (0.8867 to 0.9680)
8 Months	0.9775 (0.9314 to 0.9927)	0.9394 (0.8867 to 0.9680)
10 Months	0.9679 (0.9159 to 0.9880)	0.9309 (0.8750 to 0.9623)
12 Months	0.9679 (0.9159 to 0.9880)	0.9309 (0.8750 to 0.9623)
14 Months	0.9679 (0.9159 to 0.9880)	0.9309 (0.8750 to 0.9623)
16 Months	0.9679 (0.9159 to 0.9880)	0.9309 (0.8750 to 0.9623)
18 Months	0.9679 (0.9159 to 0.9880)	0.9309 (0.8750 to 0.9623)
20 Months	0.9679 (0.9159 to 0.9880)	0.9309 (0.8750 to 0.9623)
22 Months	0.9679 (0.9159 to 0.9880)	0.9309 (0.8750 to 0.9623)
24 Months	0.9679 (0.9159 to 0.9880)	0.9309 (0.8750 to 0.9623)
26 Months	0.9679 (0.9159 to 0.9880)	0.9309 (0.8750 to 0.9623)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	140	143
4 Months	132	133
6 Months	114	120
8 Months	103	116
10 Months	99	108
12 Months	90	101
14 Months	84	100
16 Months	77	90
18 Months	69	84
20 Months	65	81
22 Months	63	72
24 Months	62	69
26 Months	60	64
Thrombocytopenia (days)		
Number (%) of events	18 (12.1)	21 (13.8)
Number (%) of patients censored	131 (87.9)	131 (86.2)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.7448
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.1100 (0.5911 to 2.0844)
P-value	-	0.7455
Events probability (95% CI)[c]		
2 Months	0.8904 (0.8273 to 0.9314)	0.8942 (0.8332 to 0.9338)
4 Months	0.8904 (0.8273 to 0.9314)	0.8807 (0.8173 to 0.9231)
6 Months	0.8756 (0.8097 to 0.9198)	0.8807 (0.8173 to 0.9231)
8 Months	0.8756 (0.8097 to 0.9198)	0.8729 (0.8078 to 0.9170)
10 Months	0.8756 (0.8097 to 0.9198)	0.8729 (0.8078 to 0.9170)
12 Months	0.8756 (0.8097 to 0.9198)	0.8729 (0.8078 to 0.9170)
14 Months	0.8756 (0.8097 to 0.9198)	0.8729 (0.8078 to 0.9170)
16 Months	0.8756 (0.8097 to 0.9198)	0.8631 (0.7952 to 0.9097)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	0.8756 (0.8097 to 0.9198)	0.8631 (0.7952 to 0.9097)
20 Months	0.8756 (0.8097 to 0.9198)	0.8631 (0.7952 to 0.9097)
22 Months	0.8756 (0.8097 to 0.9198)	0.8631 (0.7952 to 0.9097)
24 Months	0.8756 (0.8097 to 0.9198)	0.8631 (0.7952 to 0.9097)
26 Months	0.8756 (0.8097 to 0.9198)	0.8631 (0.7952 to 0.9097)
Number of patients at risk[c]		
2 Months	127	134
4 Months	121	125
6 Months	109	114
8 Months	100	109
10 Months	96	102
12 Months	88	97
14 Months	82	96
16 Months	75	88
18 Months	68	81
20 Months	65	77
22 Months	63	71
24 Months	62	68
26 Months	60	63

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	IPd (N=152)
Tremor (days)		
Number (%) of events	7 (4.7)	12 (7.9)
Number (%) of patients censored	142 (95.3)	140 (92.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3139
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.6083 (0.6324 to 4.0905)
P-value	-	0.3184
Events probability (95% CI)[c]		
2 Months	0.9860 (0.9452 to 0.9965)	0.9733 (0.9305 to 0.9899)
4 Months	0.9638 (0.9152 to 0.9848)	0.9322 (0.8775 to 0.9629)
6 Months	0.9638 (0.9152 to 0.9848)	0.9322 (0.8775 to 0.9629)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.9549 (0.9020 to 0.9796)	0.9322 (0.8775 to 0.9629)
10 Months	0.9549 (0.9020 to 0.9796)	0.9238 (0.8663 to 0.9571)
12 Months	0.9549 (0.9020 to 0.9796)	0.9148 (0.8542 to 0.9509)
14 Months	0.9549 (0.9020 to 0.9796)	0.9148 (0.8542 to 0.9509)
16 Months	0.9549 (0.9020 to 0.9796)	0.9148 (0.8542 to 0.9509)
18 Months	0.9549 (0.9020 to 0.9796)	0.9148 (0.8542 to 0.9509)
20 Months	0.9402 (0.8744 to 0.9721)	0.9148 (0.8542 to 0.9509)
22 Months	0.9402 (0.8744 to 0.9721)	0.9148 (0.8542 to 0.9509)
24 Months	0.9402 (0.8744 to 0.9721)	0.9148 (0.8542 to 0.9509)
26 Months	0.9402 (0.8744 to 0.9721)	0.9148 (0.8542 to 0.9509)
Number of patients at risk[c]		
2 Months	140	145
4 Months	129	131
6 Months	114	119
8 Months	102	115
10 Months	98	107
12 Months	89	99
14 Months	83	98
16 Months	76	89

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	69	83
20 Months	64	80
22 Months	62	72
24 Months	61	69
26 Months	58	63
Upper respiratory tract infection (days)		
Number (%) of events	29 (19.5)	52 (34.2)
Number (%) of patients censored	120 (80.5)	100 (65.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (8.9363 to NC)	7.8193 (5.2895 to 13.0760)
Median (95% CI)	NC (NC to NC)	NC (17.5441 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0119
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.7785 (1.1284 to 2.8032)
P-value	-	0.0131

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.5623 (0.3567 to 0.8862)	-
Events probability (95% CI)[c]		
2 Months	0.9033 (0.8421 to 0.9416)	0.9138 (0.8561 to 0.9490)
4 Months	0.8745 (0.8081 to 0.9190)	0.8446 (0.7753 to 0.8939)
6 Months	0.8581 (0.7884 to 0.9062)	0.7758 (0.6976 to 0.8362)
8 Months	0.8303 (0.7547 to 0.8843)	0.7339 (0.6511 to 0.8001)
10 Months	0.8106 (0.7312 to 0.8687)	0.7164 (0.6318 to 0.7849)
12 Months	0.8106 (0.7312 to 0.8687)	0.6971 (0.6103 to 0.7682)
14 Months	0.7886 (0.7046 to 0.8512)	0.6583 (0.5681 to 0.7341)
16 Months	0.7886 (0.7046 to 0.8512)	0.6371 (0.5449 to 0.7155)
18 Months	0.7886 (0.7046 to 0.8512)	0.5925 (0.4967 to 0.6760)
20 Months	0.7745 (0.6866 to 0.8406)	0.5801 (0.4833 to 0.6651)
22 Months	0.7745 (0.6866 to 0.8406)	0.5801 (0.4833 to 0.6651)
24 Months	0.7587 (0.6661 to 0.8289)	0.5801 (0.4833 to 0.6651)
26 Months	0.7587 (0.6661 to 0.8289)	0.5801 (0.4833 to 0.6651)
Number of patients at risk[c]		
2 Months	128	136
4 Months	116	119

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	98	97
8 Months	87	87
10 Months	82	79
12 Months	76	72
14 Months	70	68
16 Months	64	60
18 Months	56	49
20 Months	51	46
22 Months	49	40
24 Months	47	40
26 Months	45	36
Urinary tract infection (days)		
Number (%) of events	14 (9.4)	19 (12.5)
Number (%) of patients censored	135 (90.6)	133 (87.5)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6126
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.1969 (0.5964 to 2.4020)
P-value	-	0.6131
Events probability (95% CI)[c]		
2 Months	0.9584 (0.9098 to 0.9811)	0.9537 (0.9053 to 0.9776)
4 Months	0.9290 (0.8720 to 0.9612)	0.9132 (0.8552 to 0.9487)
6 Months	0.9210 (0.8618 to 0.9555)	0.9132 (0.8552 to 0.9487)
8 Months	0.8938 (0.8266 to 0.9360)	0.9132 (0.8552 to 0.9487)
10 Months	0.8938 (0.8266 to 0.9360)	0.9132 (0.8552 to 0.9487)
12 Months	0.8938 (0.8266 to 0.9360)	0.9045 (0.8437 to 0.9424)
14 Months	0.8938 (0.8266 to 0.9360)	0.9045 (0.8437 to 0.9424)
16 Months	0.8938 (0.8266 to 0.9360)	0.8950 (0.8310 to 0.9356)
18 Months	0.8938 (0.8266 to 0.9360)	0.8844 (0.8168 to 0.9282)
20 Months	0.8938 (0.8266 to 0.9360)	0.8844 (0.8168 to 0.9282)
22 Months	0.8938 (0.8266 to 0.9360)	0.8726 (0.8007 to 0.9199)
24 Months	0.8938 (0.8266 to 0.9360)	0.8600 (0.7834 to 0.9110)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
26 Months	0.8938 (0.8266 to 0.9360)	0.8600 (0.7834 to 0.9110)
Number of patients at risk[c]		
2 Months	136	143
4 Months	125	130
6 Months	108	119
8 Months	94	115
10 Months	90	108
12 Months	84	100
14 Months	78	99
16 Months	72	88
18 Months	68	81
20 Months	64	78
22 Months	62	69
24 Months	61	65
26 Months	58	59
Vomiting (days)		
Number (%) of events	6 (4.0)	19 (12.5)
Number (%) of patients censored	143 (96.0)	133 (87.5)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0127
Stratified[a] Hazard ratio (95% CI) vs Pd	-	3.0383 (1.2119 to 7.6171)
P-value	-	0.0178
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.3291 (0.1313 to 0.8251)	-
Events probability (95% CI)[c]		
2 Months	0.9863 (0.9465 to 0.9966)	0.9471 (0.8969 to 0.9732)
4 Months	0.9863 (0.9465 to 0.9966)	0.9189 (0.8615 to 0.9531)
6 Months	0.9784 (0.9343 to 0.9930)	0.9189 (0.8615 to 0.9531)
8 Months	0.9604 (0.9069 to 0.9835)	0.8950 (0.8315 to 0.9355)
10 Months	0.9604 (0.9069 to 0.9835)	0.8865 (0.8210 to 0.9291)
12 Months	0.9604 (0.9069 to 0.9835)	0.8685 (0.7986 to 0.9155)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.9490 (0.8884 to 0.9771)	0.8592 (0.7871 to 0.9083)
16 Months	0.9490 (0.8884 to 0.9771)	0.8592 (0.7871 to 0.9083)
18 Months	0.9490 (0.8884 to 0.9771)	0.8592 (0.7871 to 0.9083)
20 Months	0.9490 (0.8884 to 0.9771)	0.8592 (0.7871 to 0.9083)
22 Months	0.9490 (0.8884 to 0.9771)	0.8592 (0.7871 to 0.9083)
24 Months	0.9490 (0.8884 to 0.9771)	0.8592 (0.7871 to 0.9083)
26 Months	0.9490 (0.8884 to 0.9771)	0.8592 (0.7871 to 0.9083)
Number of patients at risk[c]		
2 Months	141	141
4 Months	133	129
6 Months	115	117
8 Months	102	110
10 Months	98	102
12 Months	89	94
14 Months	82	92
16 Months	76	84
18 Months	68	80
20 Months	64	76
22 Months	62	68

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
24 Months	61	65
26 Months	58	59
Weight decreased (days)		
Number (%) of events	2 (1.3)	10 (6.6)
Number (%) of patients censored	147 (98.7)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0089
Stratified[a] Hazard ratio (95% CI) vs Pd	-	9.4245 (1.2056 to 73.6722)
P-value	-	0.0325
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.1061 (0.0136 to 0.8294)	-
Events probability (95% CI)[c]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	0.9931 (0.9517 to 0.9990)	0.9670 (0.9226 to 0.9861)
4 Months	0.9931 (0.9517 to 0.9990)	0.9467 (0.8962 to 0.9730)
6 Months	0.9931 (0.9517 to 0.9990)	0.9394 (0.8868 to 0.9680)
8 Months	0.9931 (0.9517 to 0.9990)	0.9394 (0.8868 to 0.9680)
10 Months	0.9931 (0.9517 to 0.9990)	0.9311 (0.8755 to 0.9624)
12 Months	0.9931 (0.9517 to 0.9990)	0.9311 (0.8755 to 0.9624)
14 Months	0.9931 (0.9517 to 0.9990)	0.9311 (0.8755 to 0.9624)
16 Months	0.9931 (0.9517 to 0.9990)	0.9311 (0.8755 to 0.9624)
18 Months	0.9931 (0.9517 to 0.9990)	0.9311 (0.8755 to 0.9624)
20 Months	0.9931 (0.9517 to 0.9990)	0.9311 (0.8755 to 0.9624)
22 Months	0.9931 (0.9517 to 0.9990)	0.9311 (0.8755 to 0.9624)
24 Months	0.9931 (0.9517 to 0.9990)	0.9311 (0.8755 to 0.9624)
26 Months	0.9931 (0.9517 to 0.9990)	0.9311 (0.8755 to 0.9624)
Number of patients at risk[c]		
2 Months	140	145
4 Months	132	134
6 Months	116	121
8 Months	105	116
10 Months	101	108

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.2 Treatment emergent adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	92	102
14 Months	87	101
16 Months	80	91
18 Months	72	84
20 Months	68	80
22 Months	66	71
24 Months	65	70
26 Months	62	64

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_teaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Blood and lymphatic system disorders (days)		
Number (%) of events	12 (8.1)	19 (12.5)
Number (%) of patients censored	137 (91.9)	133 (87.5)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2161
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5722 (0.7629 to 3.2399)
P-value	-	0.2200
Events probability (95% CI)[c]		
2 Months	0.9452 (0.8934 to 0.9722)	0.9008 (0.8409 to 0.9390)
4 Months	0.9381 (0.8844 to 0.9673)	0.8871 (0.8247 to 0.9283)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	0.9381 (0.8844 to 0.9673)	0.8871 (0.8247 to 0.9283)
8 Months	0.9381 (0.8844 to 0.9673)	0.8871 (0.8247 to 0.9283)
10 Months	0.9287 (0.8710 to 0.9612)	0.8788 (0.8144 to 0.9220)
12 Months	0.9287 (0.8710 to 0.9612)	0.8788 (0.8144 to 0.9220)
14 Months	0.9181 (0.8557 to 0.9543)	0.8788 (0.8144 to 0.9220)
16 Months	0.9181 (0.8557 to 0.9543)	0.8788 (0.8144 to 0.9220)
18 Months	0.9181 (0.8557 to 0.9543)	0.8788 (0.8144 to 0.9220)
20 Months	0.9044 (0.8344 to 0.9458)	0.8788 (0.8144 to 0.9220)
22 Months	0.9044 (0.8344 to 0.9458)	0.8671 (0.7980 to 0.9138)
24 Months	0.9044 (0.8344 to 0.9458)	0.8671 (0.7980 to 0.9138)
26 Months	0.9044 (0.8344 to 0.9458)	0.8671 (0.7980 to 0.9138)
Number of patients at risk[c]		
2 Months	135	135
4 Months	128	126
6 Months	114	115
8 Months	104	111
10 Months	99	106
12 Months	91	99
14 Months	84	98

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	77	89
18 Months	69	82
20 Months	65	78
22 Months	63	72
24 Months	62	69
26 Months	60	64
Cardiac disorders (days)		
Number (%) of events	5 (3.4)	10 (6.6)
Number (%) of patients censored	144 (96.6)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2690
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.8171 (0.6203 to 5.3229)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
P-value	-	0.2761
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	0.9934 (0.9539 to 0.9991)
4 Months	1.0000 (1.0000 to 1.0000)	0.9798 (0.9387 to 0.9934)
6 Months	0.9923 (0.9467 to 0.9989)	0.9798 (0.9387 to 0.9934)
8 Months	0.9923 (0.9467 to 0.9989)	0.9798 (0.9387 to 0.9934)
10 Months	0.9923 (0.9467 to 0.9989)	0.9542 (0.9003 to 0.9793)
12 Months	0.9923 (0.9467 to 0.9989)	0.9542 (0.9003 to 0.9793)
14 Months	0.9592 (0.8939 to 0.9847)	0.9542 (0.9003 to 0.9793)
16 Months	0.9592 (0.8939 to 0.9847)	0.9542 (0.9003 to 0.9793)
18 Months	0.9592 (0.8939 to 0.9847)	0.9439 (0.8847 to 0.9731)
20 Months	0.9592 (0.8939 to 0.9847)	0.9214 (0.8522 to 0.9589)
22 Months	0.9592 (0.8939 to 0.9847)	0.9214 (0.8522 to 0.9589)
24 Months	0.9592 (0.8939 to 0.9847)	0.9214 (0.8522 to 0.9589)
26 Months	0.9592 (0.8939 to 0.9847)	0.9076 (0.8318 to 0.9503)
Number of patients at risk[c]		
2 Months	142	148
4 Months	134	138

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	116	125
8 Months	105	120
10 Months	101	110
12 Months	92	104
14 Months	83	103
16 Months	76	93
18 Months	69	86
20 Months	65	80
22 Months	63	72
24 Months	62	69
26 Months	59	62
Gastrointestinal disorders (days)		
Number (%) of events	3 (2.0)	9 (5.9)
Number (%) of patients censored	146 (98.0)	143 (94.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1139
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.7481 (0.7435 to 10.1568)
P-value	-	0.1296
Events probability (95% CI)[c]		
2 Months	0.9931 (0.9517 to 0.9990)	0.9867 (0.9479 to 0.9967)
4 Months	0.9859 (0.9448 to 0.9965)	0.9800 (0.9393 to 0.9935)
6 Months	0.9859 (0.9448 to 0.9965)	0.9800 (0.9393 to 0.9935)
8 Months	0.9859 (0.9448 to 0.9965)	0.9800 (0.9393 to 0.9935)
10 Months	0.9859 (0.9448 to 0.9965)	0.9718 (0.9264 to 0.9894)
12 Months	0.9755 (0.9245 to 0.9922)	0.9718 (0.9264 to 0.9894)
14 Months	0.9755 (0.9245 to 0.9922)	0.9626 (0.9116 to 0.9844)
16 Months	0.9755 (0.9245 to 0.9922)	0.9527 (0.8964 to 0.9787)
18 Months	0.9755 (0.9245 to 0.9922)	0.9527 (0.8964 to 0.9787)
20 Months	0.9755 (0.9245 to 0.9922)	0.9527 (0.8964 to 0.9787)
22 Months	0.9755 (0.9245 to 0.9922)	0.9527 (0.8964 to 0.9787)
24 Months	0.9755 (0.9245 to 0.9922)	0.9527 (0.8964 to 0.9787)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
26 Months	0.9755 (0.9245 to 0.9922)	0.9390 (0.8729 to 0.9713)
Number of patients at risk[c]		
2 Months	141	147
4 Months	132	138
6 Months	115	125
8 Months	104	120
10 Months	100	112
12 Months	91	105
14 Months	86	103
16 Months	79	92
18 Months	71	87
20 Months	67	83
22 Months	65	75
24 Months	64	72
26 Months	61	66
General disorders and administration site conditions (days)		
Number (%) of events	15 (10.1)	20 (13.2)
Number (%) of patients censored	134 (89.9)	132 (86.8)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6487
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.1686 (0.5973 to 2.2863)
P-value	-	0.6490
Events probability (95% CI)[c]		
2 Months	0.9658 (0.9199 to 0.9856)	0.9735 (0.9310 to 0.9900)
4 Months	0.9369 (0.8822 to 0.9667)	0.9533 (0.9045 to 0.9774)
6 Months	0.9062 (0.8437 to 0.9445)	0.9326 (0.8783 to 0.9632)
8 Months	0.9062 (0.8437 to 0.9445)	0.9175 (0.8592 to 0.9524)
10 Months	0.9062 (0.8437 to 0.9445)	0.9017 (0.8393 to 0.9407)
12 Months	0.9062 (0.8437 to 0.9445)	0.9017 (0.8393 to 0.9407)
14 Months	0.9062 (0.8437 to 0.9445)	0.9017 (0.8393 to 0.9407)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	0.9062 (0.8437 to 0.9445)	0.8834 (0.8160 to 0.9273)
18 Months	0.9062 (0.8437 to 0.9445)	0.8834 (0.8160 to 0.9273)
20 Months	0.9062 (0.8437 to 0.9445)	0.8733 (0.8028 to 0.9198)
22 Months	0.9062 (0.8437 to 0.9445)	0.8733 (0.8028 to 0.9198)
24 Months	0.9062 (0.8437 to 0.9445)	0.8509 (0.7738 to 0.9033)
26 Months	0.8920 (0.8216 to 0.9357)	0.8509 (0.7738 to 0.9033)
Number of patients at risk[c]		
2 Months	139	146
4 Months	128	139
6 Months	112	126
8 Months	102	121
10 Months	98	113
12 Months	89	107
14 Months	85	107
16 Months	78	95
18 Months	71	89
20 Months	67	85
22 Months	65	78
24 Months	64	73

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
26 Months	60	67
Infections and infestations (days)		
Number (%) of events	54 (36.2)	76 (50.0)
Number (%) of patients censored	95 (63.8)	76 (50.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	4.3696 (2.2669 to 11.4333)	4.4353 (2.2669 to 7.5236)
Median (95% CI)	NC (29.5688 to NC)	20.1068 (11.3018 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0911
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.3516 (0.9517 to 1.9194)
P-value	-	0.0923
Events probability (95% CI)[c]		
2 Months	0.8496 (0.7806 to 0.8983)	0.8334 (0.7635 to 0.8842)
4 Months	0.7503 (0.6710 to 0.8131)	0.7790 (0.7035 to 0.8375)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	0.7201 (0.6384 to 0.7864)	0.7008 (0.6194 to 0.7681)
8 Months	0.7040 (0.6210 to 0.7722)	0.6631 (0.5796 to 0.7339)
10 Months	0.6952 (0.6113 to 0.7645)	0.6169 (0.5314 to 0.6914)
12 Months	0.6769 (0.5912 to 0.7484)	0.5769 (0.4901 to 0.6542)
14 Months	0.6671 (0.5804 to 0.7398)	0.5769 (0.4901 to 0.6542)
16 Months	0.6455 (0.5564 to 0.7213)	0.5507 (0.4631 to 0.6299)
18 Months	0.6342 (0.5438 to 0.7115)	0.5414 (0.4534 to 0.6213)
20 Months	0.6223 (0.5303 to 0.7013)	0.5007 (0.4111 to 0.5838)
22 Months	0.6223 (0.5303 to 0.7013)	0.4905 (0.4006 to 0.5743)
24 Months	0.6093 (0.5157 to 0.6903)	0.4788 (0.3883 to 0.5637)
26 Months	0.5960 (0.5008 to 0.6790)	0.4422 (0.3501 to 0.5302)
Number of patients at risk[c]		
2 Months	122	124
4 Months	104	112
6 Months	92	94
8 Months	81	88
10 Months	79	79
12 Months	72	70
14 Months	66	69

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	59	60
18 Months	53	54
20 Months	50	49
22 Months	48	44
24 Months	46	41
26 Months	43	34
Injury, poisoning and procedural complications (days)		
Number (%) of events	3 (2.0)	12 (7.9)
Number (%) of patients censored	146 (98.0)	140 (92.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0205
Stratified[a] Hazard ratio (95% CI) vs Pd	-	3.9871 (1.1249 to 14.1318)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
P-value	-	0.0322
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.2508 (0.0708 to 0.8889)	-
Events probability (95% CI)[c]		
2 Months	0.9863 (0.9465 to 0.9966)	0.9539 (0.9057 to 0.9778)
4 Months	0.9863 (0.9465 to 0.9966)	0.9337 (0.8803 to 0.9638)
6 Months	0.9863 (0.9465 to 0.9966)	0.9337 (0.8803 to 0.9638)
8 Months	0.9863 (0.9465 to 0.9966)	0.9259 (0.8700 to 0.9583)
10 Months	0.9863 (0.9465 to 0.9966)	0.9259 (0.8700 to 0.9583)
12 Months	0.9863 (0.9465 to 0.9966)	0.9259 (0.8700 to 0.9583)
14 Months	0.9863 (0.9465 to 0.9966)	0.9259 (0.8700 to 0.9583)
16 Months	0.9863 (0.9465 to 0.9966)	0.9259 (0.8700 to 0.9583)
18 Months	0.9730 (0.9133 to 0.9918)	0.9259 (0.8700 to 0.9583)
20 Months	0.9730 (0.9133 to 0.9918)	0.9259 (0.8700 to 0.9583)
22 Months	0.9730 (0.9133 to 0.9918)	0.9259 (0.8700 to 0.9583)
24 Months	0.9730 (0.9133 to 0.9918)	0.9259 (0.8700 to 0.9583)
26 Months	0.9730 (0.9133 to 0.9918)	0.9259 (0.8700 to 0.9583)
Number of patients at risk[c]		
2 Months	140	143

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	133	134
6 Months	116	121
8 Months	105	115
10 Months	101	108
12 Months	92	101
14 Months	86	100
16 Months	80	91
18 Months	71	84
20 Months	67	80
22 Months	65	73
24 Months	64	71
26 Months	61	66
Metabolism and nutrition disorders (days)		
Number (%) of events	6 (4.0)	10 (6.6)
Number (%) of patients censored	143 (96.0)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3768
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5736 (0.5709 to 4.3371)
P-value	-	0.3808
Events probability (95% CI)[c]		
2 Months	0.9658 (0.9197 to 0.9856)	0.9670 (0.9225 to 0.9861)
4 Months	0.9658 (0.9197 to 0.9856)	0.9533 (0.9046 to 0.9775)
6 Months	0.9582 (0.9093 to 0.9810)	0.9533 (0.9046 to 0.9775)
8 Months	0.9582 (0.9093 to 0.9810)	0.9533 (0.9046 to 0.9775)
10 Months	0.9582 (0.9093 to 0.9810)	0.9451 (0.8928 to 0.9722)
12 Months	0.9582 (0.9093 to 0.9810)	0.9451 (0.8928 to 0.9722)
14 Months	0.9582 (0.9093 to 0.9810)	0.9361 (0.8801 to 0.9664)
16 Months	0.9582 (0.9093 to 0.9810)	0.9361 (0.8801 to 0.9664)
18 Months	0.9582 (0.9093 to 0.9810)	0.9361 (0.8801 to 0.9664)
20 Months	0.9582 (0.9093 to 0.9810)	0.9250 (0.8635 to 0.9595)
22 Months	0.9582 (0.9093 to 0.9810)	0.9250 (0.8635 to 0.9595)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
24 Months	0.9582 (0.9093 to 0.9810)	0.9250 (0.8635 to 0.9595)
26 Months	0.9582 (0.9093 to 0.9810)	0.9250 (0.8635 to 0.9595)
Number of patients at risk[c]		
2 Months	137	144
4 Months	131	135
6 Months	113	124
8 Months	103	119
10 Months	100	111
12 Months	91	105
14 Months	85	103
16 Months	79	93
18 Months	72	87
20 Months	68	82
22 Months	66	74
24 Months	65	71
26 Months	62	65
Musculoskeletal and connective tissue disorders (days)		
Number (%) of events	6 (4.0)	15 (9.9)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	143 (96.0)	137 (90.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0795
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.2837 (0.8841 to 5.8988)
P-value	-	0.0881
Events probability (95% CI)[c]		
2 Months	0.9725 (0.9284 to 0.9896)	0.9537 (0.9053 to 0.9776)
4 Months	0.9725 (0.9284 to 0.9896)	0.9470 (0.8967 to 0.9731)
6 Months	0.9644 (0.9164 to 0.9851)	0.9397 (0.8872 to 0.9682)
8 Months	0.9553 (0.9026 to 0.9798)	0.9320 (0.8771 to 0.9629)
10 Months	0.9553 (0.9026 to 0.9798)	0.9320 (0.8771 to 0.9629)
12 Months	0.9553 (0.9026 to 0.9798)	0.9234 (0.8656 to 0.9570)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.9553 (0.9026 to 0.9798)	0.9146 (0.8539 to 0.9508)
16 Months	0.9553 (0.9026 to 0.9798)	0.8961 (0.8297 to 0.9375)
18 Months	0.9553 (0.9026 to 0.9798)	0.8961 (0.8297 to 0.9375)
20 Months	0.9553 (0.9026 to 0.9798)	0.8855 (0.8157 to 0.9300)
22 Months	0.9553 (0.9026 to 0.9798)	0.8855 (0.8157 to 0.9300)
24 Months	0.9553 (0.9026 to 0.9798)	0.8855 (0.8157 to 0.9300)
26 Months	0.9553 (0.9026 to 0.9798)	0.8855 (0.8157 to 0.9300)
Number of patients at risk[c]		
2 Months	138	142
4 Months	130	134
6 Months	112	123
8 Months	100	120
10 Months	96	113
12 Months	89	105
14 Months	84	103
16 Months	78	92
18 Months	71	87
20 Months	68	82
22 Months	66	74

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
24 Months	65	71
26 Months	62	65
Nervous system disorders (days)		
Number (%) of events	6 (4.0)	10 (6.6)
Number (%) of patients censored	143 (96.0)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3692
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5841 (0.5753 to 4.3622)
P-value	-	0.3734
Events probability (95% CI)[c]		
2 Months	0.9797 (0.9383 to 0.9934)	0.9868 (0.9482 to 0.9967)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.9797 (0.9383 to 0.9934)	0.9733 (0.9304 to 0.9899)
6 Months	0.9637 (0.9146 to 0.9848)	0.9733 (0.9304 to 0.9899)
8 Months	0.9548 (0.9015 to 0.9796)	0.9493 (0.8962 to 0.9756)
10 Months	0.9548 (0.9015 to 0.9796)	0.9493 (0.8962 to 0.9756)
12 Months	0.9548 (0.9015 to 0.9796)	0.9403 (0.8836 to 0.9699)
14 Months	0.9548 (0.9015 to 0.9796)	0.9403 (0.8836 to 0.9699)
16 Months	0.9548 (0.9015 to 0.9796)	0.9305 (0.8697 to 0.9635)
18 Months	0.9548 (0.9015 to 0.9796)	0.9305 (0.8697 to 0.9635)
20 Months	0.9548 (0.9015 to 0.9796)	0.9305 (0.8697 to 0.9635)
22 Months	0.9548 (0.9015 to 0.9796)	0.9183 (0.8512 to 0.9559)
24 Months	0.9548 (0.9015 to 0.9796)	0.9183 (0.8512 to 0.9559)
26 Months	0.9548 (0.9015 to 0.9796)	0.9183 (0.8512 to 0.9559)
Number of patients at risk[c]		
2 Months	140	147
4 Months	132	137
6 Months	114	124
8 Months	102	116
10 Months	98	110
12 Months	89	102

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	84	101
16 Months	79	90
18 Months	71	83
20 Months	67	79
22 Months	65	70
24 Months	64	68
26 Months	61	62
Renal and urinary disorders (days)		
Number (%) of events	10 (6.7)	9 (5.9)
Number (%) of patients censored	139 (93.3)	143 (94.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6304

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.8016 (0.3250 to 1.9770)
P-value	-	0.6311
Events probability (95% CI)[c]		
2 Months	0.9451 (0.8932 to 0.9722)	0.9603 (0.9139 to 0.9820)
4 Months	0.9451 (0.8932 to 0.9722)	0.9536 (0.9052 to 0.9776)
6 Months	0.9369 (0.8820 to 0.9667)	0.9536 (0.9052 to 0.9776)
8 Months	0.9283 (0.8704 to 0.9609)	0.9536 (0.9052 to 0.9776)
10 Months	0.9283 (0.8704 to 0.9609)	0.9453 (0.8934 to 0.9724)
12 Months	0.9283 (0.8704 to 0.9609)	0.9369 (0.8817 to 0.9668)
14 Months	0.9283 (0.8704 to 0.9609)	0.9369 (0.8817 to 0.9668)
16 Months	0.9283 (0.8704 to 0.9609)	0.9369 (0.8817 to 0.9668)
18 Months	0.9283 (0.8704 to 0.9609)	0.9369 (0.8817 to 0.9668)
20 Months	0.9283 (0.8704 to 0.9609)	0.9369 (0.8817 to 0.9668)
22 Months	0.9283 (0.8704 to 0.9609)	0.9369 (0.8817 to 0.9668)
24 Months	0.9283 (0.8704 to 0.9609)	0.9369 (0.8817 to 0.9668)
26 Months	0.9283 (0.8704 to 0.9609)	0.9369 (0.8817 to 0.9668)
Number of patients at risk[c]		
2 Months	135	144

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	128	136
6 Months	113	125
8 Months	102	121
10 Months	98	113
12 Months	89	106
14 Months	84	105
16 Months	77	95
18 Months	69	88
20 Months	66	85
22 Months	64	77
24 Months	63	74
26 Months	60	68
Respiratory, thoracic and mediastinal disorders (days)		
Number (%) of events	9 (6.0)	10 (6.6)
Number (%) of patients censored	140 (94.0)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9320
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0401 (0.4218 to 2.5648)
P-value	-	0.9320
Events probability (95% CI)[c]		
2 Months	0.9864 (0.9467 to 0.9966)	0.9736 (0.9312 to 0.9900)
4 Months	0.9864 (0.9467 to 0.9966)	0.9596 (0.9123 to 0.9817)
6 Months	0.9703 (0.9225 to 0.9888)	0.9521 (0.9020 to 0.9769)
8 Months	0.9613 (0.9090 to 0.9838)	0.9359 (0.8800 to 0.9662)
10 Months	0.9521 (0.8957 to 0.9783)	0.9359 (0.8800 to 0.9662)
12 Months	0.9521 (0.8957 to 0.9783)	0.9269 (0.8677 to 0.9602)
14 Months	0.9309 (0.8652 to 0.9652)	0.9269 (0.8677 to 0.9602)
16 Months	0.9309 (0.8652 to 0.9652)	0.9269 (0.8677 to 0.9602)
18 Months	0.9309 (0.8652 to 0.9652)	0.9269 (0.8677 to 0.9602)
20 Months	0.9309 (0.8652 to 0.9652)	0.9269 (0.8677 to 0.9602)
22 Months	0.9309 (0.8652 to 0.9652)	0.9269 (0.8677 to 0.9602)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.3 Treatment emergent serious adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
24 Months	0.9309 (0.8652 to 0.9652)	0.9269 (0.8677 to 0.9602)
26 Months	0.9309 (0.8652 to 0.9652)	0.9269 (0.8677 to 0.9602)
Number of patients at risk[c]		
2 Months	141	145
4 Months	133	135
6 Months	114	122
8 Months	104	115
10 Months	99	108
12 Months	90	100
14 Months	82	99
16 Months	76	90
18 Months	69	83
20 Months	65	79
22 Months	63	70
24 Months	62	68
26 Months	59	63

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.4 Treatment emergent serious adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Disease progression (days)		
Number (%) of events	8 (5.4)	8 (5.3)
Number (%) of patients censored	141 (94.6)	144 (94.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.7961
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.8782 (0.3286 to 2.3471)
P-value	-	0.7957
Events probability (95% CI)[c]		
2 Months	0.9794 (0.9375 to 0.9933)	0.9801 (0.9395 to 0.9935)
4 Months	0.9576 (0.9081 to 0.9808)	0.9734 (0.9307 to 0.9899)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.4 Treatment emergent serious adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	0.9501 (0.8982 to 0.9759)	0.9594 (0.9118 to 0.9816)
8 Months	0.9501 (0.8982 to 0.9759)	0.9517 (0.9013 to 0.9767)
10 Months	0.9501 (0.8982 to 0.9759)	0.9517 (0.9013 to 0.9767)
12 Months	0.9501 (0.8982 to 0.9759)	0.9517 (0.9013 to 0.9767)
14 Months	0.9501 (0.8982 to 0.9759)	0.9517 (0.9013 to 0.9767)
16 Months	0.9501 (0.8982 to 0.9759)	0.9517 (0.9013 to 0.9767)
18 Months	0.9501 (0.8982 to 0.9759)	0.9517 (0.9013 to 0.9767)
20 Months	0.9501 (0.8982 to 0.9759)	0.9410 (0.8842 to 0.9704)
22 Months	0.9501 (0.8982 to 0.9759)	0.9410 (0.8842 to 0.9704)
24 Months	0.9501 (0.8982 to 0.9759)	0.9410 (0.8842 to 0.9704)
26 Months	0.9355 (0.8709 to 0.9684)	0.9410 (0.8842 to 0.9704)
Number of patients at risk[c]		
2 Months	140	147
4 Months	130	141
6 Months	115	127
8 Months	104	123
10 Months	100	116
12 Months	91	109
14 Months	87	108

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.4 Treatment emergent serious adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	61	69
Febrile neutropenia (days)		
Number (%) of events	5 (3.4)	10 (6.6)
Number (%) of patients censored	144 (96.6)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1899
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.0207 (0.6905 to 5.9133)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.4 Treatment emergent serious adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
P-value	-	0.1991
Events probability (95% CI)[c]		
2 Months	0.9860 (0.9452 to 0.9965)	0.9471 (0.8969 to 0.9732)
4 Months	0.9860 (0.9452 to 0.9965)	0.9402 (0.8882 to 0.9684)
6 Months	0.9860 (0.9452 to 0.9965)	0.9402 (0.8882 to 0.9684)
8 Months	0.9860 (0.9452 to 0.9965)	0.9402 (0.8882 to 0.9684)
10 Months	0.9763 (0.9270 to 0.9924)	0.9402 (0.8882 to 0.9684)
12 Months	0.9763 (0.9270 to 0.9924)	0.9312 (0.8753 to 0.9625)
14 Months	0.9653 (0.9083 to 0.9871)	0.9312 (0.8753 to 0.9625)
16 Months	0.9653 (0.9083 to 0.9871)	0.9312 (0.8753 to 0.9625)
18 Months	0.9653 (0.9083 to 0.9871)	0.9312 (0.8753 to 0.9625)
20 Months	0.9511 (0.8826 to 0.9801)	0.9312 (0.8753 to 0.9625)
22 Months	0.9511 (0.8826 to 0.9801)	0.9312 (0.8753 to 0.9625)
24 Months	0.9511 (0.8826 to 0.9801)	0.9312 (0.8753 to 0.9625)
26 Months	0.9511 (0.8826 to 0.9801)	0.9312 (0.8753 to 0.9625)
Number of patients at risk[c]		
2 Months	140	141
4 Months	132	132

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.4 Treatment emergent serious adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	116	119
8 Months	105	114
10 Months	100	110
12 Months	92	102
14 Months	85	101
16 Months	78	92
18 Months	70	85
20 Months	66	81
22 Months	64	73
24 Months	63	70
26 Months	60	65
Pneumonia (days)		
Number (%) of events	31 (20.8)	35 (23.0)
Number (%) of patients censored	118 (79.2)	117 (77.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	29.5688 (9.0021 to NC)	24.5749 (11.6304 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.4 Treatment emergent serious adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9194
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0253 (0.6317 to 1.6643)
P-value	-	0.9194
Events probability (95% CI)[c]		
2 Months	0.9178 (0.8597 to 0.9525)	0.9405 (0.8888 to 0.9686)
4 Months	0.8601 (0.7915 to 0.9074)	0.9062 (0.8467 to 0.9434)
6 Months	0.8365 (0.7639 to 0.8883)	0.8622 (0.7944 to 0.9089)
8 Months	0.8279 (0.7539 to 0.8814)	0.8467 (0.7762 to 0.8964)
10 Months	0.8188 (0.7431 to 0.8741)	0.8304 (0.7572 to 0.8832)
12 Months	0.8188 (0.7431 to 0.8741)	0.8131 (0.7370 to 0.8691)
14 Months	0.8085 (0.7305 to 0.8659)	0.8044 (0.7269 to 0.8619)
16 Months	0.7972 (0.7166 to 0.8572)	0.8044 (0.7269 to 0.8619)
18 Months	0.7972 (0.7166 to 0.8572)	0.7943 (0.7149 to 0.8538)
20 Months	0.7839 (0.6996 to 0.8471)	0.7728 (0.6893 to 0.8366)
22 Months	0.7697 (0.6814 to 0.8364)	0.7616 (0.6760 to 0.8275)
24 Months	0.7697 (0.6814 to 0.8364)	0.7616 (0.6760 to 0.8275)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.4 Treatment emergent serious adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
26 Months	0.7552 (0.6632 to 0.8253)	0.7347 (0.6429 to 0.8063)
Number of patients at risk[c]		
2 Months	131	140
4 Months	116	129
6 Months	103	112
8 Months	93	106
10 Months	90	100
12 Months	83	93
14 Months	76	91
16 Months	68	83
18 Months	62	75
20 Months	57	69
22 Months	54	61
24 Months	53	58
26 Months	50	51

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_seraept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Blood and lymphatic system disorders (days)		
Number (%) of events	7 (4.7)	1 (0.7)
Number (%) of patients censored	142 (95.3)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0267
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.1337 (0.0164 to 1.0869)
P-value	-	0.0598
Events probability (95% CI)[c]		
2 Months	0.9525 (0.9029 to 0.9771)	1.0000 (1.0000 to 1.0000)
4 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
6 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
10 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
12 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
14 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
16 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
18 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
20 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
22 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
24 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
26 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
Number of patients at risk[c]		
2 Months	136	149
4 Months	130	140
6 Months	114	127
8 Months	105	122
10 Months	101	115
12 Months	92	108
14 Months	86	107
16 Months	79	97

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	71	90
20 Months	67	86
22 Months	65	77
24 Months	64	74
26 Months	62	68
Cardiac disorders (days)		
Number (%) of events	1 (0.7)	1 (0.7)
Number (%) of patients censored	148 (99.3)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9244
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.8745 (0.0547 to 13.9811)
P-value	-	0.9244

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
18 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
20 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
22 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
24 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
26 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
Eye disorders (days)		
Number (%) of events	1 (0.7)	0 (0.0)
Number (%) of patients censored	148 (99.3)	152 (100.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2966
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
14 Months	0.9889 (0.9237 to 0.9984)	1.0000 (1.0000 to 1.0000)
16 Months	0.9889 (0.9237 to 0.9984)	1.0000 (1.0000 to 1.0000)
18 Months	0.9889 (0.9237 to 0.9984)	1.0000 (1.0000 to 1.0000)
20 Months	0.9889 (0.9237 to 0.9984)	1.0000 (1.0000 to 1.0000)
22 Months	0.9889 (0.9237 to 0.9984)	1.0000 (1.0000 to 1.0000)
24 Months	0.9889 (0.9237 to 0.9984)	1.0000 (1.0000 to 1.0000)
26 Months	0.9889 (0.9237 to 0.9984)	1.0000 (1.0000 to 1.0000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	86	108
16 Months	79	98
18 Months	71	91
20 Months	67	87
22 Months	65	78
24 Months	64	75
26 Months	61	69
General disorders and administration site conditions (days)		
Number (%) of events	2 (1.3)	4 (2.6)
Number (%) of patients censored	147 (98.7)	148 (97.4)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5059
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.7693 (0.3220 to 9.7205)
P-value	-	0.5115
Events probability (95% CI)[c]		
2 Months	0.9932 (0.9530 to 0.9990)	1.0000 (1.0000 to 1.0000)
4 Months	0.9932 (0.9530 to 0.9990)	0.9932 (0.9527 to 0.9990)
6 Months	0.9856 (0.9435 to 0.9964)	0.9862 (0.9458 to 0.9965)
8 Months	0.9856 (0.9435 to 0.9964)	0.9862 (0.9458 to 0.9965)
10 Months	0.9856 (0.9435 to 0.9964)	0.9778 (0.9324 to 0.9928)
12 Months	0.9856 (0.9435 to 0.9964)	0.9778 (0.9324 to 0.9928)
14 Months	0.9856 (0.9435 to 0.9964)	0.9778 (0.9324 to 0.9928)
16 Months	0.9856 (0.9435 to 0.9964)	0.9678 (0.9155 to 0.9880)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	0.9856 (0.9435 to 0.9964)	0.9678 (0.9155 to 0.9880)
20 Months	0.9856 (0.9435 to 0.9964)	0.9678 (0.9155 to 0.9880)
22 Months	0.9856 (0.9435 to 0.9964)	0.9678 (0.9155 to 0.9880)
24 Months	0.9856 (0.9435 to 0.9964)	0.9678 (0.9155 to 0.9880)
26 Months	0.9856 (0.9435 to 0.9964)	0.9678 (0.9155 to 0.9880)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	97
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Hepatobiliary disorders (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3367
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
10 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
12 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
14 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
16 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
18 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
20 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
22 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
24 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
26 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
Infections and infestations (days)		
Number (%) of events	8 (5.4)	8 (5.3)
Number (%) of patients censored	141 (94.6)	144 (94.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8636
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.9176 (0.3442 to 2.4462)
P-value	-	0.8635

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[c]		
2 Months	0.9658 (0.9198 to 0.9856)	0.9934 (0.9539 to 0.9991)
4 Months	0.9587 (0.9105 to 0.9813)	0.9934 (0.9539 to 0.9991)
6 Months	0.9514 (0.9008 to 0.9766)	0.9793 (0.9371 to 0.9933)
8 Months	0.9429 (0.8887 to 0.9711)	0.9793 (0.9371 to 0.9933)
10 Months	0.9429 (0.8887 to 0.9711)	0.9793 (0.9371 to 0.9933)
12 Months	0.9429 (0.8887 to 0.9711)	0.9705 (0.9227 to 0.9889)
14 Months	0.9429 (0.8887 to 0.9711)	0.9705 (0.9227 to 0.9889)
16 Months	0.9429 (0.8887 to 0.9711)	0.9512 (0.8934 to 0.9780)
18 Months	0.9429 (0.8887 to 0.9711)	0.9512 (0.8934 to 0.9780)
20 Months	0.9429 (0.8887 to 0.9711)	0.9402 (0.8771 to 0.9714)
22 Months	0.9429 (0.8887 to 0.9711)	0.9402 (0.8771 to 0.9714)
24 Months	0.9429 (0.8887 to 0.9711)	0.9402 (0.8771 to 0.9714)
26 Months	0.9429 (0.8887 to 0.9711)	0.9402 (0.8771 to 0.9714)
Number of patients at risk[c]		
2 Months	139	148
4 Months	131	141
6 Months	117	127

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	105	122
10 Months	101	115
12 Months	93	107
14 Months	87	106
16 Months	80	95
18 Months	72	88
20 Months	68	83
22 Months	66	75
24 Months	65	72
26 Months	62	66
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (days)		
Number (%) of events	0 (0.0)	2 (1.3)
Number (%) of patients censored	149 (100.0)	150 (98.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2316
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9978
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
8 Months	1.0000 (1.0000 to 1.0000)	0.9919 (0.9441 to 0.9989)
10 Months	1.0000 (1.0000 to 1.0000)	0.9919 (0.9441 to 0.9989)
12 Months	1.0000 (1.0000 to 1.0000)	0.9919 (0.9441 to 0.9989)
14 Months	1.0000 (1.0000 to 1.0000)	0.9919 (0.9441 to 0.9989)
16 Months	1.0000 (1.0000 to 1.0000)	0.9919 (0.9441 to 0.9989)
18 Months	1.0000 (1.0000 to 1.0000)	0.9919 (0.9441 to 0.9989)
20 Months	1.0000 (1.0000 to 1.0000)	0.9810 (0.9251 to 0.9953)
22 Months	1.0000 (1.0000 to 1.0000)	0.9810 (0.9251 to 0.9953)
24 Months	1.0000 (1.0000 to 1.0000)	0.9810 (0.9251 to 0.9953)
26 Months	1.0000 (1.0000 to 1.0000)	0.9810 (0.9251 to 0.9953)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	122
10 Months	102	115
12 Months	93	108
14 Months	87	107
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
Nervous system disorders (days)		
Number (%) of events	2 (1.3)	1 (0.7)
Number (%) of patients censored	147 (98.7)	151 (99.3)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4923
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.4412 (0.0400 to 4.8701)
P-value	-	0.5043
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	0.9924 (0.9474 to 0.9989)	1.0000 (1.0000 to 1.0000)
8 Months	0.9924 (0.9474 to 0.9989)	1.0000 (1.0000 to 1.0000)
10 Months	0.9924 (0.9474 to 0.9989)	1.0000 (1.0000 to 1.0000)
12 Months	0.9924 (0.9474 to 0.9989)	1.0000 (1.0000 to 1.0000)
14 Months	0.9814 (0.9259 to 0.9954)	1.0000 (1.0000 to 1.0000)
16 Months	0.9814 (0.9259 to 0.9954)	1.0000 (1.0000 to 1.0000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	0.9814 (0.9259 to 0.9954)	1.0000 (1.0000 to 1.0000)
20 Months	0.9814 (0.9259 to 0.9954)	1.0000 (1.0000 to 1.0000)
22 Months	0.9814 (0.9259 to 0.9954)	0.9881 (0.9185 to 0.9983)
24 Months	0.9814 (0.9259 to 0.9954)	0.9881 (0.9185 to 0.9983)
26 Months	0.9814 (0.9259 to 0.9954)	0.9881 (0.9185 to 0.9983)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	116	128
8 Months	105	123
10 Months	101	116
12 Months	92	109
14 Months	86	108
16 Months	79	98
18 Months	71	91
20 Months	67	87
22 Months	65	77
24 Months	64	75
26 Months	61	69

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Skin and subcutaneous tissue disorders (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3300
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
6 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
10 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
12 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
14 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
16 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
18 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
20 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
22 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
24 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
26 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	140
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.5 Treatment emergent adverse event leading to discontinuation of treatment according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaesoc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Arteriosclerosis coronary artery (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3476
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9984
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
18 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
20 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
22 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
24 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
26 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
Atypical pneumonia (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3367
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
8 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
10 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
12 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
14 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
16 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
18 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
20 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
22 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
24 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
26 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	127

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	106	122
10 Months	102	115
12 Months	93	108
14 Months	87	107
16 Months	80	97
18 Months	72	90
20 Months	68	86
22 Months	66	78
24 Months	65	75
26 Months	62	69
Bronchopulmonary aspergillosis (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3428
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9984
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	0.9934 (0.9539 to 0.9991)
4 Months	1.0000 (1.0000 to 1.0000)	0.9934 (0.9539 to 0.9991)
6 Months	1.0000 (1.0000 to 1.0000)	0.9934 (0.9539 to 0.9991)
8 Months	1.0000 (1.0000 to 1.0000)	0.9934 (0.9539 to 0.9991)
10 Months	1.0000 (1.0000 to 1.0000)	0.9934 (0.9539 to 0.9991)
12 Months	1.0000 (1.0000 to 1.0000)	0.9934 (0.9539 to 0.9991)
14 Months	1.0000 (1.0000 to 1.0000)	0.9934 (0.9539 to 0.9991)
16 Months	1.0000 (1.0000 to 1.0000)	0.9934 (0.9539 to 0.9991)
18 Months	1.0000 (1.0000 to 1.0000)	0.9934 (0.9539 to 0.9991)
20 Months	1.0000 (1.0000 to 1.0000)	0.9934 (0.9539 to 0.9991)
22 Months	1.0000 (1.0000 to 1.0000)	0.9934 (0.9539 to 0.9991)
24 Months	1.0000 (1.0000 to 1.0000)	0.9934 (0.9539 to 0.9991)
26 Months	1.0000 (1.0000 to 1.0000)	0.9934 (0.9539 to 0.9991)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	142	148
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
Cerebellar infarction (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3388
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
20 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
22 Months	1.0000 (1.0000 to 1.0000)	0.9881 (0.9185 to 0.9983)
24 Months	1.0000 (1.0000 to 1.0000)	0.9881 (0.9185 to 0.9983)
26 Months	1.0000 (1.0000 to 1.0000)	0.9881 (0.9185 to 0.9983)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	77
24 Months	65	75
26 Months	62	69

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Death (days)		
Number (%) of events	1 (0.7)	2 (1.3)
Number (%) of patients censored	148 (99.3)	150 (98.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5743
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.9639 (0.1781 to 21.6585)
P-value	-	0.5816
Events probability (95% CI)[c]		
2 Months	0.9932 (0.9530 to 0.9990)	1.0000 (1.0000 to 1.0000)
4 Months	0.9932 (0.9530 to 0.9990)	0.9932 (0.9527 to 0.9990)
6 Months	0.9932 (0.9530 to 0.9990)	0.9932 (0.9527 to 0.9990)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.9932 (0.9530 to 0.9990)	0.9932 (0.9527 to 0.9990)
10 Months	0.9932 (0.9530 to 0.9990)	0.9848 (0.9400 to 0.9962)
12 Months	0.9932 (0.9530 to 0.9990)	0.9848 (0.9400 to 0.9962)
14 Months	0.9932 (0.9530 to 0.9990)	0.9848 (0.9400 to 0.9962)
16 Months	0.9932 (0.9530 to 0.9990)	0.9848 (0.9400 to 0.9962)
18 Months	0.9932 (0.9530 to 0.9990)	0.9848 (0.9400 to 0.9962)
20 Months	0.9932 (0.9530 to 0.9990)	0.9848 (0.9400 to 0.9962)
22 Months	0.9932 (0.9530 to 0.9990)	0.9848 (0.9400 to 0.9962)
24 Months	0.9932 (0.9530 to 0.9990)	0.9848 (0.9400 to 0.9962)
26 Months	0.9932 (0.9530 to 0.9990)	0.9848 (0.9400 to 0.9962)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
Decubitus ulcer (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3300
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
6 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
8 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
10 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
12 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
14 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
16 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
18 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
20 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
22 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
24 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
26 Months	1.0000 (1.0000 to 1.0000)	0.9933 (0.9533 to 0.9991)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	140
6 Months	117	128

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
Echinococciasis (days)		
Number (%) of events	1 (0.7)	0 (0.0)
Number (%) of patients censored	148 (99.3)	152 (100.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3062
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
8 Months	0.9910 (0.9378 to 0.9987)	1.0000 (1.0000 to 1.0000)
10 Months	0.9910 (0.9378 to 0.9987)	1.0000 (1.0000 to 1.0000)
12 Months	0.9910 (0.9378 to 0.9987)	1.0000 (1.0000 to 1.0000)
14 Months	0.9910 (0.9378 to 0.9987)	1.0000 (1.0000 to 1.0000)
16 Months	0.9910 (0.9378 to 0.9987)	1.0000 (1.0000 to 1.0000)
18 Months	0.9910 (0.9378 to 0.9987)	1.0000 (1.0000 to 1.0000)
20 Months	0.9910 (0.9378 to 0.9987)	1.0000 (1.0000 to 1.0000)
22 Months	0.9910 (0.9378 to 0.9987)	1.0000 (1.0000 to 1.0000)
24 Months	0.9910 (0.9378 to 0.9987)	1.0000 (1.0000 to 1.0000)
26 Months	0.9910 (0.9378 to 0.9987)	1.0000 (1.0000 to 1.0000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	105	123
10 Months	101	116
12 Months	93	109
14 Months	87	108
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
General physical health deterioration (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4497
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9985
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
16 Months	1.0000 (1.0000 to 1.0000)	0.9898 (0.9298 to 0.9986)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	1.0000 (1.0000 to 1.0000)	0.9898 (0.9298 to 0.9986)
20 Months	1.0000 (1.0000 to 1.0000)	0.9898 (0.9298 to 0.9986)
22 Months	1.0000 (1.0000 to 1.0000)	0.9898 (0.9298 to 0.9986)
24 Months	1.0000 (1.0000 to 1.0000)	0.9898 (0.9298 to 0.9986)
26 Months	1.0000 (1.0000 to 1.0000)	0.9898 (0.9298 to 0.9986)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	97
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Haemorrhage intracranial (days)		
Number (%) of events	1 (0.7)	0 (0.0)
Number (%) of patients censored	148 (99.3)	152 (100.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2786
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9984
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
14 Months	0.9890 (0.9246 to 0.9984)	1.0000 (1.0000 to 1.0000)
16 Months	0.9890 (0.9246 to 0.9984)	1.0000 (1.0000 to 1.0000)
18 Months	0.9890 (0.9246 to 0.9984)	1.0000 (1.0000 to 1.0000)
20 Months	0.9890 (0.9246 to 0.9984)	1.0000 (1.0000 to 1.0000)
22 Months	0.9890 (0.9246 to 0.9984)	1.0000 (1.0000 to 1.0000)
24 Months	0.9890 (0.9246 to 0.9984)	1.0000 (1.0000 to 1.0000)
26 Months	0.9890 (0.9246 to 0.9984)	1.0000 (1.0000 to 1.0000)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
Hepatic failure (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3367
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
8 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
10 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
12 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
14 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
16 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
18 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
20 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
22 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
24 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
26 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
Medical device site infection (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3293
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
12 Months	1.0000 (1.0000 to 1.0000)	0.9911 (0.9383 to 0.9987)
14 Months	1.0000 (1.0000 to 1.0000)	0.9911 (0.9383 to 0.9987)
16 Months	1.0000 (1.0000 to 1.0000)	0.9911 (0.9383 to 0.9987)
18 Months	1.0000 (1.0000 to 1.0000)	0.9911 (0.9383 to 0.9987)
20 Months	1.0000 (1.0000 to 1.0000)	0.9911 (0.9383 to 0.9987)
22 Months	1.0000 (1.0000 to 1.0000)	0.9911 (0.9383 to 0.9987)
24 Months	1.0000 (1.0000 to 1.0000)	0.9911 (0.9383 to 0.9987)
26 Months	1.0000 (1.0000 to 1.0000)	0.9911 (0.9383 to 0.9987)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
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	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	108
14 Months	87	107
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
Meningitis cryptococcal (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3329
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9984
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
20 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
22 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
24 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
26 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Metastases to liver (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4795
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9985
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
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	Pd (N=149)	**IPd (N=152)**
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
18 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
20 Months	1.0000 (1.0000 to 1.0000)	0.9890 (0.9246 to 0.9984)
22 Months	1.0000 (1.0000 to 1.0000)	0.9890 (0.9246 to 0.9984)
24 Months	1.0000 (1.0000 to 1.0000)	0.9890 (0.9246 to 0.9984)
26 Months	1.0000 (1.0000 to 1.0000)	0.9890 (0.9246 to 0.9984)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
Multiple organ dysfunction syndrome (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3367
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
8 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
10 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
12 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
14 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
16 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
18 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
20 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
22 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
24 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
26 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
Myelodysplastic syndrome (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3284
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
8 Months	1.0000 (1.0000 to 1.0000)	0.9919 (0.9441 to 0.9989)
10 Months	1.0000 (1.0000 to 1.0000)	0.9919 (0.9441 to 0.9989)
12 Months	1.0000 (1.0000 to 1.0000)	0.9919 (0.9441 to 0.9989)
14 Months	1.0000 (1.0000 to 1.0000)	0.9919 (0.9441 to 0.9989)
16 Months	1.0000 (1.0000 to 1.0000)	0.9919 (0.9441 to 0.9989)
18 Months	1.0000 (1.0000 to 1.0000)	0.9919 (0.9441 to 0.9989)
20 Months	1.0000 (1.0000 to 1.0000)	0.9919 (0.9441 to 0.9989)
22 Months	1.0000 (1.0000 to 1.0000)	0.9919 (0.9441 to 0.9989)
24 Months	1.0000 (1.0000 to 1.0000)	0.9919 (0.9441 to 0.9989)
26 Months	1.0000 (1.0000 to 1.0000)	0.9919 (0.9441 to 0.9989)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	122
10 Months	102	115
12 Months	93	108
14 Months	87	107
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
Myocardial infarction (days)		
Number (%) of events	1 (0.7)	0 (0.0)
Number (%) of patients censored	148 (99.3)	152 (100.0)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2827
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9984
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
16 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
20 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
22 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
24 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
26 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Neutropenia (days)		
Number (%) of events	2 (1.3)	0 (0.0)
Number (%) of patients censored	147 (98.7)	152 (100.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1547
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9964
Events probability (95% CI)[c]		
2 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
4 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
6 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
10 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
12 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
14 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
16 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
18 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
20 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
22 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
24 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
26 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
Number of patients at risk[c]		
2 Months	140	149
4 Months	132	141
6 Months	115	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
Pneumonia (days)		
Number (%) of events	3 (2.0)	2 (1.3)
Number (%) of patients censored	146 (98.0)	150 (98.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5600
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.5907 (0.0986 to 3.5396)
P-value	-	0.5645

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[c]		
2 Months	0.9860 (0.9452 to 0.9965)	1.0000 (1.0000 to 1.0000)
4 Months	0.9860 (0.9452 to 0.9965)	1.0000 (1.0000 to 1.0000)
6 Months	0.9785 (0.9347 to 0.9930)	1.0000 (1.0000 to 1.0000)
8 Months	0.9785 (0.9347 to 0.9930)	1.0000 (1.0000 to 1.0000)
10 Months	0.9785 (0.9347 to 0.9930)	1.0000 (1.0000 to 1.0000)
12 Months	0.9785 (0.9347 to 0.9930)	1.0000 (1.0000 to 1.0000)
14 Months	0.9785 (0.9347 to 0.9930)	1.0000 (1.0000 to 1.0000)
16 Months	0.9785 (0.9347 to 0.9930)	0.9903 (0.9331 to 0.9986)
18 Months	0.9785 (0.9347 to 0.9930)	0.9903 (0.9331 to 0.9986)
20 Months	0.9785 (0.9347 to 0.9930)	0.9792 (0.9190 to 0.9948)
22 Months	0.9785 (0.9347 to 0.9930)	0.9792 (0.9190 to 0.9948)
24 Months	0.9785 (0.9347 to 0.9930)	0.9792 (0.9190 to 0.9948)
26 Months	0.9785 (0.9347 to 0.9930)	0.9792 (0.9190 to 0.9948)
Number of patients at risk[c]		
2 Months	140	149
4 Months	132	141
6 Months	117	128

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	97
18 Months	72	90
20 Months	68	85
22 Months	66	76
24 Months	65	73
26 Months	62	67
Pneumonia influenzal (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3657
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9984
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
8 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
10 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
12 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
14 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
16 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
18 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
20 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
22 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
24 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)
26 Months	1.0000 (1.0000 to 1.0000)	0.9929 (0.9507 to 0.9990)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
Pneumonia streptococcal (days)		
Number (%) of events	1 (0.7)	0 (0.0)
Number (%) of patients censored	148 (99.3)	152 (100.0)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3049
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9984
Events probability (95% CI)[c]		
2 Months	0.9932 (0.9524 to 0.9990)	1.0000 (1.0000 to 1.0000)
4 Months	0.9932 (0.9524 to 0.9990)	1.0000 (1.0000 to 1.0000)
6 Months	0.9932 (0.9524 to 0.9990)	1.0000 (1.0000 to 1.0000)
8 Months	0.9932 (0.9524 to 0.9990)	1.0000 (1.0000 to 1.0000)
10 Months	0.9932 (0.9524 to 0.9990)	1.0000 (1.0000 to 1.0000)
12 Months	0.9932 (0.9524 to 0.9990)	1.0000 (1.0000 to 1.0000)
14 Months	0.9932 (0.9524 to 0.9990)	1.0000 (1.0000 to 1.0000)
16 Months	0.9932 (0.9524 to 0.9990)	1.0000 (1.0000 to 1.0000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	0.9932 (0.9524 to 0.9990)	1.0000 (1.0000 to 1.0000)
20 Months	0.9932 (0.9524 to 0.9990)	1.0000 (1.0000 to 1.0000)
22 Months	0.9932 (0.9524 to 0.9990)	1.0000 (1.0000 to 1.0000)
24 Months	0.9932 (0.9524 to 0.9990)	1.0000 (1.0000 to 1.0000)
26 Months	0.9932 (0.9524 to 0.9990)	1.0000 (1.0000 to 1.0000)
Number of patients at risk[c]		
2 Months	141	149
4 Months	133	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Pyoderma (days)		
Number (%) of events	0 (0.0)	1 (0.7)
Number (%) of patients censored	149 (100.0)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3613
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9984
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
14 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
16 Months	1.0000 (1.0000 to 1.0000)	0.9902 (0.9324 to 0.9986)
18 Months	1.0000 (1.0000 to 1.0000)	0.9902 (0.9324 to 0.9986)
20 Months	1.0000 (1.0000 to 1.0000)	0.9902 (0.9324 to 0.9986)
22 Months	1.0000 (1.0000 to 1.0000)	0.9902 (0.9324 to 0.9986)
24 Months	1.0000 (1.0000 to 1.0000)	0.9902 (0.9324 to 0.9986)
26 Months	1.0000 (1.0000 to 1.0000)	0.9902 (0.9324 to 0.9986)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	97

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	72	90
20 Months	68	86
22 Months	66	77
24 Months	65	74
26 Months	62	68
Sepsis (days)		
Number (%) of events	1 (0.7)	0 (0.0)
Number (%) of patients censored	148 (99.3)	152 (100.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2943
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9984

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	0.9929 (0.9504 to 0.9990)	1.0000 (1.0000 to 1.0000)
6 Months	0.9929 (0.9504 to 0.9990)	1.0000 (1.0000 to 1.0000)
8 Months	0.9929 (0.9504 to 0.9990)	1.0000 (1.0000 to 1.0000)
10 Months	0.9929 (0.9504 to 0.9990)	1.0000 (1.0000 to 1.0000)
12 Months	0.9929 (0.9504 to 0.9990)	1.0000 (1.0000 to 1.0000)
14 Months	0.9929 (0.9504 to 0.9990)	1.0000 (1.0000 to 1.0000)
16 Months	0.9929 (0.9504 to 0.9990)	1.0000 (1.0000 to 1.0000)
18 Months	0.9929 (0.9504 to 0.9990)	1.0000 (1.0000 to 1.0000)
20 Months	0.9929 (0.9504 to 0.9990)	1.0000 (1.0000 to 1.0000)
22 Months	0.9929 (0.9504 to 0.9990)	1.0000 (1.0000 to 1.0000)
24 Months	0.9929 (0.9504 to 0.9990)	1.0000 (1.0000 to 1.0000)
26 Months	0.9929 (0.9504 to 0.9990)	1.0000 (1.0000 to 1.0000)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
Septic shock (days)		
Number (%) of events	2 (1.3)	0 (0.0)
Number (%) of patients censored	147 (98.7)	152 (100.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1464
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9964
Events probability (95% CI)[c]		
2 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
4 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
6 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
8 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
10 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
12 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
14 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
16 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
18 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
20 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
22 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
24 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)
26 Months	0.9864 (0.9467 to 0.9966)	1.0000 (1.0000 to 1.0000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
Spinal subdural haematoma (days)		
Number (%) of events	1 (0.7)	0 (0.0)
Number (%) of patients censored	148 (99.3)	152 (100.0)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2980
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	0.9924 (0.9474 to 0.9989)	1.0000 (1.0000 to 1.0000)
8 Months	0.9924 (0.9474 to 0.9989)	1.0000 (1.0000 to 1.0000)
10 Months	0.9924 (0.9474 to 0.9989)	1.0000 (1.0000 to 1.0000)
12 Months	0.9924 (0.9474 to 0.9989)	1.0000 (1.0000 to 1.0000)
14 Months	0.9924 (0.9474 to 0.9989)	1.0000 (1.0000 to 1.0000)
16 Months	0.9924 (0.9474 to 0.9989)	1.0000 (1.0000 to 1.0000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	0.9924 (0.9474 to 0.9989)	1.0000 (1.0000 to 1.0000)
20 Months	0.9924 (0.9474 to 0.9989)	1.0000 (1.0000 to 1.0000)
22 Months	0.9924 (0.9474 to 0.9989)	1.0000 (1.0000 to 1.0000)
24 Months	0.9924 (0.9474 to 0.9989)	1.0000 (1.0000 to 1.0000)
26 Months	0.9924 (0.9474 to 0.9989)	1.0000 (1.0000 to 1.0000)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	116	128
8 Months	105	123
10 Months	101	116
12 Months	92	109
14 Months	86	108
16 Months	79	98
18 Months	71	91
20 Months	67	87
22 Months	65	78
24 Months	64	75
26 Months	61	69

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Sudden death (days)		
Number (%) of events	1 (0.7)	0 (0.0)
Number (%) of patients censored	148 (99.3)	152 (100.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2974
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	0.9923 (0.9467 to 0.9989)	1.0000 (1.0000 to 1.0000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	0.9923 (0.9467 to 0.9989)	1.0000 (1.0000 to 1.0000)
10 Months	0.9923 (0.9467 to 0.9989)	1.0000 (1.0000 to 1.0000)
12 Months	0.9923 (0.9467 to 0.9989)	1.0000 (1.0000 to 1.0000)
14 Months	0.9923 (0.9467 to 0.9989)	1.0000 (1.0000 to 1.0000)
16 Months	0.9923 (0.9467 to 0.9989)	1.0000 (1.0000 to 1.0000)
18 Months	0.9923 (0.9467 to 0.9989)	1.0000 (1.0000 to 1.0000)
20 Months	0.9923 (0.9467 to 0.9989)	1.0000 (1.0000 to 1.0000)
22 Months	0.9923 (0.9467 to 0.9989)	1.0000 (1.0000 to 1.0000)
24 Months	0.9923 (0.9467 to 0.9989)	1.0000 (1.0000 to 1.0000)
26 Months	0.9923 (0.9467 to 0.9989)	1.0000 (1.0000 to 1.0000)
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	87	108
16 Months	80	98

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	62	69
Thrombocytopenia (days)		
Number (%) of events	7 (4.7)	1 (0.7)
Number (%) of patients censored	142 (95.3)	151 (99.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0267
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.1337 (0.0164 to 1.0869)
P-value	-	0.0598

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[c]		
2 Months	0.9525 (0.9029 to 0.9771)	1.0000 (1.0000 to 1.0000)
4 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
6 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
8 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
10 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
12 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
14 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
16 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
18 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
20 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
22 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
24 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
26 Months	0.9525 (0.9029 to 0.9771)	0.9933 (0.9533 to 0.9991)
Number of patients at risk[c]		
2 Months	136	149
4 Months	130	140
6 Months	114	127

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
8 Months	105	122
10 Months	101	115
12 Months	92	108
14 Months	86	107
16 Months	79	97
18 Months	71	90
20 Months	67	86
22 Months	65	77
24 Months	64	74
26 Months	62	68
Vision blurred (days)		
Number (%) of events	1 (0.7)	0 (0.0)
Number (%) of patients censored	148 (99.3)	152 (100.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2966
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC
P-value	-	0.9975
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
4 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
6 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
8 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
10 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
12 Months	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)
14 Months	0.9889 (0.9237 to 0.9984)	1.0000 (1.0000 to 1.0000)
16 Months	0.9889 (0.9237 to 0.9984)	1.0000 (1.0000 to 1.0000)
18 Months	0.9889 (0.9237 to 0.9984)	1.0000 (1.0000 to 1.0000)
20 Months	0.9889 (0.9237 to 0.9984)	1.0000 (1.0000 to 1.0000)
22 Months	0.9889 (0.9237 to 0.9984)	1.0000 (1.0000 to 1.0000)
24 Months	0.9889 (0.9237 to 0.9984)	1.0000 (1.0000 to 1.0000)
26 Months	0.9889 (0.9237 to 0.9984)	1.0000 (1.0000 to 1.0000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.6 Treatment emergent adverse event leading to discontinuation of treatment according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	142	149
4 Months	134	141
6 Months	117	128
8 Months	106	123
10 Months	102	116
12 Months	93	109
14 Months	86	108
16 Months	79	98
18 Months	71	91
20 Months	67	87
22 Months	65	78
24 Months	64	75
26 Months	61	69

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_discaept_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Blood and lymphatic system disorders (days)		
Number (%) of events	10 (6.7)	12 (7.9)
Number (%) of patients censored	139 (93.3)	140 (92.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8432
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0882 (0.4699 to 2.5202)
P-value	-	0.8436
Events probability (95% CI)[c]		
2 Months	0.9724 (0.9280 to 0.9895)	0.9868 (0.9481 to 0.9967)
4 Months	0.9577 (0.9082 to 0.9808)	0.9590 (0.9111 to 0.9814)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	0.9329 (0.8747 to 0.9646)	0.9449 (0.8928 to 0.9721)
8 Months	0.9329 (0.8747 to 0.9646)	0.9368 (0.8819 to 0.9667)
10 Months	0.9233 (0.8615 to 0.9582)	0.9284 (0.8706 to 0.9609)
12 Months	0.9233 (0.8615 to 0.9582)	0.9284 (0.8706 to 0.9609)
14 Months	0.9233 (0.8615 to 0.9582)	0.9284 (0.8706 to 0.9609)
16 Months	0.9233 (0.8615 to 0.9582)	0.9185 (0.8568 to 0.9543)
18 Months	0.9233 (0.8615 to 0.9582)	0.9185 (0.8568 to 0.9543)
20 Months	0.9233 (0.8615 to 0.9582)	0.9185 (0.8568 to 0.9543)
22 Months	0.9233 (0.8615 to 0.9582)	0.9070 (0.8402 to 0.9468)
24 Months	0.9233 (0.8615 to 0.9582)	0.9070 (0.8402 to 0.9468)
26 Months	0.9233 (0.8615 to 0.9582)	0.9070 (0.8402 to 0.9468)
Number of patients at risk[c]		
2 Months	138	147
4 Months	128	136
6 Months	108	121
8 Months	98	116
10 Months	93	110
12 Months	85	105
14 Months	79	104

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	72	94
18 Months	64	86
20 Months	61	82
22 Months	59	76
24 Months	58	73
26 Months	55	67
Cardiac disorders (days)		
Number (%) of events	6 (4.0)	28 (18.4)
Number (%) of patients censored	143 (96.0)	124 (81.6)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (17.7413 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0004
Stratified[a] Hazard ratio (95% CI) vs Pd	-	4.3654 (1.8031 to 10.5687)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
P-value	-	0.0011
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.2291 (0.0946 to 0.5546)	-
Events probability (95% CI)[c]		
2 Months	0.9931 (0.9521 to 0.9990)	0.9337 (0.8802 to 0.9638)
4 Months	0.9931 (0.9521 to 0.9990)	0.9134 (0.8555 to 0.9488)
6 Months	0.9855 (0.9430 to 0.9964)	0.8991 (0.8381 to 0.9379)
8 Months	0.9765 (0.9284 to 0.9924)	0.8833 (0.8187 to 0.9259)
10 Months	0.9667 (0.9130 to 0.9875)	0.8668 (0.7986 to 0.9131)
12 Months	0.9667 (0.9130 to 0.9875)	0.8487 (0.7766 to 0.8991)
14 Months	0.9556 (0.8953 to 0.9816)	0.8487 (0.7766 to 0.8991)
16 Months	0.9556 (0.8953 to 0.9816)	0.8385 (0.7638 to 0.8913)
18 Months	0.9425 (0.8740 to 0.9743)	0.8062 (0.7242 to 0.8661)
20 Months	0.9425 (0.8740 to 0.9743)	0.7949 (0.7105 to 0.8571)
22 Months	0.9425 (0.8740 to 0.9743)	0.7830 (0.6961 to 0.8478)
24 Months	0.9425 (0.8740 to 0.9743)	0.7830 (0.6961 to 0.8478)
26 Months	0.9425 (0.8740 to 0.9743)	0.7693 (0.6790 to 0.8372)
Number of patients at risk[c]		
2 Months	142	139

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	134	130
6 Months	116	117
8 Months	104	110
10 Months	99	101
12 Months	90	92
14 Months	83	92
16 Months	76	82
18 Months	68	73
20 Months	64	69
22 Months	62	62
24 Months	61	59
26 Months	58	54
Eye disorders (days)		
Number (%) of events	16 (10.7)	18 (11.8)
Number (%) of patients censored	133 (89.3)	134 (88.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (27.1376 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9809
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0083 (0.5138 to 1.9787)
P-value	-	0.9809
Events probability (95% CI)[c]		
2 Months	0.9727 (0.9290 to 0.9897)	0.9868 (0.9482 to 0.9967)
4 Months	0.9074 (0.8457 to 0.9452)	0.9800 (0.9394 to 0.9935)
6 Months	0.9074 (0.8457 to 0.9452)	0.9800 (0.9394 to 0.9935)
8 Months	0.9074 (0.8457 to 0.9452)	0.9397 (0.8827 to 0.9695)
10 Months	0.9074 (0.8457 to 0.9452)	0.9225 (0.8602 to 0.9577)
12 Months	0.9074 (0.8457 to 0.9452)	0.9134 (0.8485 to 0.9513)
14 Months	0.8962 (0.8298 to 0.9376)	0.9134 (0.8485 to 0.9513)
16 Months	0.8839 (0.8125 to 0.9293)	0.8932 (0.8221 to 0.9370)
18 Months	0.8839 (0.8125 to 0.9293)	0.8932 (0.8221 to 0.9370)
20 Months	0.8701 (0.7928 to 0.9200)	0.8703 (0.7921 to 0.9206)
22 Months	0.8701 (0.7928 to 0.9200)	0.8582 (0.7766 to 0.9117)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
24 Months	0.8701 (0.7928 to 0.9200)	0.8446 (0.7587 to 0.9019)
26 Months	0.8701 (0.7928 to 0.9200)	0.8446 (0.7587 to 0.9019)
Number of patients at risk[c]		
2 Months	139	147
4 Months	122	138
6 Months	106	125
8 Months	96	115
10 Months	93	106
12 Months	84	98
14 Months	78	97
16 Months	72	86
18 Months	64	79
20 Months	59	75
22 Months	57	66
24 Months	56	62
26 Months	53	56
Gastrointestinal disorders (days)		
Number (%) of events	79 (53.0)	83 (54.6)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	70 (47.0)	69 (45.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	0.8214 (0.5585 to 1.9713)	0.7228 (0.4600 to 1.2485)
Median (95% CI)	7.2608 (3.8439 to 24.4107)	8.5749 (3.4825 to 21.3224)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9484
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.9898 (0.7253 to 1.3508)
P-value	-	0.9484
Events probability (95% CI)[c]		
2 Months	0.6768 (0.5941 to 0.7463)	0.6495 (0.5677 to 0.7197)
4 Months	0.5651 (0.4791 to 0.6423)	0.5667 (0.4833 to 0.6418)
6 Months	0.5132 (0.4260 to 0.5936)	0.5593 (0.4758 to 0.6347)
8 Months	0.4843 (0.3964 to 0.5666)	0.5130 (0.4289 to 0.5908)
10 Months	0.4740 (0.3858 to 0.5570)	0.4967 (0.4125 to 0.5752)
12 Months	0.4632 (0.3747 to 0.5470)	0.4517 (0.3669 to 0.5326)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.4525 (0.3637 to 0.5370)	0.4332 (0.3485 to 0.5149)
16 Months	0.4406 (0.3513 to 0.5261)	0.4234 (0.3386 to 0.5055)
18 Months	0.4406 (0.3513 to 0.5261)	0.4234 (0.3386 to 0.5055)
20 Months	0.4254 (0.3347 to 0.5130)	0.4234 (0.3386 to 0.5055)
22 Months	0.4254 (0.3347 to 0.5130)	0.4109 (0.3254 to 0.4943)
24 Months	0.4254 (0.3347 to 0.5130)	0.4109 (0.3254 to 0.4943)
26 Months	0.4076 (0.3148 to 0.4983)	0.4109 (0.3254 to 0.4943)
Number of patients at risk[c]		
2 Months	95	96
4 Months	74	80
6 Months	57	73
8 Months	47	64
10 Months	45	56
12 Months	43	49
14 Months	41	47
16 Months	35	41
18 Months	29	39
20 Months	25	38
22 Months	24	32

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
24 Months	24	31
26 Months	22	28
General disorders and administration site conditions (days)		
Number (%) of events	83 (55.7)	78 (51.3)
Number (%) of patients censored	66 (44.3)	74 (48.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	0.9856 (0.4928 to 1.5441)	2.0698 (0.8871 to 3.2197)
Median (95% CI)	6.0780 (3.7454 to 11.9261)	17.5441 (6.5380 to 30.8830)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1186
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.7802 (0.5708 to 1.0664)
P-value	-	0.1195
Events probability (95% CI)[c]		
2 Months	0.6488 (0.5650 to 0.7204)	0.7694 (0.6939 to 0.8286)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.5459 (0.4603 to 0.6236)	0.6476 (0.5654 to 0.7182)
6 Months	0.5056 (0.4196 to 0.5852)	0.6048 (0.5213 to 0.6783)
8 Months	0.4546 (0.3688 to 0.5362)	0.5661 (0.4815 to 0.6422)
10 Months	0.4362 (0.3505 to 0.5186)	0.5315 (0.4457 to 0.6100)
12 Months	0.4159 (0.3301 to 0.4993)	0.5220 (0.4358 to 0.6013)
14 Months	0.4055 (0.3197 to 0.4894)	0.5125 (0.4260 to 0.5925)
16 Months	0.4055 (0.3197 to 0.4894)	0.5014 (0.4141 to 0.5824)
18 Months	0.4055 (0.3197 to 0.4894)	0.4895 (0.4012 to 0.5718)
20 Months	0.4055 (0.3197 to 0.4894)	0.4772 (0.3881 to 0.5609)
22 Months	0.4055 (0.3197 to 0.4894)	0.4772 (0.3881 to 0.5609)
24 Months	0.4055 (0.3197 to 0.4894)	0.4511 (0.3601 to 0.5376)
26 Months	0.4055 (0.3197 to 0.4894)	0.4370 (0.3450 to 0.5251)
Number of patients at risk[c]		
2 Months	91	115
4 Months	73	94
6 Months	60	79
8 Months	51	71
10 Months	45	60
12 Months	41	55

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	38	53
16 Months	36	46
18 Months	34	40
20 Months	32	39
22 Months	31	37
24 Months	31	33
26 Months	29	29
Infections and infestations (days)		
Number (%) of events	86 (57.7)	103 (67.8)
Number (%) of patients censored	63 (42.3)	49 (32.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	1.6756 (1.3470 to 1.9055)	0.8871 (0.7228 to 1.9055)
Median (95% CI)	6.5051 (2.5955 to 9.1663)	3.9097 (2.7926 to 5.0595)
75% quantile (95% CI)	NC (27.1704 to NC)	NC (11.2690 to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1530

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.2331 (0.9242 to 1.6453)
P-value	-	0.1545
Events probability (95% CI)[c]		
2 Months	0.6598 (0.5761 to 0.7309)	0.6684 (0.5871 to 0.7374)
4 Months	0.5272 (0.4414 to 0.6059)	0.4799 (0.3969 to 0.5581)
6 Months	0.5016 (0.4153 to 0.5817)	0.3734 (0.2938 to 0.4527)
8 Months	0.4278 (0.3414 to 0.5113)	0.3485 (0.2701 to 0.4279)
10 Months	0.3982 (0.3122 to 0.4827)	0.3299 (0.2521 to 0.4095)
12 Months	0.3877 (0.3019 to 0.4726)	0.3099 (0.2328 to 0.3899)
14 Months	0.3772 (0.2916 to 0.4625)	0.2799 (0.2045 to 0.3600)
16 Months	0.3772 (0.2916 to 0.4625)	0.2699 (0.1952 to 0.3499)
18 Months	0.3772 (0.2916 to 0.4625)	0.2582 (0.1840 to 0.3385)
20 Months	0.3503 (0.2639 to 0.4377)	0.2582 (0.1840 to 0.3385)
22 Months	0.3503 (0.2639 to 0.4377)	0.2582 (0.1840 to 0.3385)
24 Months	0.3503 (0.2639 to 0.4377)	0.2582 (0.1840 to 0.3385)
26 Months	0.3503 (0.2639 to 0.4377)	0.2582 (0.1840 to 0.3385)
Number of patients at risk[c]		
2 Months	93	99

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	68	66
6 Months	57	45
8 Months	45	42
10 Months	40	35
12 Months	37	31
14 Months	34	28
16 Months	30	24
18 Months	28	20
20 Months	24	19
22 Months	22	16
24 Months	21	16
26 Months	19	13
Injury, poisoning and procedural complications (days)		
Number (%) of events	16 (10.7)	68 (44.7)
Number (%) of patients censored	133 (89.3)	84 (55.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0986 to 0.1971)
Median (95% CI)	NC (NC to NC)	NC (8.5092 to NC)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	<.0001
Stratified[a] Hazard ratio (95% CI) vs Pd	-	5.6279 (3.2120 to 9.8611)
P-value	-	<.0001
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.1777 (0.1014 to 0.3113)	-
Events probability (95% CI)[c]		
2 Months	0.9722 (0.9275 to 0.9895)	0.6447 (0.5630 to 0.7150)
4 Months	0.9504 (0.8987 to 0.9760)	0.6310 (0.5489 to 0.7022)
6 Months	0.9428 (0.8889 to 0.9710)	0.6236 (0.5412 to 0.6954)
8 Months	0.9082 (0.8435 to 0.9470)	0.5917 (0.5079 to 0.6661)
10 Months	0.8894 (0.8195 to 0.9333)	0.5832 (0.4988 to 0.6582)
12 Months	0.8894 (0.8195 to 0.9333)	0.5734 (0.4884 to 0.6495)
14 Months	0.8894 (0.8195 to 0.9333)	0.5734 (0.4884 to 0.6495)
16 Months	0.8894 (0.8195 to 0.9333)	0.5518 (0.4647 to 0.6304)
18 Months	0.8894 (0.8195 to 0.9333)	0.5518 (0.4647 to 0.6304)
20 Months	0.8894 (0.8195 to 0.9333)	0.5398 (0.4515 to 0.6200)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
22 Months	0.8894 (0.8195 to 0.9333)	0.5398 (0.4515 to 0.6200)
24 Months	0.8894 (0.8195 to 0.9333)	0.5398 (0.4515 to 0.6200)
26 Months	0.8894 (0.8195 to 0.9333)	0.5398 (0.4515 to 0.6200)
Number of patients at risk[c]		
2 Months	137	96
4 Months	129	89
6 Months	113	79
8 Months	98	71
10 Months	93	64
12 Months	84	58
14 Months	78	57
16 Months	72	49
18 Months	64	46
20 Months	60	42
22 Months	58	37
24 Months	57	36
26 Months	54	33
Investigations (days)		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of events	12 (8.1)	18 (11.8)
Number (%) of patients censored	137 (91.9)	134 (88.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3306
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.4495 (0.6833 to 3.0749)
P-value	-	0.3334
Events probability (95% CI)[c]		
2 Months	0.9792 (0.9369 to 0.9932)	0.9670 (0.9226 to 0.9861)
4 Months	0.9649 (0.9177 to 0.9852)	0.9332 (0.8793 to 0.9635)
6 Months	0.9564 (0.9052 to 0.9802)	0.9259 (0.8702 to 0.9583)
8 Months	0.9564 (0.9052 to 0.9802)	0.9259 (0.8702 to 0.9583)
10 Months	0.9564 (0.9052 to 0.9802)	0.9093 (0.8484 to 0.9464)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	0.9564 (0.9052 to 0.9802)	0.9003 (0.8367 to 0.9400)
14 Months	0.9231 (0.8550 to 0.9600)	0.8911 (0.8249 to 0.9332)
16 Months	0.9231 (0.8550 to 0.9600)	0.8911 (0.8249 to 0.9332)
18 Months	0.9231 (0.8550 to 0.9600)	0.8911 (0.8249 to 0.9332)
20 Months	0.9231 (0.8550 to 0.9600)	0.8798 (0.8095 to 0.9253)
22 Months	0.9231 (0.8550 to 0.9600)	0.8674 (0.7925 to 0.9167)
24 Months	0.9075 (0.8299 to 0.9507)	0.8674 (0.7925 to 0.9167)
26 Months	0.8916 (0.8063 to 0.9406)	0.8536 (0.7735 to 0.9071)
Number of patients at risk[c]		
2 Months	138	145
4 Months	128	132
6 Months	111	119
8 Months	100	114
10 Months	97	105
12 Months	88	98
14 Months	80	96
16 Months	73	86
18 Months	65	79
20 Months	61	74

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
22 Months	59	66
24 Months	57	65
26 Months	54	58
Metabolism and nutrition disorders (days)		
Number (%) of events	15 (10.1)	26 (17.1)
Number (%) of patients censored	134 (89.9)	126 (82.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (16.5585 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1290
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.6300 (0.8620 to 3.0821)
P-value	-	0.1328
Events probability (95% CI)[c]		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	0.9448 (0.8926 to 0.9720)	0.9338 (0.8804 to 0.9638)
4 Months	0.9155 (0.8559 to 0.9511)	0.8859 (0.8227 to 0.9275)
6 Months	0.8994 (0.8357 to 0.9392)	0.8859 (0.8227 to 0.9275)
8 Months	0.8994 (0.8357 to 0.9392)	0.8702 (0.8039 to 0.9153)
10 Months	0.8994 (0.8357 to 0.9392)	0.8619 (0.7937 to 0.9088)
12 Months	0.8994 (0.8357 to 0.9392)	0.8533 (0.7834 to 0.9021)
14 Months	0.8994 (0.8357 to 0.9392)	0.8355 (0.7619 to 0.8880)
16 Months	0.8994 (0.8357 to 0.9392)	0.8355 (0.7619 to 0.8880)
18 Months	0.8994 (0.8357 to 0.9392)	0.8046 (0.7244 to 0.8637)
20 Months	0.8994 (0.8357 to 0.9392)	0.8046 (0.7244 to 0.8637)
22 Months	0.8994 (0.8357 to 0.9392)	0.8046 (0.7244 to 0.8637)
24 Months	0.8994 (0.8357 to 0.9392)	0.8046 (0.7244 to 0.8637)
26 Months	0.8844 (0.8121 to 0.9301)	0.8046 (0.7244 to 0.8637)
Number of patients at risk[c]		
2 Months	134	139
4 Months	123	126
6 Months	106	116
8 Months	96	110
10 Months	92	103

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	84	96
14 Months	79	93
16 Months	74	84
18 Months	67	74
20 Months	63	71
22 Months	61	64
24 Months	60	62
26 Months	57	56
Musculoskeletal and connective tissue disorders (days)		
Number (%) of events	73 (49.0)	88 (57.9)
Number (%) of patients censored	76 (51.0)	64 (42.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	2.3655 (1.0513 to 3.9097)	2.1027 (1.3142 to 3.4497)
Median (95% CI)	10.8419 (5.6181 to 31.4415)	8.7064 (6.6037 to 15.6057)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6013

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
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	Pd (N=149)	**IPd (N=152)**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0867 (0.7948 to 1.4859)
P-value	-	0.6024
Events probability (95% CI)[c]		
2 Months	0.7785 (0.7015 to 0.8379)	0.7750 (0.6997 to 0.8336)
4 Months	0.6666 (0.5817 to 0.7381)	0.6380 (0.5552 to 0.7095)
6 Months	0.5730 (0.4837 to 0.6524)	0.6090 (0.5252 to 0.6825)
8 Months	0.5349 (0.4443 to 0.6172)	0.5154 (0.4299 to 0.5943)
10 Months	0.5126 (0.4208 to 0.5969)	0.4757 (0.3905 to 0.5560)
12 Months	0.4760 (0.3822 to 0.5638)	0.4429 (0.3582 to 0.5241)
14 Months	0.4634 (0.3692 to 0.5523)	0.4260 (0.3417 to 0.5076)
16 Months	0.4494 (0.3543 to 0.5398)	0.4071 (0.3230 to 0.4894)
18 Months	0.4494 (0.3543 to 0.5398)	0.4071 (0.3230 to 0.4894)
20 Months	0.4494 (0.3543 to 0.5398)	0.3967 (0.3125 to 0.4795)
22 Months	0.4334 (0.3370 to 0.5258)	0.3967 (0.3125 to 0.4795)
24 Months	0.4334 (0.3370 to 0.5258)	0.3967 (0.3125 to 0.4795)
26 Months	0.4334 (0.3370 to 0.5258)	0.3967 (0.3125 to 0.4795)
Number of patients at risk[c]		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	109	115
4 Months	87	91
6 Months	62	79
8 Months	50	66
10 Months	46	59
12 Months	38	53
14 Months	33	50
16 Months	32	43
18 Months	31	39
20 Months	28	38
22 Months	27	34
24 Months	26	34
26 Months	25	31
Nervous system disorders (days)		
Number (%) of events	44 (29.5)	56 (36.8)
Number (%) of patients censored	105 (70.5)	96 (63.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	7.6550 (3.8439 to 21.0267)	5.2895 (2.1355 to 8.0164)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
Median (95% CI)	NC (NC to NC)	NC (31.0801 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2618
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.2578 (0.8419 to 1.8792)
P-value	-	0.2628
Events probability (95% CI)[c]		
2 Months	0.8677 (0.8005 to 0.9136)	0.8477 (0.7798 to 0.8961)
4 Months	0.8222 (0.7481 to 0.8763)	0.7798 (0.7045 to 0.8381)
6 Months	0.7716 (0.6905 to 0.8339)	0.7127 (0.6315 to 0.7792)
8 Months	0.7443 (0.6599 to 0.8108)	0.6805 (0.5967 to 0.7505)
10 Months	0.7348 (0.6492 to 0.8026)	0.6462 (0.5600 to 0.7198)
12 Months	0.7243 (0.6372 to 0.7938)	0.6281 (0.5407 to 0.7036)
14 Months	0.7243 (0.6372 to 0.7938)	0.6188 (0.5307 to 0.6951)
16 Months	0.7243 (0.6372 to 0.7938)	0.6089 (0.5201 to 0.6863)
18 Months	0.7124 (0.6234 to 0.7840)	0.6089 (0.5201 to 0.6863)
20 Months	0.6707 (0.5739 to 0.7504)	0.5981 (0.5082 to 0.6768)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
22 Months	0.6558 (0.5564 to 0.7382)	0.5981 (0.5082 to 0.6768)
24 Months	0.6558 (0.5564 to 0.7382)	0.5981 (0.5082 to 0.6768)
26 Months	0.6402 (0.5382 to 0.7254)	0.5981 (0.5082 to 0.6768)
Number of patients at risk[c]		
2 Months	121	126
4 Months	108	111
6 Months	89	92
8 Months	79	83
10 Months	74	73
12 Months	69	67
14 Months	65	66
16 Months	62	59
18 Months	54	56
20 Months	47	55
22 Months	44	49
24 Months	43	46
26 Months	39	41
Psychiatric disorders (days)		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

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16.2.7.1.39 Analysis according to SOC/PT
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	Pd (N=149)	**IPd (N=152)**
Number (%) of events	28 (18.8)	30 (19.7)
Number (%) of patients censored	121 (81.2)	122 (80.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (7.9836 to NC)	NC (12.2875 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9353
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.9789 (0.5846 to 1.6390)
P-value	-	0.9353
Events probability (95% CI)[c]		
2 Months	0.9116 (0.8526 to 0.9477)	0.9074 (0.8487 to 0.9441)
4 Months	0.8751 (0.8089 to 0.9195)	0.8800 (0.8163 to 0.9227)
6 Months	0.8416 (0.7689 to 0.8931)	0.8362 (0.7653 to 0.8872)
8 Months	0.8235 (0.7473 to 0.8785)	0.8362 (0.7653 to 0.8872)
10 Months	0.8235 (0.7473 to 0.8785)	0.8275 (0.7551 to 0.8802)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	0.8129 (0.7344 to 0.8703)	0.8275 (0.7551 to 0.8802)
14 Months	0.8021 (0.7212 to 0.8617)	0.8184 (0.7442 to 0.8730)
16 Months	0.7899 (0.7061 to 0.8523)	0.8087 (0.7325 to 0.8652)
18 Months	0.7899 (0.7061 to 0.8523)	0.7985 (0.7201 to 0.8571)
20 Months	0.7899 (0.7061 to 0.8523)	0.7985 (0.7201 to 0.8571)
22 Months	0.7899 (0.7061 to 0.8523)	0.7985 (0.7201 to 0.8571)
24 Months	0.7738 (0.6845 to 0.8408)	0.7985 (0.7201 to 0.8571)
26 Months	0.7738 (0.6845 to 0.8408)	0.7852 (0.7029 to 0.8471)
Number of patients at risk[c]		
2 Months	129	135
4 Months	116	125
6 Months	97	109
8 Months	87	104
10 Months	84	96
12 Months	75	91
14 Months	70	89
16 Months	62	79
18 Months	55	74
20 Months	51	70

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
22 Months	49	63
24 Months	47	60
26 Months	44	54
Renal and urinary disorders (days)		
Number (%) of events	13 (8.7)	14 (9.2)
Number (%) of patients censored	136 (91.3)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9568
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.9793 (0.4588 to 2.0901)
P-value	-	0.9568
Events probability (95% CI)[c]		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
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	Pd (N=149)	**IPd (N=152)**
2 Months	0.9449 (0.8929 to 0.9721)	0.9471 (0.8969 to 0.9732)
4 Months	0.9306 (0.8747 to 0.9620)	0.9269 (0.8719 to 0.9588)
6 Months	0.9306 (0.8747 to 0.9620)	0.9269 (0.8719 to 0.9588)
8 Months	0.9035 (0.8388 to 0.9431)	0.9111 (0.8516 to 0.9475)
10 Months	0.9035 (0.8388 to 0.9431)	0.9111 (0.8516 to 0.9475)
12 Months	0.9035 (0.8388 to 0.9431)	0.9111 (0.8516 to 0.9475)
14 Months	0.9035 (0.8388 to 0.9431)	0.9111 (0.8516 to 0.9475)
16 Months	0.9035 (0.8388 to 0.9431)	0.9111 (0.8516 to 0.9475)
18 Months	0.9035 (0.8388 to 0.9431)	0.9111 (0.8516 to 0.9475)
20 Months	0.9035 (0.8388 to 0.9431)	0.9111 (0.8516 to 0.9475)
22 Months	0.9035 (0.8388 to 0.9431)	0.9111 (0.8516 to 0.9475)
24 Months	0.9035 (0.8388 to 0.9431)	0.8985 (0.8323 to 0.9395)
26 Months	0.9035 (0.8388 to 0.9431)	0.8985 (0.8323 to 0.9395)
Number of patients at risk[c]		
2 Months	134	141
4 Months	125	132
6 Months	109	119
8 Months	96	113
10 Months	92	107

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	87	100
14 Months	81	99
16 Months	74	89
18 Months	67	83
20 Months	63	80
22 Months	61	72
24 Months	60	68
26 Months	57	62
Reproductive system and breast disorders (days)		
Number (%) of events	4 (2.7)	10 (6.6)
Number (%) of patients censored	145 (97.3)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1525

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.2810 (0.7139 to 7.2878)
P-value	-	0.1641
Events probability (95% CI)[c]		
2 Months	0.9863 (0.9462 to 0.9965)	0.9934 (0.9539 to 0.9991)
4 Months	0.9863 (0.9462 to 0.9965)	0.9800 (0.9391 to 0.9935)
6 Months	0.9781 (0.9334 to 0.9929)	0.9729 (0.9293 to 0.9897)
8 Months	0.9690 (0.9188 to 0.9883)	0.9648 (0.9173 to 0.9852)
10 Months	0.9690 (0.9188 to 0.9883)	0.9648 (0.9173 to 0.9852)
12 Months	0.9690 (0.9188 to 0.9883)	0.9560 (0.9040 to 0.9801)
14 Months	0.9690 (0.9188 to 0.9883)	0.9378 (0.8785 to 0.9686)
16 Months	0.9690 (0.9188 to 0.9883)	0.9280 (0.8651 to 0.9622)
18 Months	0.9690 (0.9188 to 0.9883)	0.9280 (0.8651 to 0.9622)
20 Months	0.9690 (0.9188 to 0.9883)	0.9169 (0.8495 to 0.9549)
22 Months	0.9690 (0.9188 to 0.9883)	0.9169 (0.8495 to 0.9549)
24 Months	0.9690 (0.9188 to 0.9883)	0.9169 (0.8495 to 0.9549)
26 Months	0.9690 (0.9188 to 0.9883)	0.9169 (0.8495 to 0.9549)
Number of patients at risk[c]		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	140	148
4 Months	132	138
6 Months	114	125
8 Months	103	119
10 Months	99	113
12 Months	91	105
14 Months	85	102
16 Months	78	91
18 Months	70	85
20 Months	66	81
22 Months	64	73
24 Months	63	70
26 Months	60	64
Respiratory, thoracic and mediastinal disorders (days)		
Number (%) of events	43 (28.9)	66 (43.4)
Number (%) of patients censored	106 (71.1)	86 (56.6)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	5.6838 (1.7084 to NC)	3.8768 (1.8727 to 4.5667)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Median (95% CI)	NC (NC to NC)	27.3676 (10.2177 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0368
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5033 (1.0227 to 2.2097)
P-value	-	0.0381
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6652 (0.4526 to 0.9778)	-
Events probability (95% CI)[c]		
2 Months	0.8006 (0.7258 to 0.8569)	0.8075 (0.7350 to 0.8621)
4 Months	0.7639 (0.6855 to 0.8253)	0.7382 (0.6595 to 0.8014)
6 Months	0.7471 (0.6668 to 0.8109)	0.6656 (0.5824 to 0.7359)
8 Months	0.7385 (0.6571 to 0.8034)	0.6328 (0.5476 to 0.7062)
10 Months	0.7110 (0.6264 to 0.7798)	0.5971 (0.5098 to 0.6739)
12 Months	0.7015 (0.6159 to 0.7716)	0.5781 (0.4897 to 0.6567)
14 Months	0.6913 (0.6045 to 0.7629)	0.5482 (0.4582 to 0.6294)
16 Months	0.6913 (0.6045 to 0.7629)	0.5275 (0.4365 to 0.6104)
18 Months	0.6913 (0.6045 to 0.7629)	0.5275 (0.4365 to 0.6104)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
20 Months	0.6913 (0.6045 to 0.7629)	0.5275 (0.4365 to 0.6104)
22 Months	0.6913 (0.6045 to 0.7629)	0.5275 (0.4365 to 0.6104)
24 Months	0.6766 (0.5863 to 0.7514)	0.5275 (0.4365 to 0.6104)
26 Months	0.6766 (0.5863 to 0.7514)	0.5124 (0.4194 to 0.5978)
Number of patients at risk[c]		
2 Months	113	120
4 Months	101	104
6 Months	88	83
8 Months	82	75
10 Months	76	65
12 Months	69	59
14 Months	64	55
16 Months	58	48
18 Months	52	43
20 Months	49	42
22 Months	47	37
24 Months	45	35
26 Months	42	32

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Skin and subcutaneous tissue disorders (days)		
Number (%) of events	37 (24.8)	46 (30.3)
Number (%) of patients censored	112 (75.2)	106 (69.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	9.1992 (3.6140 to NC)	9.2320 (2.8255 to 22.5380)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4930
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.1640 (0.7537 to 1.7978)
P-value	-	0.4935
Events probability (95% CI)[c]		
2 Months	0.8505 (0.7819 to 0.8990)	0.8481 (0.7803 to 0.8964)
4 Months	0.8137 (0.7399 to 0.8683)	0.8142 (0.7423 to 0.8678)
6 Months	0.7792 (0.7003 to 0.8397)	0.8068 (0.7340 to 0.8616)
8 Months	0.7521 (0.6695 to 0.8168)	0.7823 (0.7059 to 0.8411)

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
10 Months	0.7418 (0.6576 to 0.8083)	0.7385 (0.6563 to 0.8039)
12 Months	0.7418 (0.6576 to 0.8083)	0.7201 (0.6358 to 0.7881)
14 Months	0.7304 (0.6441 to 0.7989)	0.7106 (0.6253 to 0.7800)
16 Months	0.7304 (0.6441 to 0.7989)	0.6906 (0.6029 to 0.7628)
18 Months	0.7304 (0.6441 to 0.7989)	0.6793 (0.5900 to 0.7532)
20 Months	0.7304 (0.6441 to 0.7989)	0.6793 (0.5900 to 0.7532)
22 Months	0.7304 (0.6441 to 0.7989)	0.6793 (0.5900 to 0.7532)
24 Months	0.7304 (0.6441 to 0.7989)	0.6662 (0.5747 to 0.7425)
26 Months	0.7304 (0.6441 to 0.7989)	0.6662 (0.5747 to 0.7425)
Number of patients at risk[c]		
2 Months	120	126
4 Months	108	115
6 Months	87	101
8 Months	76	93
10 Months	72	81
12 Months	66	76
14 Months	62	74
16 Months	56	66
18 Months	50	59

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
20 Months	46	57
22 Months	44	52
24 Months	43	48
26 Months	40	43
Vascular disorders (days)		
Number (%) of events	15 (10.1)	23 (15.1)
Number (%) of patients censored	134 (89.9)	129 (84.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (24.6407 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2497
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.4630 (0.7625 to 2.8074)
P-value	-	0.2525

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[c]		
2 Months	0.9725 (0.9285 to 0.9896)	0.9535 (0.9050 to 0.9776)
4 Months	0.9508 (0.8994 to 0.9762)	0.9121 (0.8533 to 0.9480)
6 Months	0.9192 (0.8585 to 0.9545)	0.9049 (0.8446 to 0.9426)
8 Months	0.9012 (0.8354 to 0.9416)	0.8970 (0.8347 to 0.9366)
10 Months	0.9012 (0.8354 to 0.9416)	0.8887 (0.8245 to 0.9305)
12 Months	0.8905 (0.8209 to 0.9341)	0.8614 (0.7904 to 0.9098)
14 Months	0.8905 (0.8209 to 0.9341)	0.8428 (0.7678 to 0.8952)
16 Months	0.8905 (0.8209 to 0.9341)	0.8428 (0.7678 to 0.8952)
18 Months	0.8776 (0.8027 to 0.9253)	0.8428 (0.7678 to 0.8952)
20 Months	0.8776 (0.8027 to 0.9253)	0.8428 (0.7678 to 0.8952)
22 Months	0.8776 (0.8027 to 0.9253)	0.8428 (0.7678 to 0.8952)
24 Months	0.8776 (0.8027 to 0.9253)	0.8428 (0.7678 to 0.8952)
26 Months	0.8776 (0.8027 to 0.9253)	0.8285 (0.7480 to 0.8852)
Number of patients at risk[c]		
2 Months	138	142
4 Months	128	128
6 Months	108	115
8 Months	95	109

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.7 Treatment emergent not severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
10 Months	91	101
12 Months	83	93
14 Months	78	90
16 Months	72	83
18 Months	64	76
20 Months	60	72
22 Months	58	64
24 Months	57	61
26 Months	54	54

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Arthralgia (days)		
Number (%) of events	15 (10.1)	14 (9.2)
Number (%) of patients censored	134 (89.9)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6633
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.8504 (0.4102 to 1.7631)
P-value	-	0.6631
Events probability (95% CI)[c]		
2 Months	0.9658 (0.9197 to 0.9856)	0.9670 (0.9225 to 0.9861)
4 Months	0.9367 (0.8818 to 0.9666)	0.9388 (0.8857 to 0.9677)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	0.9286 (0.8711 to 0.9610)	0.9388 (0.8857 to 0.9677)
8 Months	0.9012 (0.8350 to 0.9417)	0.9224 (0.8639 to 0.9564)
10 Months	0.9012 (0.8350 to 0.9417)	0.9224 (0.8639 to 0.9564)
12 Months	0.9012 (0.8350 to 0.9417)	0.9134 (0.8519 to 0.9501)
14 Months	0.8896 (0.8190 to 0.9338)	0.9041 (0.8396 to 0.9435)
16 Months	0.8896 (0.8190 to 0.9338)	0.9041 (0.8396 to 0.9435)
18 Months	0.8767 (0.8010 to 0.9250)	0.9041 (0.8396 to 0.9435)
20 Months	0.8767 (0.8010 to 0.9250)	0.9041 (0.8396 to 0.9435)
22 Months	0.8767 (0.8010 to 0.9250)	0.9041 (0.8396 to 0.9435)
24 Months	0.8767 (0.8010 to 0.9250)	0.9041 (0.8396 to 0.9435)
26 Months	0.8767 (0.8010 to 0.9250)	0.9041 (0.8396 to 0.9435)
Number of patients at risk[c]		
2 Months	137	144
4 Months	125	132
6 Months	107	119
8 Months	94	112
10 Months	91	105
12 Months	82	98
14 Months	75	96

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	69	87
18 Months	61	81
20 Months	58	79
22 Months	57	71
24 Months	56	68
26 Months	53	62
Asthenia (days)		
Number (%) of events	26 (17.4)	21 (13.8)
Number (%) of patients censored	123 (82.6)	131 (86.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (9.3306 to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3655
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.7653 (0.4282 to 1.3680)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
P-value	-	0.3668
Events probability (95% CI)[c]		
2 Months	0.9107 (0.8511 to 0.9471)	0.9406 (0.8890 to 0.9686)
4 Months	0.8881 (0.8237 to 0.9300)	0.8930 (0.8312 to 0.9331)
6 Months	0.8629 (0.7930 to 0.9105)	0.8782 (0.8135 to 0.9215)
8 Months	0.8452 (0.7717 to 0.8966)	0.8622 (0.7942 to 0.9090)
10 Months	0.8258 (0.7483 to 0.8813)	0.8622 (0.7942 to 0.9090)
12 Months	0.8152 (0.7354 to 0.8730)	0.8528 (0.7826 to 0.9018)
14 Months	0.8044 (0.7223 to 0.8645)	0.8528 (0.7826 to 0.9018)
16 Months	0.8044 (0.7223 to 0.8645)	0.8528 (0.7826 to 0.9018)
18 Months	0.8044 (0.7223 to 0.8645)	0.8528 (0.7826 to 0.9018)
20 Months	0.8044 (0.7223 to 0.8645)	0.8528 (0.7826 to 0.9018)
22 Months	0.8044 (0.7223 to 0.8645)	0.8528 (0.7826 to 0.9018)
24 Months	0.8044 (0.7223 to 0.8645)	0.8528 (0.7826 to 0.9018)
26 Months	0.8044 (0.7223 to 0.8645)	0.8528 (0.7826 to 0.9018)
Number of patients at risk[c]		
2 Months	128	140
4 Months	118	125

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	101	112
8 Months	90	106
10 Months	84	99
12 Months	77	91
14 Months	71	90
16 Months	67	83
18 Months	61	78
20 Months	57	74
22 Months	55	66
24 Months	54	63
26 Months	51	57
Back pain (days)		
Number (%) of events	24 (16.1)	25 (16.4)
Number (%) of patients censored	125 (83.9)	127 (83.6)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (27.5647 to NC)	NC (34.9569 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8875
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.9603 (0.5481 to 1.6827)
P-value	-	0.8875
Events probability (95% CI)[c]		
2 Months	0.9449 (0.8928 to 0.9721)	0.9537 (0.9054 to 0.9777)
4 Months	0.8934 (0.8293 to 0.9344)	0.8988 (0.8376 to 0.9377)
6 Months	0.8778 (0.8105 to 0.9223)	0.8839 (0.8197 to 0.9262)
8 Months	0.8693 (0.8002 to 0.9157)	0.8522 (0.7819 to 0.9013)
10 Months	0.8693 (0.8002 to 0.9157)	0.8439 (0.7722 to 0.8946)
12 Months	0.8486 (0.7739 to 0.9001)	0.8351 (0.7616 to 0.8875)
14 Months	0.8380 (0.7607 to 0.8920)	0.8262 (0.7511 to 0.8804)
16 Months	0.8380 (0.7607 to 0.8920)	0.8262 (0.7511 to 0.8804)
18 Months	0.8380 (0.7607 to 0.8920)	0.8262 (0.7511 to 0.8804)
20 Months	0.8380 (0.7607 to 0.8920)	0.8262 (0.7511 to 0.8804)
22 Months	0.8380 (0.7607 to 0.8920)	0.8262 (0.7511 to 0.8804)
24 Months	0.8380 (0.7607 to 0.8920)	0.8262 (0.7511 to 0.8804)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
26 Months	0.8380 (0.7607 to 0.8920)	0.8262 (0.7511 to 0.8804)
Number of patients at risk[c]		
2 Months	134	142
4 Months	119	127
6 Months	103	113
8 Months	93	106
10 Months	89	101
12 Months	80	94
14 Months	75	92
16 Months	69	84
18 Months	62	78
20 Months	58	74
22 Months	56	67
24 Months	55	65
26 Months	53	59
Bone pain (days)		
Number (%) of events	8 (5.4)	11 (7.2)
Number (%) of patients censored	141 (94.6)	141 (92.8)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5923
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.2819 (0.5153 to 3.1893)
P-value	-	0.5932
Events probability (95% CI)[c]		
2 Months	0.9797 (0.9383 to 0.9934)	0.9802 (0.9399 to 0.9936)
4 Months	0.9797 (0.9383 to 0.9934)	0.9530 (0.9040 to 0.9773)
6 Months	0.9712 (0.9245 to 0.9891)	0.9530 (0.9040 to 0.9773)
8 Months	0.9712 (0.9245 to 0.9891)	0.9530 (0.9040 to 0.9773)
10 Months	0.9516 (0.8942 to 0.9783)	0.9530 (0.9040 to 0.9773)
12 Months	0.9411 (0.8787 to 0.9719)	0.9356 (0.8793 to 0.9662)
14 Months	0.9411 (0.8787 to 0.9719)	0.9356 (0.8793 to 0.9662)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	0.9411 (0.8787 to 0.9719)	0.9155 (0.8510 to 0.9528)
18 Months	0.9411 (0.8787 to 0.9719)	0.9155 (0.8510 to 0.9528)
20 Months	0.9411 (0.8787 to 0.9719)	0.9155 (0.8510 to 0.9528)
22 Months	0.9411 (0.8787 to 0.9719)	0.9155 (0.8510 to 0.9528)
24 Months	0.9411 (0.8787 to 0.9719)	0.9155 (0.8510 to 0.9528)
26 Months	0.9411 (0.8787 to 0.9719)	0.9155 (0.8510 to 0.9528)
Number of patients at risk[c]		
2 Months	139	146
4 Months	132	134
6 Months	114	121
8 Months	103	116
10 Months	97	113
12 Months	88	104
14 Months	82	103
16 Months	78	91
18 Months	70	85
20 Months	66	81
22 Months	64	72
24 Months	63	70

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
26 Months	61	65
Bronchitis (days)		
Number (%) of events	16 (10.7)	36 (23.7)
Number (%) of patients censored	133 (89.3)	116 (76.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	14.8172 (4.9610 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0054
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.2563 (1.2512 to 4.0686)
P-value	-	0.0068
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.4432 (0.2458 to 0.7992)	-
Events probability (95% CI)[c]		
2 Months	0.9725 (0.9284 to 0.9896)	0.9006 (0.8405 to 0.9388)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
4 Months	0.9576 (0.9081 to 0.9808)	0.8453 (0.7763 to 0.8944)
6 Months	0.9339 (0.8766 to 0.9651)	0.8009 (0.7260 to 0.8573)
8 Months	0.9159 (0.8527 to 0.9527)	0.7768 (0.6989 to 0.8369)
10 Months	0.9159 (0.8527 to 0.9527)	0.7768 (0.6989 to 0.8369)
12 Months	0.9159 (0.8527 to 0.9527)	0.7768 (0.6989 to 0.8369)
14 Months	0.9050 (0.8376 to 0.9454)	0.7675 (0.6880 to 0.8292)
16 Months	0.8923 (0.8193 to 0.9369)	0.7483 (0.6660 to 0.8131)
18 Months	0.8791 (0.8011 to 0.9279)	0.7483 (0.6660 to 0.8131)
20 Months	0.8791 (0.8011 to 0.9279)	0.7483 (0.6660 to 0.8131)
22 Months	0.8791 (0.8011 to 0.9279)	0.7483 (0.6660 to 0.8131)
24 Months	0.8635 (0.7784 to 0.9175)	0.7483 (0.6660 to 0.8131)
26 Months	0.8635 (0.7784 to 0.9175)	0.7342 (0.6480 to 0.8024)
Number of patients at risk[c]		
2 Months	138	134
4 Months	128	118
6 Months	110	102
8 Months	97	94
10 Months	93	88
12 Months	84	83

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	77	82
16 Months	69	73
18 Months	63	69
20 Months	59	65
22 Months	57	56
24 Months	55	55
26 Months	52	49
Constipation (days)		
Number (%) of events	30 (20.1)	25 (16.4)
Number (%) of patients censored	119 (79.9)	127 (83.6)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (5.5852 to NC)	NC (26.4476 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2993

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.7550 (0.4434 to 1.2857)
P-value	-	0.3008
Events probability (95% CI)[c]		
2 Months	0.8632 (0.7959 to 0.9095)	0.8942 (0.8331 to 0.9338)
4 Months	0.8338 (0.7622 to 0.8854)	0.8669 (0.8013 to 0.9120)
6 Months	0.8176 (0.7435 to 0.8721)	0.8595 (0.7927 to 0.9061)
8 Months	0.8084 (0.7326 to 0.8647)	0.8430 (0.7729 to 0.8930)
10 Months	0.8084 (0.7326 to 0.8647)	0.8430 (0.7729 to 0.8930)
12 Months	0.8084 (0.7326 to 0.8647)	0.8430 (0.7729 to 0.8930)
14 Months	0.8084 (0.7326 to 0.8647)	0.8335 (0.7612 to 0.8856)
16 Months	0.8084 (0.7326 to 0.8647)	0.8335 (0.7612 to 0.8856)
18 Months	0.8084 (0.7326 to 0.8647)	0.8335 (0.7612 to 0.8856)
20 Months	0.8084 (0.7326 to 0.8647)	0.8335 (0.7612 to 0.8856)
22 Months	0.7611 (0.6688 to 0.8309)	0.8335 (0.7612 to 0.8856)
24 Months	0.7611 (0.6688 to 0.8309)	0.8335 (0.7612 to 0.8856)
26 Months	0.7611 (0.6688 to 0.8309)	0.8335 (0.7612 to 0.8856)
Number of patients at risk[c]		
2 Months	122	133

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	112	122
6 Months	97	108
8 Months	85	101
10 Months	81	95
12 Months	74	89
14 Months	70	88
16 Months	63	79
18 Months	56	73
20 Months	52	72
22 Months	47	63
24 Months	46	61
26 Months	45	55
Cough (days)		
Number (%) of events	11 (7.4)	14 (9.2)
Number (%) of patients censored	138 (92.6)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.7140
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.1592 (0.5257 to 2.5557)
P-value	-	0.7143
Events probability (95% CI)[c]		
2 Months	0.9588 (0.9107 to 0.9813)	0.9732 (0.9303 to 0.9899)
4 Months	0.9444 (0.8918 to 0.9718)	0.9524 (0.9028 to 0.9770)
6 Months	0.9362 (0.8808 to 0.9664)	0.9382 (0.8846 to 0.9674)
8 Months	0.9362 (0.8808 to 0.9664)	0.9059 (0.8431 to 0.9444)
10 Months	0.9268 (0.8675 to 0.9601)	0.8974 (0.8323 to 0.9381)
12 Months	0.9268 (0.8675 to 0.9601)	0.8974 (0.8323 to 0.9381)
14 Months	0.9162 (0.8525 to 0.9532)	0.8974 (0.8323 to 0.9381)
16 Months	0.9162 (0.8525 to 0.9532)	0.8974 (0.8323 to 0.9381)
18 Months	0.9162 (0.8525 to 0.9532)	0.8974 (0.8323 to 0.9381)
20 Months	0.9162 (0.8525 to 0.9532)	0.8974 (0.8323 to 0.9381)
22 Months	0.9162 (0.8525 to 0.9532)	0.8974 (0.8323 to 0.9381)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
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	Pd (N=149)	**IPd (N=152)**
24 Months	0.9162 (0.8525 to 0.9532)	0.8974 (0.8323 to 0.9381)
26 Months	0.9162 (0.8525 to 0.9532)	0.8974 (0.8323 to 0.9381)
Number of patients at risk[c]		
2 Months	136	145
4 Months	127	134
6 Months	111	120
8 Months	102	111
10 Months	97	103
12 Months	88	97
14 Months	81	96
16 Months	74	88
18 Months	68	81
20 Months	64	78
22 Months	62	70
24 Months	61	67
26 Months	58	61
Decreased appetite (days)		
Number (%) of events	8 (5.4)	17 (11.2)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	141 (94.6)	135 (88.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1001
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.9988 (0.8611 to 4.6396)
P-value	-	0.1070
Events probability (95% CI)[c]		
2 Months	0.9793 (0.9371 to 0.9933)	0.9469 (0.8967 to 0.9731)
4 Months	0.9574 (0.9076 to 0.9807)	0.9128 (0.8545 to 0.9484)
6 Months	0.9490 (0.8958 to 0.9754)	0.9128 (0.8545 to 0.9484)
8 Months	0.9490 (0.8958 to 0.9754)	0.9049 (0.8446 to 0.9426)
10 Months	0.9490 (0.8958 to 0.9754)	0.8965 (0.8339 to 0.9364)
12 Months	0.9490 (0.8958 to 0.9754)	0.8965 (0.8339 to 0.9364)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.9490 (0.8958 to 0.9754)	0.8965 (0.8339 to 0.9364)
16 Months	0.9490 (0.8958 to 0.9754)	0.8965 (0.8339 to 0.9364)
18 Months	0.9490 (0.8958 to 0.9754)	0.8763 (0.8071 to 0.9218)
20 Months	0.9490 (0.8958 to 0.9754)	0.8763 (0.8071 to 0.9218)
22 Months	0.9490 (0.8958 to 0.9754)	0.8763 (0.8071 to 0.9218)
24 Months	0.9490 (0.8958 to 0.9754)	0.8763 (0.8071 to 0.9218)
26 Months	0.9337 (0.8670 to 0.9676)	0.8763 (0.8071 to 0.9218)
Number of patients at risk[c]		
2 Months	139	141
4 Months	129	130
6 Months	112	119
8 Months	101	114
10 Months	97	107
12 Months	88	101
14 Months	82	100
16 Months	76	91
18 Months	69	82
20 Months	65	79
22 Months	63	71

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
24 Months	62	68
26 Months	59	62
Diarrhoea (days)		
Number (%) of events	32 (21.5)	46 (30.3)
Number (%) of patients censored	117 (78.5)	106 (69.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	26.9076 (7.0308 to NC)	10.1191 (4.1725 to 19.5154)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2021
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.3408 (0.8531 to 2.1073)
P-value	-	0.2037
Events probability (95% CI)[c]		
2 Months	0.8970 (0.8349 to 0.9366)	0.8678 (0.8026 to 0.9126)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
4 Months	0.8458 (0.7751 to 0.8957)	0.8265 (0.7556 to 0.8784)
6 Months	0.8289 (0.7552 to 0.8821)	0.8121 (0.7394 to 0.8663)
8 Months	0.8199 (0.7445 to 0.8748)	0.7731 (0.6955 to 0.8333)
10 Months	0.8101 (0.7328 to 0.8670)	0.7570 (0.6776 to 0.8194)
12 Months	0.8001 (0.7209 to 0.8590)	0.7217 (0.6381 to 0.7891)
14 Months	0.7890 (0.7074 to 0.8502)	0.7126 (0.6282 to 0.7813)
16 Months	0.7774 (0.6933 to 0.8411)	0.6934 (0.6068 to 0.7646)
18 Months	0.7774 (0.6933 to 0.8411)	0.6830 (0.5952 to 0.7557)
20 Months	0.7635 (0.6757 to 0.8305)	0.6718 (0.5825 to 0.7462)
22 Months	0.7635 (0.6757 to 0.8305)	0.6596 (0.5685 to 0.7360)
24 Months	0.7635 (0.6757 to 0.8305)	0.6596 (0.5685 to 0.7360)
26 Months	0.7635 (0.6757 to 0.8305)	0.6596 (0.5685 to 0.7360)
Number of patients at risk[c]		
2 Months	127	129
4 Months	114	118
6 Months	97	106
8 Months	86	97
10 Months	83	88
12 Months	77	80

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
14 Months	71	78
16 Months	64	69
18 Months	56	63
20 Months	51	59
22 Months	50	53
24 Months	49	52
26 Months	46	47
Dyspnoea (days)		
Number (%) of events	13 (8.7)	23 (15.1)
Number (%) of patients censored	136 (91.3)	129 (84.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1280

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.6863 (0.8538 to 3.3307)
P-value	-	0.1324
Events probability (95% CI)[c]		
2 Months	0.9448 (0.8926 to 0.9720)	0.9471 (0.8970 to 0.9732)
4 Months	0.9302 (0.8741 to 0.9618)	0.9269 (0.8718 to 0.9588)
6 Months	0.9218 (0.8630 to 0.9560)	0.8831 (0.8185 to 0.9258)
8 Months	0.9132 (0.8518 to 0.9499)	0.8749 (0.8085 to 0.9195)
10 Months	0.9040 (0.8397 to 0.9433)	0.8575 (0.7872 to 0.9060)
12 Months	0.9040 (0.8397 to 0.9433)	0.8487 (0.7766 to 0.8990)
14 Months	0.9040 (0.8397 to 0.9433)	0.8393 (0.7651 to 0.8916)
16 Months	0.9040 (0.8397 to 0.9433)	0.8393 (0.7651 to 0.8916)
18 Months	0.9040 (0.8397 to 0.9433)	0.8393 (0.7651 to 0.8916)
20 Months	0.9040 (0.8397 to 0.9433)	0.8276 (0.7501 to 0.8829)
22 Months	0.9040 (0.8397 to 0.9433)	0.8276 (0.7501 to 0.8829)
24 Months	0.9040 (0.8397 to 0.9433)	0.8276 (0.7501 to 0.8829)
26 Months	0.9040 (0.8397 to 0.9433)	0.8276 (0.7501 to 0.8829)
Number of patients at risk[c]		
2 Months	134	141

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
4 Months	124	132
6 Months	109	113
8 Months	99	107
10 Months	94	98
12 Months	87	91
14 Months	83	89
16 Months	76	79
18 Months	68	73
20 Months	65	69
22 Months	63	61
24 Months	62	59
26 Months	59	54
Fatigue (days)		
Number (%) of events	32 (21.5)	27 (17.8)
Number (%) of patients censored	117 (78.5)	125 (82.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (2.5298 to NC)	NC (15.8686 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

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	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2612
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.7458 (0.4463 to 1.2462)
P-value	-	0.2629
Events probability (95% CI)[c]		
2 Months	0.8422 (0.7721 to 0.8922)	0.9206 (0.8645 to 0.9541)
4 Months	0.8058 (0.7311 to 0.8617)	0.8929 (0.8311 to 0.9330)
6 Months	0.8058 (0.7311 to 0.8617)	0.8782 (0.8134 to 0.9215)
8 Months	0.7798 (0.7012 to 0.8401)	0.8540 (0.7844 to 0.9025)
10 Months	0.7705 (0.6905 to 0.8323)	0.8453 (0.7739 to 0.8956)
12 Months	0.7705 (0.6905 to 0.8323)	0.8453 (0.7739 to 0.8956)
14 Months	0.7705 (0.6905 to 0.8323)	0.8360 (0.7626 to 0.8883)
16 Months	0.7705 (0.6905 to 0.8323)	0.8255 (0.7496 to 0.8802)
18 Months	0.7705 (0.6905 to 0.8323)	0.8255 (0.7496 to 0.8802)
20 Months	0.7705 (0.6905 to 0.8323)	0.8142 (0.7354 to 0.8716)
22 Months	0.7705 (0.6905 to 0.8323)	0.8142 (0.7354 to 0.8716)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
24 Months	0.7705 (0.6905 to 0.8323)	0.8013 (0.7188 to 0.8619)
26 Months	0.7705 (0.6905 to 0.8323)	0.8013 (0.7188 to 0.8619)
Number of patients at risk[c]		
2 Months	119	137
4 Months	107	125
6 Months	95	111
8 Months	84	104
10 Months	79	96
12 Months	73	92
14 Months	69	90
16 Months	64	79
18 Months	58	73
20 Months	55	70
22 Months	54	63
24 Months	53	60
26 Months	51	54
Headache (days)		
Number (%) of events	9 (6.0)	16 (10.5)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	140 (94.0)	136 (89.5)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1683
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.8028 (0.7701 to 4.2204)
P-value	-	0.1745
Events probability (95% CI)[c]		
2 Months	0.9720 (0.9271 to 0.9894)	0.9734 (0.9306 to 0.9899)
4 Months	0.9720 (0.9271 to 0.9894)	0.9667 (0.9218 to 0.9860)
6 Months	0.9473 (0.8924 to 0.9746)	0.9297 (0.8730 to 0.9616)
8 Months	0.9473 (0.8924 to 0.9746)	0.9217 (0.8628 to 0.9560)
10 Months	0.9473 (0.8924 to 0.9746)	0.9053 (0.8421 to 0.9440)
12 Months	0.9473 (0.8924 to 0.9746)	0.8968 (0.8314 to 0.9377)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
14 Months	0.9473 (0.8924 to 0.9746)	0.8877 (0.8200 to 0.9310)
16 Months	0.9473 (0.8924 to 0.9746)	0.8877 (0.8200 to 0.9310)
18 Months	0.9473 (0.8924 to 0.9746)	0.8877 (0.8200 to 0.9310)
20 Months	0.9473 (0.8924 to 0.9746)	0.8877 (0.8200 to 0.9310)
22 Months	0.9321 (0.8642 to 0.9667)	0.8877 (0.8200 to 0.9310)
24 Months	0.9321 (0.8642 to 0.9667)	0.8877 (0.8200 to 0.9310)
26 Months	0.9321 (0.8642 to 0.9667)	0.8877 (0.8200 to 0.9310)
Number of patients at risk[c]		
2 Months	137	145
4 Months	129	138
6 Months	111	121
8 Months	101	115
10 Months	97	107
12 Months	89	99
14 Months	83	97
16 Months	76	88
18 Months	68	82
20 Months	64	79
22 Months	61	70

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
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16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
24 Months	60	67
26 Months	57	61
Infusion related reaction (days)		
Number (%) of events	2 (1.3)	54 (35.5)
Number (%) of patients censored	147 (98.7)	98 (64.5)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0986 to 0.1971)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	<.0001
Stratified[a] Hazard ratio (95% CI) vs Pd	-	31.6625 (7.7153 to 129.9380)
P-value	-	<.0001
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.0316 (0.0077 to 0.1296)	-
Events probability (95% CI)[c]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

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	Pd (N=149)	**IPd (N=152)**
2 Months	0.9931 (0.9517 to 0.9990)	0.6513 (0.5698 to 0.7212)
4 Months	0.9931 (0.9517 to 0.9990)	0.6513 (0.5698 to 0.7212)
6 Months	0.9931 (0.9517 to 0.9990)	0.6513 (0.5698 to 0.7212)
8 Months	0.9845 (0.9390 to 0.9961)	0.6513 (0.5698 to 0.7212)
10 Months	0.9845 (0.9390 to 0.9961)	0.6513 (0.5698 to 0.7212)
12 Months	0.9845 (0.9390 to 0.9961)	0.6513 (0.5698 to 0.7212)
14 Months	0.9845 (0.9390 to 0.9961)	0.6513 (0.5698 to 0.7212)
16 Months	0.9845 (0.9390 to 0.9961)	0.6513 (0.5698 to 0.7212)
18 Months	0.9845 (0.9390 to 0.9961)	0.6513 (0.5698 to 0.7212)
20 Months	0.9845 (0.9390 to 0.9961)	0.6399 (0.5566 to 0.7116)
22 Months	0.9845 (0.9390 to 0.9961)	0.6399 (0.5566 to 0.7116)
24 Months	0.9845 (0.9390 to 0.9961)	0.6399 (0.5566 to 0.7116)
26 Months	0.9845 (0.9390 to 0.9961)	0.6399 (0.5566 to 0.7116)
Number of patients at risk[c]		
2 Months	141	97
4 Months	134	91
6 Months	117	82
8 Months	105	78
10 Months	101	72

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
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	Pd (N=149)	**IPd (N=152)**
12 Months	92	67
14 Months	86	66
16 Months	80	60
18 Months	72	57
20 Months	68	53
22 Months	66	48
24 Months	65	47
26 Months	62	43
Insomnia (days)		
Number (%) of events	13 (8.7)	15 (9.9)
Number (%) of patients censored	136 (91.3)	137 (90.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8658

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
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	Pd (N=149)	IPd (N=152)
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0660 (0.5071 to 2.2411)
P-value	-	0.8661
Events probability (95% CI)[c]		
2 Months	0.9388 (0.8857 to 0.9677)	0.9603 (0.9139 to 0.9820)
4 Months	0.9314 (0.8762 to 0.9625)	0.9532 (0.9044 to 0.9774)
6 Months	0.9233 (0.8656 to 0.9569)	0.9233 (0.8656 to 0.9569)
8 Months	0.9233 (0.8656 to 0.9569)	0.9073 (0.8453 to 0.9452)
10 Months	0.9233 (0.8656 to 0.9569)	0.8984 (0.8340 to 0.9388)
12 Months	0.9127 (0.8503 to 0.9499)	0.8984 (0.8340 to 0.9388)
14 Months	0.9127 (0.8503 to 0.9499)	0.8891 (0.8219 to 0.9319)
16 Months	0.9002 (0.8317 to 0.9418)	0.8891 (0.8219 to 0.9319)
18 Months	0.9002 (0.8317 to 0.9418)	0.8891 (0.8219 to 0.9319)
20 Months	0.9002 (0.8317 to 0.9418)	0.8891 (0.8219 to 0.9319)
22 Months	0.9002 (0.8317 to 0.9418)	0.8891 (0.8219 to 0.9319)
24 Months	0.9002 (0.8317 to 0.9418)	0.8891 (0.8219 to 0.9319)
26 Months	0.9002 (0.8317 to 0.9418)	0.8891 (0.8219 to 0.9319)
Number of patients at risk[c]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	133	143
4 Months	124	134
6 Months	107	117
8 Months	97	110
10 Months	93	102
12 Months	83	96
14 Months	77	94
16 Months	69	85
18 Months	62	79
20 Months	58	75
22 Months	56	68
24 Months	55	65
26 Months	52	59
Muscle spasms (days)		
Number (%) of events	16 (10.7)	15 (9.9)
Number (%) of patients censored	133 (89.3)	137 (90.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6860
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.8646 (0.4270 to 1.7506)
P-value	-	0.6860
Events probability (95% CI)[c]		
2 Months	0.9513 (0.9006 to 0.9765)	0.9669 (0.9224 to 0.9861)
4 Months	0.9224 (0.8643 to 0.9563)	0.9392 (0.8863 to 0.9679)
6 Months	0.9061 (0.8434 to 0.9444)	0.9316 (0.8765 to 0.9626)
8 Months	0.9061 (0.8434 to 0.9444)	0.9074 (0.8454 to 0.9453)
10 Months	0.8857 (0.8163 to 0.9300)	0.8990 (0.8348 to 0.9391)
12 Months	0.8857 (0.8163 to 0.9300)	0.8990 (0.8348 to 0.9391)
14 Months	0.8857 (0.8163 to 0.9300)	0.8895 (0.8226 to 0.9322)
16 Months	0.8723 (0.7971 to 0.9209)	0.8895 (0.8226 to 0.9322)
18 Months	0.8723 (0.7971 to 0.9209)	0.8895 (0.8226 to 0.9322)
20 Months	0.8723 (0.7971 to 0.9209)	0.8895 (0.8226 to 0.9322)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
22 Months	0.8723 (0.7971 to 0.9209)	0.8895 (0.8226 to 0.9322)
24 Months	0.8723 (0.7971 to 0.9209)	0.8895 (0.8226 to 0.9322)
26 Months	0.8723 (0.7971 to 0.9209)	0.8895 (0.8226 to 0.9322)
Number of patients at risk[c]		
2 Months	135	144
4 Months	123	132
6 Months	104	118
8 Months	93	110
10 Months	87	102
12 Months	79	96
14 Months	73	94
16 Months	65	84
18 Months	57	77
20 Months	53	73
22 Months	51	67
24 Months	50	64
26 Months	47	58
Muscular weakness (days)		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of events	7 (4.7)	12 (7.9)
Number (%) of patients censored	142 (95.3)	140 (92.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3746
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5219 (0.5982 to 3.8721)
P-value	-	0.3781
Events probability (95% CI)[c]		
2 Months	0.9865 (0.9472 to 0.9966)	0.9867 (0.9477 to 0.9966)
4 Months	0.9646 (0.9169 to 0.9851)	0.9732 (0.9303 to 0.9899)
6 Months	0.9570 (0.9067 to 0.9805)	0.9585 (0.9099 to 0.9812)
8 Months	0.9570 (0.9067 to 0.9805)	0.9506 (0.8990 to 0.9762)
10 Months	0.9570 (0.9067 to 0.9805)	0.9506 (0.8990 to 0.9762)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	0.9466 (0.8902 to 0.9744)	0.9420 (0.8869 to 0.9707)
14 Months	0.9466 (0.8902 to 0.9744)	0.9420 (0.8869 to 0.9707)
16 Months	0.9466 (0.8902 to 0.9744)	0.9128 (0.8467 to 0.9512)
18 Months	0.9466 (0.8902 to 0.9744)	0.9128 (0.8467 to 0.9512)
20 Months	0.9466 (0.8902 to 0.9744)	0.9128 (0.8467 to 0.9512)
22 Months	0.9466 (0.8902 to 0.9744)	0.9128 (0.8467 to 0.9512)
24 Months	0.9466 (0.8902 to 0.9744)	0.9000 (0.8279 to 0.9429)
26 Months	0.9466 (0.8902 to 0.9744)	0.9000 (0.8279 to 0.9429)
Number of patients at risk[c]		
2 Months	140	147
4 Months	129	138
6 Months	111	124
8 Months	100	119
10 Months	96	112
12 Months	86	104
14 Months	80	103
16 Months	73	91
18 Months	65	84
20 Months	61	80

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
22 Months	60	71
24 Months	59	68
26 Months	56	62
Musculoskeletal chest pain (days)		
Number (%) of events	7 (4.7)	14 (9.2)
Number (%) of patients censored	142 (95.3)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1866
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.8299 (0.7363 to 4.5477)
P-value	-	0.1933
Events probability (95% CI)[c]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	0.9930 (0.9514 to 0.9990)	0.9669 (0.9224 to 0.9861)
4 Months	0.9715 (0.9258 to 0.9892)	0.9321 (0.8773 to 0.9629)
6 Months	0.9634 (0.9141 to 0.9846)	0.9248 (0.8682 to 0.9577)
8 Months	0.9547 (0.9016 to 0.9795)	0.9248 (0.8682 to 0.9577)
10 Months	0.9547 (0.9016 to 0.9795)	0.9080 (0.8465 to 0.9457)
12 Months	0.9443 (0.8858 to 0.9733)	0.9080 (0.8465 to 0.9457)
14 Months	0.9443 (0.8858 to 0.9733)	0.9080 (0.8465 to 0.9457)
16 Months	0.9443 (0.8858 to 0.9733)	0.9080 (0.8465 to 0.9457)
18 Months	0.9443 (0.8858 to 0.9733)	0.9080 (0.8465 to 0.9457)
20 Months	0.9443 (0.8858 to 0.9733)	0.8968 (0.8305 to 0.9381)
22 Months	0.9443 (0.8858 to 0.9733)	0.8968 (0.8305 to 0.9381)
24 Months	0.9443 (0.8858 to 0.9733)	0.8968 (0.8305 to 0.9381)
26 Months	0.9443 (0.8858 to 0.9733)	0.8968 (0.8305 to 0.9381)
Number of patients at risk[c]		
2 Months	141	144
4 Months	130	131
6 Months	112	119
8 Months	100	115
10 Months	98	106

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	88	99
14 Months	82	98
16 Months	75	90
18 Months	67	84
20 Months	63	79
22 Months	61	70
24 Months	60	67
26 Months	58	61
Myalgia (days)		
Number (%) of events	5 (3.4)	11 (7.2)
Number (%) of patients censored	144 (96.6)	141 (92.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0968

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.5481 (0.8112 to 8.0042)
P-value	-	0.1092
Events probability (95% CI)[c]		
2 Months	0.9862 (0.9459 to 0.9965)	0.9670 (0.9225 to 0.9861)
4 Months	0.9862 (0.9459 to 0.9965)	0.9532 (0.9044 to 0.9774)
6 Months	0.9776 (0.9318 to 0.9928)	0.9461 (0.8951 to 0.9727)
8 Months	0.9687 (0.9180 to 0.9882)	0.9461 (0.8951 to 0.9727)
10 Months	0.9687 (0.9180 to 0.9882)	0.9461 (0.8951 to 0.9727)
12 Months	0.9687 (0.9180 to 0.9882)	0.9461 (0.8951 to 0.9727)
14 Months	0.9687 (0.9180 to 0.9882)	0.9370 (0.8819 to 0.9669)
16 Months	0.9687 (0.9180 to 0.9882)	0.9278 (0.8690 to 0.9608)
18 Months	0.9687 (0.9180 to 0.9882)	0.9278 (0.8690 to 0.9608)
20 Months	0.9687 (0.9180 to 0.9882)	0.9278 (0.8690 to 0.9608)
22 Months	0.9687 (0.9180 to 0.9882)	0.9278 (0.8690 to 0.9608)
24 Months	0.9687 (0.9180 to 0.9882)	0.9278 (0.8690 to 0.9608)
26 Months	0.9687 (0.9180 to 0.9882)	0.9278 (0.8690 to 0.9608)
Number of patients at risk[c]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	139	144
4 Months	131	134
6 Months	113	120
8 Months	102	117
10 Months	98	110
12 Months	89	104
14 Months	83	102
16 Months	76	92
18 Months	69	85
20 Months	65	82
22 Months	63	75
24 Months	62	72
26 Months	59	66
Nasopharyngitis (days)		
Number (%) of events	10 (6.7)	21 (13.8)
Number (%) of patients censored	139 (93.3)	131 (86.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (21.3224 to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

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16.2.7.1.39 Analysis according to SOC/PT
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	Pd (N=149)	**IPd (N=152)**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0919
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.8934 (0.8900 to 4.0280)
P-value	-	0.0974
Events probability (95% CI)[c]		
2 Months	0.9791 (0.9367 to 0.9932)	0.9734 (0.9306 to 0.9899)
4 Months	0.9648 (0.9175 to 0.9852)	0.9458 (0.8946 to 0.9726)
6 Months	0.9648 (0.9175 to 0.9852)	0.9313 (0.8759 to 0.9625)
8 Months	0.9561 (0.9046 to 0.9801)	0.9233 (0.8656 to 0.9569)
10 Months	0.9561 (0.9046 to 0.9801)	0.9064 (0.8437 to 0.9447)
12 Months	0.9351 (0.8727 to 0.9675)	0.9064 (0.8437 to 0.9447)
14 Months	0.9351 (0.8727 to 0.9675)	0.8878 (0.8198 to 0.9312)
16 Months	0.9228 (0.8542 to 0.9598)	0.8775 (0.8064 to 0.9237)
18 Months	0.9228 (0.8542 to 0.9598)	0.8668 (0.7926 to 0.9158)
20 Months	0.9228 (0.8542 to 0.9598)	0.8441 (0.7638 to 0.8989)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
22 Months	0.9228 (0.8542 to 0.9598)	0.8185 (0.7312 to 0.8797)
24 Months	0.9074 (0.8299 to 0.9506)	0.8185 (0.7312 to 0.8797)
26 Months	0.9074 (0.8299 to 0.9506)	0.8185 (0.7312 to 0.8797)
Number of patients at risk[c]		
2 Months	139	145
4 Months	129	134
6 Months	112	119
8 Months	100	114
10 Months	96	105
12 Months	85	98
14 Months	80	95
16 Months	74	85
18 Months	66	78
20 Months	62	73
22 Months	60	62
24 Months	58	60
26 Months	55	55
Nausea (days)		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of events	14 (9.4)	23 (15.1)
Number (%) of patients censored	135 (90.6)	129 (84.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1408
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.6396 (0.8435 to 3.1869)
P-value	-	0.1448
Events probability (95% CI)[c]		
2 Months	0.9520 (0.9019 to 0.9768)	0.8878 (0.8258 to 0.9287)
4 Months	0.9227 (0.8646 to 0.9565)	0.8739 (0.8094 to 0.9177)
6 Months	0.9144 (0.8540 to 0.9506)	0.8666 (0.8007 to 0.9118)
8 Months	0.9052 (0.8418 to 0.9440)	0.8587 (0.7913 to 0.9056)
10 Months	0.8954 (0.8288 to 0.9370)	0.8587 (0.7913 to 0.9056)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	0.8954 (0.8288 to 0.9370)	0.8409 (0.7696 to 0.8916)
14 Months	0.8954 (0.8288 to 0.9370)	0.8409 (0.7696 to 0.8916)
16 Months	0.8954 (0.8288 to 0.9370)	0.8409 (0.7696 to 0.8916)
18 Months	0.8954 (0.8288 to 0.9370)	0.8409 (0.7696 to 0.8916)
20 Months	0.8954 (0.8288 to 0.9370)	0.8409 (0.7696 to 0.8916)
22 Months	0.8954 (0.8288 to 0.9370)	0.8409 (0.7696 to 0.8916)
24 Months	0.8954 (0.8288 to 0.9370)	0.8409 (0.7696 to 0.8916)
26 Months	0.8954 (0.8288 to 0.9370)	0.8409 (0.7696 to 0.8916)
Number of patients at risk[c]		
2 Months	135	132
4 Months	123	122
6 Months	105	111
8 Months	96	105
10 Months	91	98
12 Months	83	92
14 Months	78	91
16 Months	72	83
18 Months	65	76
20 Months	61	72

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
22 Months	59	65
24 Months	58	62
26 Months	56	56
Oedema peripheral (days)		
Number (%) of events	18 (12.1)	29 (19.1)
Number (%) of patients censored	131 (87.9)	123 (80.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	24.9692 (13.5031 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2525
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.4090 (0.7809 to 2.5424)
P-value	-	0.2548
Events probability (95% CI)[c]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	0.9243 (0.8675 to 0.9574)	0.9868 (0.9481 to 0.9967)
4 Months	0.9099 (0.8499 to 0.9467)	0.9528 (0.9034 to 0.9772)
6 Months	0.8938 (0.8297 to 0.9347)	0.9385 (0.8850 to 0.9675)
8 Months	0.8938 (0.8297 to 0.9347)	0.9065 (0.8439 to 0.9447)
10 Months	0.8844 (0.8176 to 0.9278)	0.8642 (0.7925 to 0.9125)
12 Months	0.8844 (0.8176 to 0.9278)	0.8465 (0.7714 to 0.8986)
14 Months	0.8844 (0.8176 to 0.9278)	0.8278 (0.7492 to 0.8836)
16 Months	0.8844 (0.8176 to 0.9278)	0.8278 (0.7492 to 0.8836)
18 Months	0.8844 (0.8176 to 0.9278)	0.8053 (0.7216 to 0.8661)
20 Months	0.8844 (0.8176 to 0.9278)	0.7817 (0.6933 to 0.8475)
22 Months	0.8689 (0.7936 to 0.9181)	0.7573 (0.6644 to 0.8278)
24 Months	0.8689 (0.7936 to 0.9181)	0.7573 (0.6644 to 0.8278)
26 Months	0.8689 (0.7936 to 0.9181)	0.7430 (0.6470 to 0.8166)
Number of patients at risk[c]		
2 Months	132	147
4 Months	123	136
6 Months	104	121
8 Months	95	112
10 Months	90	100

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	82	91
14 Months	77	88
16 Months	71	78
18 Months	63	69
20 Months	59	66
22 Months	56	58
24 Months	55	55
26 Months	53	48
Oropharyngeal pain (days)		
Number (%) of events	4 (2.7)	11 (7.2)
Number (%) of patients censored	145 (97.3)	141 (92.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1306

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.3673 (0.7489 to 7.4831)
P-value	-	0.1422
Events probability (95% CI)[c]		
2 Months	0.9862 (0.9460 to 0.9965)	0.9801 (0.9397 to 0.9935)
4 Months	0.9862 (0.9460 to 0.9965)	0.9733 (0.9303 to 0.9899)
6 Months	0.9786 (0.9349 to 0.9930)	0.9662 (0.9206 to 0.9858)
8 Months	0.9694 (0.9200 to 0.9885)	0.9583 (0.9092 to 0.9811)
10 Months	0.9694 (0.9200 to 0.9885)	0.9497 (0.8969 to 0.9758)
12 Months	0.9694 (0.9200 to 0.9885)	0.9497 (0.8969 to 0.9758)
14 Months	0.9694 (0.9200 to 0.9885)	0.9311 (0.8707 to 0.9638)
16 Months	0.9694 (0.9200 to 0.9885)	0.9311 (0.8707 to 0.9638)
18 Months	0.9694 (0.9200 to 0.9885)	0.9311 (0.8707 to 0.9638)
20 Months	0.9694 (0.9200 to 0.9885)	0.9197 (0.8541 to 0.9566)
22 Months	0.9694 (0.9200 to 0.9885)	0.9197 (0.8541 to 0.9566)
24 Months	0.9694 (0.9200 to 0.9885)	0.9197 (0.8541 to 0.9566)
26 Months	0.9694 (0.9200 to 0.9885)	0.9060 (0.8332 to 0.9480)
Number of patients at risk[c]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	140	146
4 Months	132	137
6 Months	115	123
8 Months	103	117
10 Months	99	109
12 Months	90	103
14 Months	84	100
16 Months	77	90
18 Months	69	84
20 Months	65	80
22 Months	63	71
24 Months	62	68
26 Months	59	62
Pain in extremity (days)		
Number (%) of events	4 (2.7)	11 (7.2)
Number (%) of patients censored	145 (97.3)	141 (92.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1227
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.3973 (0.7624 to 7.5378)
P-value	-	0.1347
Events probability (95% CI)[c]		
2 Months	0.9798 (0.9387 to 0.9934)	0.9934 (0.9539 to 0.9991)
4 Months	0.9725 (0.9282 to 0.9896)	0.9934 (0.9539 to 0.9991)
6 Months	0.9725 (0.9282 to 0.9896)	0.9859 (0.9444 to 0.9965)
8 Months	0.9725 (0.9282 to 0.9896)	0.9620 (0.9109 to 0.9840)
10 Months	0.9725 (0.9282 to 0.9896)	0.9366 (0.8769 to 0.9679)
12 Months	0.9725 (0.9282 to 0.9896)	0.9274 (0.8647 to 0.9617)
14 Months	0.9725 (0.9282 to 0.9896)	0.9181 (0.8527 to 0.9553)
16 Months	0.9725 (0.9282 to 0.9896)	0.9181 (0.8527 to 0.9553)
18 Months	0.9725 (0.9282 to 0.9896)	0.9181 (0.8527 to 0.9553)
20 Months	0.9725 (0.9282 to 0.9896)	0.9181 (0.8527 to 0.9553)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
22 Months	0.9725 (0.9282 to 0.9896)	0.9181 (0.8527 to 0.9553)
24 Months	0.9725 (0.9282 to 0.9896)	0.9181 (0.8527 to 0.9553)
26 Months	0.9725 (0.9282 to 0.9896)	0.9181 (0.8527 to 0.9553)
Number of patients at risk[c]		
2 Months	139	148
4 Months	130	140
6 Months	113	126
8 Months	103	118
10 Months	99	108
12 Months	90	101
14 Months	84	99
16 Months	77	90
18 Months	71	83
20 Months	67	80
22 Months	65	71
24 Months	64	68
26 Months	61	63
Peripheral sensory neuropathy (days)		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
Number (%) of events	11 (7.4)	15 (9.9)
Number (%) of patients censored	138 (92.6)	137 (90.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4292
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.3802 (0.6188 to 3.0788)
P-value	-	0.4311
Events probability (95% CI)[c]		
2 Months	0.9862 (0.9461 to 0.9965)	0.9670 (0.9225 to 0.9861)
4 Months	0.9715 (0.9258 to 0.9892)	0.9535 (0.9050 to 0.9776)
6 Months	0.9629 (0.9129 to 0.9845)	0.9232 (0.8653 to 0.9568)
8 Months	0.9536 (0.8989 to 0.9790)	0.9232 (0.8653 to 0.9568)
10 Months	0.9438 (0.8849 to 0.9731)	0.9145 (0.8538 to 0.9507)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	0.9330 (0.8690 to 0.9663)	0.9145 (0.8538 to 0.9507)
14 Months	0.9216 (0.8529 to 0.9590)	0.9145 (0.8538 to 0.9507)
16 Months	0.9216 (0.8529 to 0.9590)	0.9145 (0.8538 to 0.9507)
18 Months	0.9216 (0.8529 to 0.9590)	0.9145 (0.8538 to 0.9507)
20 Months	0.9216 (0.8529 to 0.9590)	0.8916 (0.8214 to 0.9353)
22 Months	0.9216 (0.8529 to 0.9590)	0.8785 (0.8029 to 0.9264)
24 Months	0.9216 (0.8529 to 0.9590)	0.8785 (0.8029 to 0.9264)
26 Months	0.9054 (0.8267 to 0.9495)	0.8785 (0.8029 to 0.9264)
Number of patients at risk[c]		
2 Months	139	144
4 Months	129	134
6 Months	111	117
8 Months	99	112
10 Months	94	104
12 Months	86	98
14 Months	79	97
16 Months	72	88
18 Months	64	81
20 Months	60	76

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
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	Pd (N=149)	**IPd (N=152)**
22 Months	58	67
24 Months	57	64
26 Months	53	58
Pneumonia (days)		
Number (%) of events	12 (8.1)	14 (9.2)
Number (%) of patients censored	137 (91.9)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8428
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0811 (0.4995 to 2.3401)
P-value	-	0.8431
Events probability (95% CI)[c]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	0.9791 (0.9365 to 0.9932)	0.9934 (0.9539 to 0.9991)
4 Months	0.9571 (0.9070 to 0.9805)	0.9589 (0.9109 to 0.9814)
6 Months	0.9571 (0.9070 to 0.9805)	0.9589 (0.9109 to 0.9814)
8 Months	0.9571 (0.9070 to 0.9805)	0.9589 (0.9109 to 0.9814)
10 Months	0.9475 (0.8923 to 0.9748)	0.9421 (0.8872 to 0.9708)
12 Months	0.9475 (0.8923 to 0.9748)	0.9421 (0.8872 to 0.9708)
14 Months	0.9362 (0.8748 to 0.9680)	0.9240 (0.8625 to 0.9586)
16 Months	0.9239 (0.8561 to 0.9605)	0.9143 (0.8495 to 0.9520)
18 Months	0.9109 (0.8370 to 0.9522)	0.9143 (0.8495 to 0.9520)
20 Months	0.9109 (0.8370 to 0.9522)	0.9143 (0.8495 to 0.9520)
22 Months	0.9109 (0.8370 to 0.9522)	0.9143 (0.8495 to 0.9520)
24 Months	0.9109 (0.8370 to 0.9522)	0.9008 (0.8291 to 0.9435)
26 Months	0.9109 (0.8370 to 0.9522)	0.9008 (0.8291 to 0.9435)
Number of patients at risk[c]		
2 Months	139	148
4 Months	128	135
6 Months	113	125
8 Months	102	120
10 Months	97	111

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	88	104
14 Months	81	101
16 Months	73	90
18 Months	65	83
20 Months	61	79
22 Months	59	71
24 Months	58	67
26 Months	55	61
Pruritus (days)		
Number (%) of events	11 (7.4)	9 (5.9)
Number (%) of patients censored	138 (92.6)	143 (94.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5964

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
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	Pd (N=149)	IPd (N=152)
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.7886 (0.3268 to 1.9033)
P-value	-	0.5973
Events probability (95% CI)[c]		
2 Months	0.9253 (0.8692 to 0.9579)	0.9474 (0.8975 to 0.9733)
4 Months	0.9253 (0.8692 to 0.9579)	0.9474 (0.8975 to 0.9733)
6 Months	0.9253 (0.8692 to 0.9579)	0.9474 (0.8975 to 0.9733)
8 Months	0.9253 (0.8692 to 0.9579)	0.9474 (0.8975 to 0.9733)
10 Months	0.9253 (0.8692 to 0.9579)	0.9474 (0.8975 to 0.9733)
12 Months	0.9253 (0.8692 to 0.9579)	0.9474 (0.8975 to 0.9733)
14 Months	0.9253 (0.8692 to 0.9579)	0.9382 (0.8839 to 0.9675)
16 Months	0.9253 (0.8692 to 0.9579)	0.9382 (0.8839 to 0.9675)
18 Months	0.9253 (0.8692 to 0.9579)	0.9382 (0.8839 to 0.9675)
20 Months	0.9253 (0.8692 to 0.9579)	0.9382 (0.8839 to 0.9675)
22 Months	0.9253 (0.8692 to 0.9579)	0.9382 (0.8839 to 0.9675)
24 Months	0.9253 (0.8692 to 0.9579)	0.9382 (0.8839 to 0.9675)
26 Months	0.9253 (0.8692 to 0.9579)	0.9382 (0.8839 to 0.9675)
Number of patients at risk[c]		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	131	141
4 Months	123	133
6 Months	106	120
8 Months	96	115
10 Months	92	108
12 Months	85	103
14 Months	80	101
16 Months	73	91
18 Months	65	85
20 Months	61	82
22 Months	59	74
24 Months	58	71
26 Months	55	66
Pyrexia (days)		
Number (%) of events	19 (12.8)	23 (15.1)
Number (%) of patients censored	130 (87.2)	129 (84.9)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (34.9569 to NC)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

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	Pd (N=149)	**IPd (N=152)**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8918
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0432 (0.5664 to 1.9214)
P-value	-	0.8920
Events probability (95% CI)[c]		
2 Months	0.9240 (0.8669 to 0.9572)	0.9539 (0.9058 to 0.9778)
4 Months	0.9019 (0.8399 to 0.9407)	0.9268 (0.8716 to 0.9588)
6 Months	0.8860 (0.8204 to 0.9287)	0.9194 (0.8624 to 0.9534)
8 Months	0.8774 (0.8098 to 0.9221)	0.8961 (0.8333 to 0.9362)
10 Months	0.8680 (0.7981 to 0.9150)	0.8793 (0.8125 to 0.9235)
12 Months	0.8580 (0.7853 to 0.9074)	0.8619 (0.7913 to 0.9100)
14 Months	0.8580 (0.7853 to 0.9074)	0.8529 (0.7803 to 0.9029)
16 Months	0.8580 (0.7853 to 0.9074)	0.8427 (0.7676 to 0.8952)
18 Months	0.8580 (0.7853 to 0.9074)	0.8427 (0.7676 to 0.8952)
20 Months	0.8580 (0.7853 to 0.9074)	0.8427 (0.7676 to 0.8952)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
22 Months	0.8580 (0.7853 to 0.9074)	0.8427 (0.7676 to 0.8952)
24 Months	0.8580 (0.7853 to 0.9074)	0.8427 (0.7676 to 0.8952)
26 Months	0.8580 (0.7853 to 0.9074)	0.8427 (0.7676 to 0.8952)
Number of patients at risk[c]		
2 Months	131	143
4 Months	122	133
6 Months	105	120
8 Months	97	112
10 Months	92	103
12 Months	82	96
14 Months	77	94
16 Months	70	84
18 Months	64	77
20 Months	61	74
22 Months	59	66
24 Months	58	63
26 Months	55	59
Rash (days)		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

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	Pd (N=149)	**IPd (N=152)**
Number (%) of events	8 (5.4)	11 (7.2)
Number (%) of patients censored	141 (94.6)	141 (92.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6308
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.2500 (0.5022 to 3.1115)
P-value	-	0.6315
Events probability (95% CI)[c]		
2 Months	0.9657 (0.9195 to 0.9856)	0.9802 (0.9398 to 0.9936)
4 Months	0.9513 (0.9005 to 0.9765)	0.9666 (0.9216 to 0.9860)
6 Months	0.9513 (0.9005 to 0.9765)	0.9596 (0.9121 to 0.9816)
8 Months	0.9513 (0.9005 to 0.9765)	0.9596 (0.9121 to 0.9816)
10 Months	0.9413 (0.8851 to 0.9704)	0.9512 (0.9001 to 0.9765)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	0.9413 (0.8851 to 0.9704)	0.9337 (0.8757 to 0.9651)
14 Months	0.9413 (0.8851 to 0.9704)	0.9337 (0.8757 to 0.9651)
16 Months	0.9413 (0.8851 to 0.9704)	0.9337 (0.8757 to 0.9651)
18 Months	0.9413 (0.8851 to 0.9704)	0.9337 (0.8757 to 0.9651)
20 Months	0.9413 (0.8851 to 0.9704)	0.9337 (0.8757 to 0.9651)
22 Months	0.9413 (0.8851 to 0.9704)	0.9337 (0.8757 to 0.9651)
24 Months	0.9413 (0.8851 to 0.9704)	0.9337 (0.8757 to 0.9651)
26 Months	0.9413 (0.8851 to 0.9704)	0.9337 (0.8757 to 0.9651)
Number of patients at risk[c]		
2 Months	137	146
4 Months	127	137
6 Months	110	123
8 Months	99	118
10 Months	94	110
12 Months	85	102
14 Months	79	101
16 Months	72	91
18 Months	66	84
20 Months	62	81

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
22 Months	60	73
24 Months	59	70
26 Months	56	64
Upper respiratory tract infection (days)		
Number (%) of events	28 (18.8)	50 (32.9)
Number (%) of patients censored	121 (81.2)	102 (67.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (9.1663 to NC)	7.9179 (5.3881 to 13.3060)
Median (95% CI)	NC (NC to NC)	NC (19.0554 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0129
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.7861 (1.1236 to 2.8393)
P-value	-	0.0142
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.5599 (0.3522 to 0.8900)	-

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
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	Pd (N=149)	IPd (N=152)
Events probability (95% CI)[c]		
2 Months	0.9100 (0.8501 to 0.9468)	0.9138 (0.8561 to 0.9490)
4 Months	0.8813 (0.8159 to 0.9245)	0.8581 (0.7906 to 0.9051)
6 Months	0.8649 (0.7961 to 0.9117)	0.7889 (0.7115 to 0.8477)
8 Months	0.8372 (0.7623 to 0.8901)	0.7467 (0.6644 to 0.8117)
10 Months	0.8176 (0.7388 to 0.8746)	0.7291 (0.6449 to 0.7965)
12 Months	0.8176 (0.7388 to 0.8746)	0.7097 (0.6231 to 0.7798)
14 Months	0.7956 (0.7122 to 0.8573)	0.6708 (0.5806 to 0.7458)
16 Months	0.7956 (0.7122 to 0.8573)	0.6491 (0.5567 to 0.7270)
18 Months	0.7956 (0.7122 to 0.8573)	0.6037 (0.5073 to 0.6871)
20 Months	0.7817 (0.6943 to 0.8468)	0.5911 (0.4935 to 0.6761)
22 Months	0.7817 (0.6943 to 0.8468)	0.5911 (0.4935 to 0.6761)
24 Months	0.7660 (0.6740 to 0.8352)	0.5911 (0.4935 to 0.6761)
26 Months	0.7660 (0.6740 to 0.8352)	0.5911 (0.4935 to 0.6761)
Number of patients at risk[c]		
2 Months	129	136
4 Months	117	120
6 Months	99	98
8 Months	88	88

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
10 Months	83	80
12 Months	77	73
14 Months	71	69
16 Months	65	60
18 Months	57	49
20 Months	52	46
22 Months	50	40
24 Months	48	40
26 Months	46	36
Urinary tract infection (days)		
Number (%) of events	13 (8.7)	14 (9.2)
Number (%) of patients censored	136 (91.3)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8798
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.9428 (0.4396 to 2.0220)
P-value	-	0.8797
Events probability (95% CI)[c]		
2 Months	0.9584 (0.9098 to 0.9811)	0.9736 (0.9311 to 0.9900)
4 Months	0.9365 (0.8814 to 0.9664)	0.9393 (0.8866 to 0.9680)
6 Months	0.9284 (0.8708 to 0.9609)	0.9393 (0.8866 to 0.9680)
8 Months	0.9101 (0.8464 to 0.9482)	0.9393 (0.8866 to 0.9680)
10 Months	0.9001 (0.8331 to 0.9411)	0.9393 (0.8866 to 0.9680)
12 Months	0.9001 (0.8331 to 0.9411)	0.9304 (0.8740 to 0.9621)
14 Months	0.9001 (0.8331 to 0.9411)	0.9304 (0.8740 to 0.9621)
16 Months	0.9001 (0.8331 to 0.9411)	0.9206 (0.8602 to 0.9556)
18 Months	0.9001 (0.8331 to 0.9411)	0.9206 (0.8602 to 0.9556)
20 Months	0.9001 (0.8331 to 0.9411)	0.9206 (0.8602 to 0.9556)
22 Months	0.9001 (0.8331 to 0.9411)	0.9085 (0.8420 to 0.9478)
24 Months	0.9001 (0.8331 to 0.9411)	0.8955 (0.8230 to 0.9393)
26 Months	0.9001 (0.8331 to 0.9411)	0.8955 (0.8230 to 0.9393)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
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	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	136	145
4 Months	126	132
6 Months	108	120
8 Months	95	115
10 Months	90	108
12 Months	84	100
14 Months	78	99
16 Months	72	88
18 Months	68	82
20 Months	64	79
22 Months	62	70
24 Months	61	66
26 Months	58	60
Vomiting (days)		
Number (%) of events	6 (4.0)	18 (11.8)
Number (%) of patients censored	143 (96.0)	134 (88.2)
Kaplan-Meier estimates of Events in months		

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0196
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.8659 (1.1361 to 7.2297)
P-value	-	0.0257
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.3489 (0.1383 to 0.8802)	-
Events probability (95% CI)[c]		
2 Months	0.9863 (0.9465 to 0.9966)	0.9471 (0.8969 to 0.9732)
4 Months	0.9863 (0.9465 to 0.9966)	0.9258 (0.8699 to 0.9582)
6 Months	0.9784 (0.9343 to 0.9930)	0.9258 (0.8699 to 0.9582)
8 Months	0.9604 (0.9069 to 0.9835)	0.9019 (0.8396 to 0.9409)
10 Months	0.9604 (0.9069 to 0.9835)	0.8934 (0.8289 to 0.9345)
12 Months	0.9604 (0.9069 to 0.9835)	0.8753 (0.8061 to 0.9210)
14 Months	0.9490 (0.8884 to 0.9771)	0.8659 (0.7944 to 0.9138)
16 Months	0.9490 (0.8884 to 0.9771)	0.8659 (0.7944 to 0.9138)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
18 Months	0.9490 (0.8884 to 0.9771)	0.8659 (0.7944 to 0.9138)
20 Months	0.9490 (0.8884 to 0.9771)	0.8659 (0.7944 to 0.9138)
22 Months	0.9490 (0.8884 to 0.9771)	0.8659 (0.7944 to 0.9138)
24 Months	0.9490 (0.8884 to 0.9771)	0.8659 (0.7944 to 0.9138)
26 Months	0.9490 (0.8884 to 0.9771)	0.8659 (0.7944 to 0.9138)
Number of patients at risk[c]		
2 Months	141	141
4 Months	133	130
6 Months	115	118
8 Months	102	110
10 Months	98	102
12 Months	89	94
14 Months	82	92
16 Months	76	84
18 Months	68	80
20 Months	64	76
22 Months	62	68
24 Months	61	65
26 Months	58	59

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Weight decreased (days)		
Number (%) of events	2 (1.3)	10 (6.6)
Number (%) of patients censored	147 (98.7)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0089
Stratified[a] Hazard ratio (95% CI) vs Pd	-	9.4245 (1.2056 to 73.6722)
P-value	-	0.0325
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.1061 (0.0136 to 0.8294)	-
Events probability (95% CI)[c]		
2 Months	0.9931 (0.9517 to 0.9990)	0.9670 (0.9226 to 0.9861)
4 Months	0.9931 (0.9517 to 0.9990)	0.9467 (0.8962 to 0.9730)

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	0.9931 (0.9517 to 0.9990)	0.9394 (0.8868 to 0.9680)
8 Months	0.9931 (0.9517 to 0.9990)	0.9394 (0.8868 to 0.9680)
10 Months	0.9931 (0.9517 to 0.9990)	0.9311 (0.8755 to 0.9624)
12 Months	0.9931 (0.9517 to 0.9990)	0.9311 (0.8755 to 0.9624)
14 Months	0.9931 (0.9517 to 0.9990)	0.9311 (0.8755 to 0.9624)
16 Months	0.9931 (0.9517 to 0.9990)	0.9311 (0.8755 to 0.9624)
18 Months	0.9931 (0.9517 to 0.9990)	0.9311 (0.8755 to 0.9624)
20 Months	0.9931 (0.9517 to 0.9990)	0.9311 (0.8755 to 0.9624)
22 Months	0.9931 (0.9517 to 0.9990)	0.9311 (0.8755 to 0.9624)
24 Months	0.9931 (0.9517 to 0.9990)	0.9311 (0.8755 to 0.9624)
26 Months	0.9931 (0.9517 to 0.9990)	0.9311 (0.8755 to 0.9624)
Number of patients at risk[c]		
2 Months	140	145
4 Months	132	134
6 Months	116	121
8 Months	105	116
10 Months	101	108
12 Months	92	102
14 Months	87	101

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.8 Treatment emergent not severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	80	91
18 Months	72	84
20 Months	68	80
22 Months	66	71
24 Months	65	70
26 Months	62	64

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae12pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Blood and lymphatic system disorders (days)		
Number (%) of events	63 (42.3)	94 (61.8)
Number (%) of patients censored	86 (57.7)	58 (38.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	0.9528 (0.7556 to 1.9384)	0.6571 (0.5585 to 0.7885)
Median (95% CI)	NC (7.6222 to NC)	2.7926 (0.9528 to 10.4476)
75% quantile (95% CI)	NC (NC to NC)	NC (36.1396 to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0013
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.6801 (1.2198 to 2.3139)
P-value	-	0.0015
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.5952 (0.4322 to 0.8198)	-
Events probability (95% CI)[c]		
2 Months	0.6784 (0.5959 to 0.7475)	0.5232 (0.4406 to 0.5992)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.6213 (0.5370 to 0.6947)	0.4621 (0.3808 to 0.5394)
6 Months	0.5910 (0.5058 to 0.6664)	0.4550 (0.3739 to 0.5324)
8 Months	0.5826 (0.4970 to 0.6587)	0.4464 (0.3652 to 0.5242)
10 Months	0.5826 (0.4970 to 0.6587)	0.4282 (0.3468 to 0.5069)
12 Months	0.5826 (0.4970 to 0.6587)	0.4188 (0.3374 to 0.4981)
14 Months	0.5826 (0.4970 to 0.6587)	0.4093 (0.3278 to 0.4890)
16 Months	0.5826 (0.4970 to 0.6587)	0.4093 (0.3278 to 0.4890)
18 Months	0.5702 (0.4829 to 0.6481)	0.3988 (0.3171 to 0.4792)
20 Months	0.5702 (0.4829 to 0.6481)	0.3988 (0.3171 to 0.4792)
22 Months	0.5563 (0.4668 to 0.6366)	0.3764 (0.2941 to 0.4583)
24 Months	0.5563 (0.4668 to 0.6366)	0.3528 (0.2701 to 0.4363)
26 Months	0.5563 (0.4668 to 0.6366)	0.3528 (0.2701 to 0.4363)
Number of patients at risk[c]		
2 Months	98	78
4 Months	86	65
6 Months	76	54
8 Months	67	51
10 Months	65	46
12 Months	60	44

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	54	43
16 Months	50	42
18 Months	45	38
20 Months	42	38
22 Months	40	33
24 Months	39	28
26 Months	37	26
Cardiac disorders (days)		
Number (%) of events	4 (2.7)	11 (7.2)
Number (%) of patients censored	145 (97.3)	141 (92.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1044

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.5014 (0.7957 to 7.8639)
P-value	-	0.1167
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	0.9934 (0.9539 to 0.9991)
4 Months	1.0000 (1.0000 to 1.0000)	0.9798 (0.9387 to 0.9934)
6 Months	0.9923 (0.9467 to 0.9989)	0.9798 (0.9387 to 0.9934)
8 Months	0.9923 (0.9467 to 0.9989)	0.9718 (0.9263 to 0.9894)
10 Months	0.9923 (0.9467 to 0.9989)	0.9462 (0.8899 to 0.9741)
12 Months	0.9923 (0.9467 to 0.9989)	0.9462 (0.8899 to 0.9741)
14 Months	0.9592 (0.8939 to 0.9847)	0.9462 (0.8899 to 0.9741)
16 Months	0.9592 (0.8939 to 0.9847)	0.9462 (0.8899 to 0.9741)
18 Months	0.9592 (0.8939 to 0.9847)	0.9358 (0.8746 to 0.9677)
20 Months	0.9592 (0.8939 to 0.9847)	0.9245 (0.8582 to 0.9605)
22 Months	0.9592 (0.8939 to 0.9847)	0.9127 (0.8415 to 0.9528)
24 Months	0.9592 (0.8939 to 0.9847)	0.9127 (0.8415 to 0.9528)
26 Months	0.9592 (0.8939 to 0.9847)	0.8988 (0.8213 to 0.9439)
Number of patients at risk[c]		
2 Months	142	148

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	134	138
6 Months	116	125
8 Months	105	119
10 Months	101	109
12 Months	92	103
14 Months	83	102
16 Months	76	92
18 Months	69	85
20 Months	65	80
22 Months	63	71
24 Months	62	68
26 Months	59	61
Gastrointestinal disorders (days)		
Number (%) of events	5 (3.4)	13 (8.6)
Number (%) of patients censored	144 (96.6)	139 (91.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0704
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.5089 (0.8940 to 7.0405)
P-value	-	0.0806
Events probability (95% CI)[c]		
2 Months	0.9931 (0.9517 to 0.9990)	0.9734 (0.9307 to 0.9899)
4 Months	0.9788 (0.9356 to 0.9931)	0.9527 (0.9033 to 0.9772)
6 Months	0.9788 (0.9356 to 0.9931)	0.9451 (0.8930 to 0.9722)
8 Months	0.9788 (0.9356 to 0.9931)	0.9451 (0.8930 to 0.9722)
10 Months	0.9788 (0.9356 to 0.9931)	0.9451 (0.8930 to 0.9722)
12 Months	0.9788 (0.9356 to 0.9931)	0.9451 (0.8930 to 0.9722)
14 Months	0.9788 (0.9356 to 0.9931)	0.9359 (0.8798 to 0.9663)
16 Months	0.9788 (0.9356 to 0.9931)	0.9359 (0.8798 to 0.9663)
18 Months	0.9655 (0.9066 to 0.9875)	0.9359 (0.8798 to 0.9663)
20 Months	0.9655 (0.9066 to 0.9875)	0.9359 (0.8798 to 0.9663)
22 Months	0.9655 (0.9066 to 0.9875)	0.9359 (0.8798 to 0.9663)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
24 Months	0.9655 (0.9066 to 0.9875)	0.9359 (0.8798 to 0.9663)
26 Months	0.9655 (0.9066 to 0.9875)	0.9219 (0.8561 to 0.9584)
Number of patients at risk[c]		
2 Months	141	145
4 Months	131	134
6 Months	114	120
8 Months	103	116
10 Months	100	109
12 Months	92	103
14 Months	87	101
16 Months	80	91
18 Months	71	85
20 Months	67	81
22 Months	65	72
24 Months	64	69
26 Months	61	62
General disorders and administration site conditions (days)		
Number (%) of events	15 (10.1)	21 (13.8)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	134 (89.9)	131 (86.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (26.5791 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4804
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.2696 (0.6532 to 2.4678)
P-value	-	0.4814
Events probability (95% CI)[c]		
2 Months	0.9586 (0.9102 to 0.9812)	0.9471 (0.8971 to 0.9732)
4 Months	0.9370 (0.8824 to 0.9667)	0.9335 (0.8798 to 0.9636)
6 Months	0.9211 (0.8619 to 0.9556)	0.9193 (0.8621 to 0.9533)
8 Months	0.9123 (0.8504 to 0.9494)	0.9038 (0.8427 to 0.9420)
10 Months	0.9029 (0.8380 to 0.9427)	0.8955 (0.8323 to 0.9358)
12 Months	0.9029 (0.8380 to 0.9427)	0.8955 (0.8323 to 0.9358)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.9029 (0.8380 to 0.9427)	0.8955 (0.8323 to 0.9358)
16 Months	0.9029 (0.8380 to 0.9427)	0.8762 (0.8073 to 0.9217)
18 Months	0.9029 (0.8380 to 0.9427)	0.8762 (0.8073 to 0.9217)
20 Months	0.9029 (0.8380 to 0.9427)	0.8656 (0.7934 to 0.9139)
22 Months	0.9029 (0.8380 to 0.9427)	0.8656 (0.7934 to 0.9139)
24 Months	0.9029 (0.8380 to 0.9427)	0.8415 (0.7619 to 0.8963)
26 Months	0.8884 (0.8154 to 0.9336)	0.8415 (0.7619 to 0.8963)
Number of patients at risk[c]		
2 Months	137	142
4 Months	127	133
6 Months	113	120
8 Months	101	116
10 Months	96	108
12 Months	87	101
14 Months	83	101
16 Months	76	89
18 Months	69	84
20 Months	65	80
22 Months	63	72

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
24 Months	62	67
26 Months	59	61
Infections and infestations (days)		
Number (%) of events	52 (34.9)	77 (50.7)
Number (%) of patients censored	97 (65.1)	75 (49.3)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	4.3696 (2.2669 to 14.9158)	4.0411 (2.0041 to 6.2752)
Median (95% CI)	NC (29.5688 to NC)	19.3183 (11.2690 to 36.3696)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0446
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.4342 (1.0068 to 2.0430)
P-value	-	0.0458
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6972 (0.4895 to 0.9932)	-
Events probability (95% CI)[c]		

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	0.8424 (0.7723 to 0.8923)	0.8267 (0.7561 to 0.8786)
4 Months	0.7559 (0.6767 to 0.8183)	0.7522 (0.6747 to 0.8138)
6 Months	0.7252 (0.6434 to 0.7913)	0.6879 (0.6060 to 0.7562)
8 Months	0.7088 (0.6256 to 0.7768)	0.6420 (0.5577 to 0.7144)
10 Months	0.7088 (0.6256 to 0.7768)	0.6028 (0.5170 to 0.6783)
12 Months	0.6989 (0.6145 to 0.7684)	0.5621 (0.4751 to 0.6402)
14 Months	0.6888 (0.6031 to 0.7597)	0.5536 (0.4663 to 0.6323)
16 Months	0.6669 (0.5783 to 0.7411)	0.5357 (0.4480 to 0.6156)
18 Months	0.6552 (0.5650 to 0.7312)	0.5263 (0.4383 to 0.6069)
20 Months	0.6429 (0.5509 to 0.7208)	0.4852 (0.3957 to 0.5689)
22 Months	0.6429 (0.5509 to 0.7208)	0.4749 (0.3852 to 0.5593)
24 Months	0.6295 (0.5355 to 0.7096)	0.4749 (0.3852 to 0.5593)
26 Months	0.6158 (0.5199 to 0.6981)	0.4376 (0.3460 to 0.5254)
Number of patients at risk[c]		
2 Months	120	123
4 Months	103	109
6 Months	91	91
8 Months	80	84
10 Months	79	76

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	71	67
14 Months	66	65
16 Months	60	58
18 Months	53	52
20 Months	50	47
22 Months	48	43
24 Months	46	40
26 Months	43	33
Injury, poisoning and procedural complications (days)		
Number (%) of events	1 (0.7)	9 (5.9)
Number (%) of patients censored	148 (99.3)	143 (94.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0150

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	8.4651 (1.0719 to 66.8545)
P-value	-	0.0428
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.1181 (0.0150 to 0.9330)	-
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	0.9671 (0.9227 to 0.9862)
4 Months	1.0000 (1.0000 to 1.0000)	0.9536 (0.9052 to 0.9776)
6 Months	1.0000 (1.0000 to 1.0000)	0.9536 (0.9052 to 0.9776)
8 Months	1.0000 (1.0000 to 1.0000)	0.9536 (0.9052 to 0.9776)
10 Months	1.0000 (1.0000 to 1.0000)	0.9536 (0.9052 to 0.9776)
12 Months	1.0000 (1.0000 to 1.0000)	0.9536 (0.9052 to 0.9776)
14 Months	1.0000 (1.0000 to 1.0000)	0.9445 (0.8916 to 0.9720)
16 Months	1.0000 (1.0000 to 1.0000)	0.9445 (0.8916 to 0.9720)
18 Months	0.9865 (0.9079 to 0.9981)	0.9445 (0.8916 to 0.9720)
20 Months	0.9865 (0.9079 to 0.9981)	0.9445 (0.8916 to 0.9720)
22 Months	0.9865 (0.9079 to 0.9981)	0.9445 (0.8916 to 0.9720)
24 Months	0.9865 (0.9079 to 0.9981)	0.9445 (0.8916 to 0.9720)
26 Months	0.9865 (0.9079 to 0.9981)	0.9445 (0.8916 to 0.9720)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	142	145
4 Months	134	137
6 Months	117	124
8 Months	106	119
10 Months	102	112
12 Months	93	105
14 Months	87	103
16 Months	80	94
18 Months	71	87
20 Months	67	83
22 Months	65	76
24 Months	64	73
26 Months	61	68
Metabolism and nutrition disorders (days)		
Number (%) of events	8 (5.4)	15 (9.9)
Number (%) of patients censored	141 (94.6)	137 (90.1)
Kaplan-Meier estimates of Events in months		

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1624
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.8271 (0.7743 to 4.3112)
P-value	-	0.1688
Events probability (95% CI)[c]		
2 Months	0.9661 (0.9205 to 0.9858)	0.9539 (0.9056 to 0.9777)
4 Months	0.9518 (0.9016 to 0.9768)	0.9334 (0.8796 to 0.9636)
6 Months	0.9444 (0.8917 to 0.9718)	0.9259 (0.8701 to 0.9583)
8 Months	0.9444 (0.8917 to 0.9718)	0.9259 (0.8701 to 0.9583)
10 Months	0.9444 (0.8917 to 0.9718)	0.9091 (0.8480 to 0.9463)
12 Months	0.9444 (0.8917 to 0.9718)	0.9091 (0.8480 to 0.9463)
14 Months	0.9444 (0.8917 to 0.9718)	0.9000 (0.8361 to 0.9398)
16 Months	0.9444 (0.8917 to 0.9718)	0.9000 (0.8361 to 0.9398)
18 Months	0.9444 (0.8917 to 0.9718)	0.9000 (0.8361 to 0.9398)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
20 Months	0.9444 (0.8917 to 0.9718)	0.8890 (0.8210 to 0.9322)
22 Months	0.9444 (0.8917 to 0.9718)	0.8890 (0.8210 to 0.9322)
24 Months	0.9444 (0.8917 to 0.9718)	0.8890 (0.8210 to 0.9322)
26 Months	0.9444 (0.8917 to 0.9718)	0.8890 (0.8210 to 0.9322)
Number of patients at risk[c]		
2 Months	138	143
4 Months	130	133
6 Months	112	120
8 Months	102	115
10 Months	99	106
12 Months	90	100
14 Months	85	98
16 Months	78	89
18 Months	71	83
20 Months	67	80
22 Months	65	72
24 Months	64	69
26 Months	62	63

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Musculoskeletal and connective tissue disorders (days)		
Number (%) of events	8 (5.4)	14 (9.2)
Number (%) of patients censored	141 (94.6)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2793
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.6102 (0.6739 to 3.8478)
P-value	-	0.2838
Events probability (95% CI)[c]		
2 Months	0.9523 (0.9025 to 0.9770)	0.9669 (0.9224 to 0.9861)
4 Months	0.9523 (0.9025 to 0.9770)	0.9602 (0.9136 to 0.9819)
6 Months	0.9523 (0.9025 to 0.9770)	0.9459 (0.8946 to 0.9726)
8 Months	0.9434 (0.8895 to 0.9714)	0.9459 (0.8946 to 0.9726)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
10 Months	0.9434 (0.8895 to 0.9714)	0.9377 (0.8835 to 0.9672)
12 Months	0.9434 (0.8895 to 0.9714)	0.9292 (0.8719 to 0.9614)
14 Months	0.9434 (0.8895 to 0.9714)	0.9292 (0.8719 to 0.9614)
16 Months	0.9434 (0.8895 to 0.9714)	0.9107 (0.8471 to 0.9486)
18 Months	0.9434 (0.8895 to 0.9714)	0.9107 (0.8471 to 0.9486)
20 Months	0.9434 (0.8895 to 0.9714)	0.9107 (0.8471 to 0.9486)
22 Months	0.9434 (0.8895 to 0.9714)	0.9107 (0.8471 to 0.9486)
24 Months	0.9434 (0.8895 to 0.9714)	0.8987 (0.8298 to 0.9407)
26 Months	0.9434 (0.8895 to 0.9714)	0.8853 (0.8104 to 0.9318)
Number of patients at risk[c]		
2 Months	137	145
4 Months	129	136
6 Months	113	123
8 Months	101	122
10 Months	97	114
12 Months	90	106
14 Months	85	105
16 Months	79	94
18 Months	72	88

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
20 Months	68	84
22 Months	66	76
24 Months	65	72
26 Months	62	65
Nervous system disorders (days)		
Number (%) of events	9 (6.0)	14 (9.2)
Number (%) of patients censored	140 (94.0)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3411
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.4983 (0.6481 to 3.4638)
P-value	-	0.3443

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Events probability (95% CI)[c]		
2 Months	0.9592 (0.9115 to 0.9815)	0.9603 (0.9137 to 0.9819)
4 Months	0.9518 (0.9015 to 0.9767)	0.9397 (0.8872 to 0.9682)
6 Months	0.9443 (0.8916 to 0.9718)	0.9397 (0.8872 to 0.9682)
8 Months	0.9443 (0.8916 to 0.9718)	0.9237 (0.8661 to 0.9571)
10 Months	0.9443 (0.8916 to 0.9718)	0.9237 (0.8661 to 0.9571)
12 Months	0.9339 (0.8758 to 0.9654)	0.9147 (0.8541 to 0.9509)
14 Months	0.9339 (0.8758 to 0.9654)	0.9147 (0.8541 to 0.9509)
16 Months	0.9339 (0.8758 to 0.9654)	0.9147 (0.8541 to 0.9509)
18 Months	0.9339 (0.8758 to 0.9654)	0.9147 (0.8541 to 0.9509)
20 Months	0.9339 (0.8758 to 0.9654)	0.9147 (0.8541 to 0.9509)
22 Months	0.9339 (0.8758 to 0.9654)	0.9025 (0.8359 to 0.9430)
24 Months	0.9339 (0.8758 to 0.9654)	0.9025 (0.8359 to 0.9430)
26 Months	0.9339 (0.8758 to 0.9654)	0.9025 (0.8359 to 0.9430)
Number of patients at risk[c]		
2 Months	137	143
4 Months	128	132
6 Months	112	119
8 Months	101	113

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
10 Months	97	107
12 Months	87	99
14 Months	82	98
16 Months	75	89
18 Months	67	82
20 Months	63	78
22 Months	61	70
24 Months	60	68
26 Months	57	62
Renal and urinary disorders (days)		
Number (%) of events	10 (6.7)	9 (5.9)
Number (%) of patients censored	139 (93.3)	143 (94.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5819
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.7765 (0.3149 to 1.9151)
P-value	-	0.5829
Events probability (95% CI)[c]		
2 Months	0.9515 (0.9009 to 0.9766)	0.9868 (0.9482 to 0.9967)
4 Months	0.9444 (0.8918 to 0.9718)	0.9800 (0.9392 to 0.9935)
6 Months	0.9362 (0.8807 to 0.9663)	0.9725 (0.9281 to 0.9896)
8 Months	0.9362 (0.8807 to 0.9663)	0.9725 (0.9281 to 0.9896)
10 Months	0.9362 (0.8807 to 0.9663)	0.9560 (0.9042 to 0.9801)
12 Months	0.9261 (0.8662 to 0.9598)	0.9473 (0.8922 to 0.9747)
14 Months	0.9261 (0.8662 to 0.9598)	0.9382 (0.8796 to 0.9688)
16 Months	0.9261 (0.8662 to 0.9598)	0.9382 (0.8796 to 0.9688)
18 Months	0.9261 (0.8662 to 0.9598)	0.9280 (0.8652 to 0.9622)
20 Months	0.9261 (0.8662 to 0.9598)	0.9280 (0.8652 to 0.9622)
22 Months	0.9261 (0.8662 to 0.9598)	0.9280 (0.8652 to 0.9622)
24 Months	0.9261 (0.8662 to 0.9598)	0.9280 (0.8652 to 0.9622)
26 Months	0.9261 (0.8662 to 0.9598)	0.9280 (0.8652 to 0.9622)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number of patients at risk[c]		
2 Months	135	147
4 Months	127	138
6 Months	113	126
8 Months	102	121
10 Months	99	112
12 Months	90	105
14 Months	85	103
16 Months	78	93
18 Months	70	86
20 Months	67	83
22 Months	65	76
24 Months	64	73
26 Months	61	67
Respiratory, thoracic and mediastinal disorders (days)		
Number (%) of events	11 (7.4)	14 (9.2)
Number (%) of patients censored	138 (92.6)	138 (90.8)
Kaplan-Meier estimates of Events in months		

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6539
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.1981 (0.5431 to 2.6433)
P-value	-	0.6543
Events probability (95% CI)[c]		
2 Months	0.9797 (0.9383 to 0.9934)	0.9603 (0.9138 to 0.9820)
4 Months	0.9797 (0.9383 to 0.9934)	0.9463 (0.8955 to 0.9728)
6 Months	0.9636 (0.9143 to 0.9847)	0.9388 (0.8855 to 0.9677)
8 Months	0.9546 (0.9010 to 0.9795)	0.9148 (0.8545 to 0.9509)
10 Months	0.9356 (0.8743 to 0.9675)	0.9065 (0.8439 to 0.9448)
12 Months	0.9356 (0.8743 to 0.9675)	0.8975 (0.8324 to 0.9383)
14 Months	0.9141 (0.8445 to 0.9534)	0.8975 (0.8324 to 0.9383)
16 Months	0.9141 (0.8445 to 0.9534)	0.8975 (0.8324 to 0.9383)
18 Months	0.9141 (0.8445 to 0.9534)	0.8975 (0.8324 to 0.9383)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.9 Treatment emergent severe adverse event according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
20 Months	0.9141 (0.8445 to 0.9534)	0.8975 (0.8324 to 0.9383)
22 Months	0.9141 (0.8445 to 0.9534)	0.8975 (0.8324 to 0.9383)
24 Months	0.9141 (0.8445 to 0.9534)	0.8975 (0.8324 to 0.9383)
26 Months	0.9141 (0.8445 to 0.9534)	0.8975 (0.8324 to 0.9383)
Number of patients at risk[c]		
2 Months	140	143
4 Months	132	133
6 Months	113	121
8 Months	102	113
10 Months	96	105
12 Months	87	97
14 Months	80	96
16 Months	74	87
18 Months	67	80
20 Months	63	76
22 Months	61	69
24 Months	60	66
26 Months	58	61

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.10 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Febrile neutropenia (days)		
Number (%) of events	5 (3.4)	18 (11.8)
Number (%) of patients censored	144 (96.6)	134 (88.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0059
Stratified[a] Hazard ratio (95% CI) vs Pd	-	3.6697 (1.3622 to 9.8861)
P-value	-	0.0101
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.2725 (0.1012 to 0.7341)	-
Events probability (95% CI)[c]		
2 Months	0.9860 (0.9452 to 0.9965)	0.9073 (0.8485 to 0.9440)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.10 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.9860 (0.9452 to 0.9965)	0.9005 (0.8404 to 0.9388)
6 Months	0.9860 (0.9452 to 0.9965)	0.8865 (0.8238 to 0.9279)
8 Months	0.9860 (0.9452 to 0.9965)	0.8865 (0.8238 to 0.9279)
10 Months	0.9763 (0.9270 to 0.9924)	0.8865 (0.8238 to 0.9279)
12 Months	0.9763 (0.9270 to 0.9924)	0.8777 (0.8126 to 0.9213)
14 Months	0.9653 (0.9083 to 0.9871)	0.8777 (0.8126 to 0.9213)
16 Months	0.9653 (0.9083 to 0.9871)	0.8777 (0.8126 to 0.9213)
18 Months	0.9653 (0.9083 to 0.9871)	0.8777 (0.8126 to 0.9213)
20 Months	0.9511 (0.8826 to 0.9801)	0.8777 (0.8126 to 0.9213)
22 Months	0.9511 (0.8826 to 0.9801)	0.8777 (0.8126 to 0.9213)
24 Months	0.9511 (0.8826 to 0.9801)	0.8777 (0.8126 to 0.9213)
26 Months	0.9511 (0.8826 to 0.9801)	0.8777 (0.8126 to 0.9213)
Number of patients at risk[c]		
2 Months	140	135
4 Months	132	129
6 Months	116	114
8 Months	105	110
10 Months	100	107
12 Months	92	99

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.10 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	85	98
16 Months	78	89
18 Months	70	83
20 Months	66	79
22 Months	64	71
24 Months	63	68
26 Months	60	63
Lower respiratory tract infection (days)		
Number (%) of events	4 (2.7)	8 (5.3)
Number (%) of patients censored	145 (97.3)	144 (94.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4848

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.10 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5317 (0.4590 to 5.1112)
P-value	-	0.4880
Events probability (95% CI)[c]		
2 Months	0.9932 (0.9530 to 0.9990)	0.9934 (0.9539 to 0.9991)
4 Months	0.9860 (0.9451 to 0.9965)	0.9863 (0.9462 to 0.9966)
6 Months	0.9775 (0.9315 to 0.9927)	0.9863 (0.9462 to 0.9966)
8 Months	0.9684 (0.9175 to 0.9881)	0.9863 (0.9462 to 0.9966)
10 Months	0.9684 (0.9175 to 0.9881)	0.9613 (0.9092 to 0.9838)
12 Months	0.9684 (0.9175 to 0.9881)	0.9613 (0.9092 to 0.9838)
14 Months	0.9684 (0.9175 to 0.9881)	0.9613 (0.9092 to 0.9838)
16 Months	0.9684 (0.9175 to 0.9881)	0.9613 (0.9092 to 0.9838)
18 Months	0.9684 (0.9175 to 0.9881)	0.9510 (0.8932 to 0.9779)
20 Months	0.9684 (0.9175 to 0.9881)	0.9287 (0.8607 to 0.9642)
22 Months	0.9684 (0.9175 to 0.9881)	0.9287 (0.8607 to 0.9642)
24 Months	0.9684 (0.9175 to 0.9881)	0.9287 (0.8607 to 0.9642)
26 Months	0.9684 (0.9175 to 0.9881)	0.9287 (0.8607 to 0.9642)
Number of patients at risk[c]		
2 Months	141	148

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.10 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	132	139
6 Months	114	127
8 Months	102	122
10 Months	99	112
12 Months	90	106
14 Months	84	105
16 Months	78	95
18 Months	70	87
20 Months	66	82
22 Months	64	73
24 Months	63	70
26 Months	60	64
Neutropenia (days)		
Number (%) of events	52 (34.9)	75 (49.3)
Number (%) of patients censored	97 (65.1)	77 (50.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	1.9384 (0.9856 to 4.6653)	0.8542 (0.7556 to 1.0185)
Median (95% CI)	NC (NC to NC)	22.6037 (3.0554 to NC)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.10 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0154
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5445 (1.0838 to 2.2011)
P-value	-	0.0162
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6474 (0.4543 to 0.9227)	-
Events probability (95% CI)[c]		
2 Months	0.7463 (0.6674 to 0.8092)	0.6220 (0.5395 to 0.6940)
4 Months	0.6958 (0.6136 to 0.7639)	0.5809 (0.4977 to 0.6551)
6 Months	0.6639 (0.5795 to 0.7352)	0.5809 (0.4977 to 0.6551)
8 Months	0.6549 (0.5698 to 0.7273)	0.5643 (0.4804 to 0.6398)
10 Months	0.6549 (0.5698 to 0.7273)	0.5455 (0.4604 to 0.6227)
12 Months	0.6549 (0.5698 to 0.7273)	0.5359 (0.4504 to 0.6139)
14 Months	0.6549 (0.5698 to 0.7273)	0.5260 (0.4399 to 0.6049)
16 Months	0.6549 (0.5698 to 0.7273)	0.5260 (0.4399 to 0.6049)
18 Months	0.6418 (0.5543 to 0.7166)	0.5150 (0.4281 to 0.5951)
20 Months	0.6418 (0.5543 to 0.7166)	0.5150 (0.4281 to 0.5951)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.10 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
22 Months	0.6272 (0.5367 to 0.7050)	0.5021 (0.4139 to 0.5839)
24 Months	0.6272 (0.5367 to 0.7050)	0.4617 (0.3697 to 0.5486)
26 Months	0.6272 (0.5367 to 0.7050)	0.4617 (0.3697 to 0.5486)
Number of patients at risk[c]		
2 Months	108	92
4 Months	93	81
6 Months	80	71
8 Months	71	66
10 Months	69	57
12 Months	64	54
14 Months	58	53
16 Months	53	51
18 Months	48	46
20 Months	45	46
22 Months	43	39
24 Months	42	33
26 Months	39	30
Pneumonia (days)		

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.10 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of events	31 (20.8)	35 (23.0)
Number (%) of patients censored	118 (79.2)	117 (77.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	29.5688 (7.0308 to NC)	24.5749 (8.6078 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8720
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0406 (0.6410 to 1.6894)
P-value	-	0.8721
Events probability (95% CI)[c]		
2 Months	0.9042 (0.8435 to 0.9421)	0.9207 (0.8646 to 0.9542)
4 Months	0.8536 (0.7842 to 0.9020)	0.8866 (0.8238 to 0.9279)
6 Months	0.8299 (0.7567 to 0.8828)	0.8496 (0.7804 to 0.8984)
8 Months	0.8214 (0.7467 to 0.8758)	0.8262 (0.7533 to 0.8793)
10 Months	0.8214 (0.7467 to 0.8758)	0.8181 (0.7440 to 0.8726)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.10 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	0.8214 (0.7467 to 0.8758)	0.8009 (0.7240 to 0.8584)
14 Months	0.8111 (0.7341 to 0.8677)	0.8009 (0.7240 to 0.8584)
16 Months	0.8000 (0.7204 to 0.8591)	0.8009 (0.7240 to 0.8584)
18 Months	0.8000 (0.7204 to 0.8591)	0.7909 (0.7121 to 0.8504)
20 Months	0.7866 (0.7032 to 0.8491)	0.7698 (0.6870 to 0.8333)
22 Months	0.7723 (0.6848 to 0.8384)	0.7588 (0.6740 to 0.8244)
24 Months	0.7723 (0.6848 to 0.8384)	0.7588 (0.6740 to 0.8244)
26 Months	0.7578 (0.6664 to 0.8273)	0.7324 (0.6417 to 0.8036)
Number of patients at risk[c]		
2 Months	129	137
4 Months	115	126
6 Months	102	110
8 Months	92	104
10 Months	90	99
12 Months	83	92
14 Months	77	91
16 Months	69	83
18 Months	62	76
20 Months	57	70

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.10 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
22 Months	54	62
24 Months	53	59
26 Months	50	52
Thrombocytopenia (days)		
Number (%) of events	18 (12.1)	20 (13.2)
Number (%) of patients censored	131 (87.9)	132 (86.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8814
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0497 (0.5550 to 1.9852)
P-value	-	0.8815
Events probability (95% CI)[c]		

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.10 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	0.8904 (0.8273 to 0.9314)	0.9009 (0.8409 to 0.9390)
4 Months	0.8904 (0.8273 to 0.9314)	0.8873 (0.8250 to 0.9284)
6 Months	0.8756 (0.8097 to 0.9198)	0.8873 (0.8250 to 0.9284)
8 Months	0.8756 (0.8097 to 0.9198)	0.8795 (0.8155 to 0.9224)
10 Months	0.8756 (0.8097 to 0.9198)	0.8795 (0.8155 to 0.9224)
12 Months	0.8756 (0.8097 to 0.9198)	0.8795 (0.8155 to 0.9224)
14 Months	0.8756 (0.8097 to 0.9198)	0.8795 (0.8155 to 0.9224)
16 Months	0.8756 (0.8097 to 0.9198)	0.8698 (0.8027 to 0.9152)
18 Months	0.8756 (0.8097 to 0.9198)	0.8698 (0.8027 to 0.9152)
20 Months	0.8756 (0.8097 to 0.9198)	0.8698 (0.8027 to 0.9152)
22 Months	0.8756 (0.8097 to 0.9198)	0.8698 (0.8027 to 0.9152)
24 Months	0.8756 (0.8097 to 0.9198)	0.8698 (0.8027 to 0.9152)
26 Months	0.8756 (0.8097 to 0.9198)	0.8698 (0.8027 to 0.9152)
Number of patients at risk[c]		
2 Months	127	135
4 Months	121	126
6 Months	109	115
8 Months	100	110
10 Months	96	103

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.10 Treatment emergent severe adverse event according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	88	98
14 Months	82	97
16 Months	75	89
18 Months	68	82
20 Months	65	78
22 Months	63	72
24 Months	62	69
26 Months	60	64

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae34pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Blood and lymphatic system disorders (days)		
Number (%) of events	63 (42.3)	94 (61.8)
Number (%) of patients censored	86 (57.7)	58 (38.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	0.9528 (0.7556 to 1.9384)	0.6571 (0.5585 to 0.7885)
Median (95% CI)	NC (7.6222 to NC)	2.7926 (0.9528 to 10.4476)
75% quantile (95% CI)	NC (NC to NC)	NC (36.1396 to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0013
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.6801 (1.2198 to 2.3139)
P-value	-	0.0015
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.5952 (0.4322 to 0.8198)	-
Events probability (95% CI)[c]		
2 Months	0.6784 (0.5959 to 0.7475)	0.5232 (0.4406 to 0.5992)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.6213 (0.5370 to 0.6947)	0.4621 (0.3808 to 0.5394)
6 Months	0.5910 (0.5058 to 0.6664)	0.4550 (0.3739 to 0.5324)
8 Months	0.5826 (0.4970 to 0.6587)	0.4464 (0.3652 to 0.5242)
10 Months	0.5826 (0.4970 to 0.6587)	0.4282 (0.3468 to 0.5069)
12 Months	0.5826 (0.4970 to 0.6587)	0.4188 (0.3374 to 0.4981)
14 Months	0.5826 (0.4970 to 0.6587)	0.4093 (0.3278 to 0.4890)
16 Months	0.5826 (0.4970 to 0.6587)	0.4093 (0.3278 to 0.4890)
18 Months	0.5702 (0.4829 to 0.6481)	0.3988 (0.3171 to 0.4792)
20 Months	0.5702 (0.4829 to 0.6481)	0.3988 (0.3171 to 0.4792)
22 Months	0.5563 (0.4668 to 0.6366)	0.3764 (0.2941 to 0.4583)
24 Months	0.5563 (0.4668 to 0.6366)	0.3528 (0.2701 to 0.4363)
26 Months	0.5563 (0.4668 to 0.6366)	0.3528 (0.2701 to 0.4363)
Number of patients at risk[c]		
2 Months	98	78
4 Months	86	65
6 Months	76	54
8 Months	67	51
10 Months	65	46
12 Months	60	44

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	54	43
16 Months	50	42
18 Months	45	38
20 Months	42	38
22 Months	40	33
24 Months	39	28
26 Months	37	26
Cardiac disorders (days)		
Number (%) of events	5 (3.4)	11 (7.2)
Number (%) of patients censored	144 (96.6)	141 (92.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1829

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.0225 (0.7019 to 5.8277)
P-value	-	0.1921
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	0.9934 (0.9539 to 0.9991)
4 Months	1.0000 (1.0000 to 1.0000)	0.9798 (0.9387 to 0.9934)
6 Months	0.9923 (0.9467 to 0.9989)	0.9798 (0.9387 to 0.9934)
8 Months	0.9923 (0.9467 to 0.9989)	0.9718 (0.9263 to 0.9894)
10 Months	0.9923 (0.9467 to 0.9989)	0.9462 (0.8899 to 0.9741)
12 Months	0.9923 (0.9467 to 0.9989)	0.9462 (0.8899 to 0.9741)
14 Months	0.9592 (0.8939 to 0.9847)	0.9462 (0.8899 to 0.9741)
16 Months	0.9592 (0.8939 to 0.9847)	0.9462 (0.8899 to 0.9741)
18 Months	0.9592 (0.8939 to 0.9847)	0.9358 (0.8746 to 0.9677)
20 Months	0.9592 (0.8939 to 0.9847)	0.9245 (0.8582 to 0.9605)
22 Months	0.9592 (0.8939 to 0.9847)	0.9127 (0.8415 to 0.9528)
24 Months	0.9592 (0.8939 to 0.9847)	0.9127 (0.8415 to 0.9528)
26 Months	0.9592 (0.8939 to 0.9847)	0.8988 (0.8213 to 0.9439)
Number of patients at risk[c]		
2 Months	142	148

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	134	138
6 Months	116	125
8 Months	105	119
10 Months	101	109
12 Months	92	103
14 Months	83	102
16 Months	76	92
18 Months	69	85
20 Months	65	80
22 Months	63	71
24 Months	62	68
26 Months	59	61
Gastrointestinal disorders (days)		
Number (%) of events	5 (3.4)	13 (8.6)
Number (%) of patients censored	144 (96.6)	139 (91.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0704
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.5089 (0.8940 to 7.0405)
P-value	-	0.0806
Events probability (95% CI)[c]		
2 Months	0.9931 (0.9517 to 0.9990)	0.9734 (0.9307 to 0.9899)
4 Months	0.9788 (0.9356 to 0.9931)	0.9527 (0.9033 to 0.9772)
6 Months	0.9788 (0.9356 to 0.9931)	0.9451 (0.8930 to 0.9722)
8 Months	0.9788 (0.9356 to 0.9931)	0.9451 (0.8930 to 0.9722)
10 Months	0.9788 (0.9356 to 0.9931)	0.9451 (0.8930 to 0.9722)
12 Months	0.9788 (0.9356 to 0.9931)	0.9451 (0.8930 to 0.9722)
14 Months	0.9788 (0.9356 to 0.9931)	0.9359 (0.8798 to 0.9663)
16 Months	0.9788 (0.9356 to 0.9931)	0.9359 (0.8798 to 0.9663)
18 Months	0.9655 (0.9066 to 0.9875)	0.9359 (0.8798 to 0.9663)
20 Months	0.9655 (0.9066 to 0.9875)	0.9359 (0.8798 to 0.9663)
22 Months	0.9655 (0.9066 to 0.9875)	0.9359 (0.8798 to 0.9663)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
24 Months	0.9655 (0.9066 to 0.9875)	0.9359 (0.8798 to 0.9663)
26 Months	0.9655 (0.9066 to 0.9875)	0.9219 (0.8561 to 0.9584)
Number of patients at risk[c]		
2 Months	141	145
4 Months	131	134
6 Months	114	120
8 Months	103	116
10 Months	100	109
12 Months	92	103
14 Months	87	101
16 Months	80	91
18 Months	71	85
20 Months	67	81
22 Months	65	72
24 Months	64	69
26 Months	61	62
General disorders and administration site conditions (days)		
Number (%) of events	20 (13.4)	27 (17.8)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	129 (86.6)	125 (82.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (31.3758 to NC)	NC (22.4723 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4540
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.2474 (0.6986 to 2.2272)
P-value	-	0.4549
Events probability (95% CI)[c]		
2 Months	0.9454 (0.8937 to 0.9723)	0.9338 (0.8805 to 0.9639)
4 Months	0.9169 (0.8582 to 0.9519)	0.9136 (0.8558 to 0.9489)
6 Months	0.8870 (0.8219 to 0.9292)	0.8859 (0.8228 to 0.9275)
8 Months	0.8785 (0.8115 to 0.9228)	0.8710 (0.8051 to 0.9158)
10 Months	0.8695 (0.8003 to 0.9159)	0.8552 (0.7863 to 0.9033)
12 Months	0.8695 (0.8003 to 0.9159)	0.8552 (0.7863 to 0.9033)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	0.8695 (0.8003 to 0.9159)	0.8552 (0.7863 to 0.9033)
16 Months	0.8695 (0.8003 to 0.9159)	0.8368 (0.7638 to 0.8889)
18 Months	0.8695 (0.8003 to 0.9159)	0.8368 (0.7638 to 0.8889)
20 Months	0.8695 (0.8003 to 0.9159)	0.8266 (0.7512 to 0.8810)
22 Months	0.8695 (0.8003 to 0.9159)	0.8266 (0.7512 to 0.8810)
24 Months	0.8695 (0.8003 to 0.9159)	0.8037 (0.7224 to 0.8633)
26 Months	0.8554 (0.7800 to 0.9065)	0.8037 (0.7224 to 0.8633)
Number of patients at risk[c]		
2 Months	137	140
4 Months	126	133
6 Months	113	120
8 Months	101	116
10 Months	96	108
12 Months	87	101
14 Months	83	101
16 Months	76	89
18 Months	69	84
20 Months	65	80
22 Months	63	72

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
24 Months	62	67
26 Months	59	61
Infections and infestations (days)		
Number (%) of events	54 (36.2)	79 (52.0)
Number (%) of patients censored	95 (63.8)	73 (48.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	3.6140 (2.1355 to 13.7988)	4.0411 (2.0041 to 5.9795)
Median (95% CI)	NC (27.8275 to NC)	19.0554 (10.5462 to 36.3696)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0520
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.4097 (0.9953 to 1.9967)
P-value	-	0.0532
Events probability (95% CI)[c]		
2 Months	0.8360 (0.7653 to 0.8870)	0.8267 (0.7561 to 0.8786)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	0.7437 (0.6640 to 0.8072)	0.7522 (0.6747 to 0.8138)
6 Months	0.7135 (0.6315 to 0.7804)	0.6745 (0.5922 to 0.7438)
8 Months	0.6973 (0.6140 to 0.7661)	0.6295 (0.5452 to 0.7026)
10 Months	0.6973 (0.6140 to 0.7661)	0.5911 (0.5055 to 0.6669)
12 Months	0.6877 (0.6032 to 0.7577)	0.5512 (0.4647 to 0.6294)
14 Months	0.6777 (0.5921 to 0.7492)	0.5428 (0.4562 to 0.6215)
16 Months	0.6562 (0.5679 to 0.7307)	0.5253 (0.4383 to 0.6051)
18 Months	0.6447 (0.5549 to 0.7209)	0.5161 (0.4288 to 0.5965)
20 Months	0.6325 (0.5411 to 0.7106)	0.4758 (0.3873 to 0.5590)
22 Months	0.6325 (0.5411 to 0.7106)	0.4657 (0.3770 to 0.5495)
24 Months	0.6193 (0.5260 to 0.6995)	0.4657 (0.3770 to 0.5495)
26 Months	0.6059 (0.5107 to 0.6882)	0.4291 (0.3388 to 0.5161)
Number of patients at risk[c]		
2 Months	120	123
4 Months	103	109
6 Months	91	91
8 Months	80	84
10 Months	79	76
12 Months	71	67

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
14 Months	66	65
16 Months	60	58
18 Months	53	52
20 Months	50	47
22 Months	48	43
24 Months	46	40
26 Months	43	33
Injury, poisoning and procedural complications (days)		
Number (%) of events	1 (0.7)	9 (5.9)
Number (%) of patients censored	148 (99.3)	143 (94.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0150

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	8.4651 (1.0719 to 66.8545)
P-value	-	0.0428
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.1181 (0.0150 to 0.9330)	-
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	0.9671 (0.9227 to 0.9862)
4 Months	1.0000 (1.0000 to 1.0000)	0.9536 (0.9052 to 0.9776)
6 Months	1.0000 (1.0000 to 1.0000)	0.9536 (0.9052 to 0.9776)
8 Months	1.0000 (1.0000 to 1.0000)	0.9536 (0.9052 to 0.9776)
10 Months	1.0000 (1.0000 to 1.0000)	0.9536 (0.9052 to 0.9776)
12 Months	1.0000 (1.0000 to 1.0000)	0.9536 (0.9052 to 0.9776)
14 Months	1.0000 (1.0000 to 1.0000)	0.9445 (0.8916 to 0.9720)
16 Months	1.0000 (1.0000 to 1.0000)	0.9445 (0.8916 to 0.9720)
18 Months	0.9865 (0.9079 to 0.9981)	0.9445 (0.8916 to 0.9720)
20 Months	0.9865 (0.9079 to 0.9981)	0.9445 (0.8916 to 0.9720)
22 Months	0.9865 (0.9079 to 0.9981)	0.9445 (0.8916 to 0.9720)
24 Months	0.9865 (0.9079 to 0.9981)	0.9445 (0.8916 to 0.9720)
26 Months	0.9865 (0.9079 to 0.9981)	0.9445 (0.8916 to 0.9720)
Number of patients at risk[c]		

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	142	145
4 Months	134	137
6 Months	117	124
8 Months	106	119
10 Months	102	112
12 Months	93	105
14 Months	87	103
16 Months	80	94
18 Months	71	87
20 Months	67	83
22 Months	65	76
24 Months	64	73
26 Months	61	68
Metabolism and nutrition disorders (days)		
Number (%) of events	8 (5.4)	15 (9.9)
Number (%) of patients censored	141 (94.6)	137 (90.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
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16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1624
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.8271 (0.7743 to 4.3112)
P-value	-	0.1688
Events probability (95% CI)[c]		
2 Months	0.9661 (0.9205 to 0.9858)	0.9539 (0.9056 to 0.9777)
4 Months	0.9518 (0.9016 to 0.9768)	0.9334 (0.8796 to 0.9636)
6 Months	0.9444 (0.8917 to 0.9718)	0.9259 (0.8701 to 0.9583)
8 Months	0.9444 (0.8917 to 0.9718)	0.9259 (0.8701 to 0.9583)
10 Months	0.9444 (0.8917 to 0.9718)	0.9091 (0.8480 to 0.9463)
12 Months	0.9444 (0.8917 to 0.9718)	0.9091 (0.8480 to 0.9463)
14 Months	0.9444 (0.8917 to 0.9718)	0.9000 (0.8361 to 0.9398)
16 Months	0.9444 (0.8917 to 0.9718)	0.9000 (0.8361 to 0.9398)
18 Months	0.9444 (0.8917 to 0.9718)	0.9000 (0.8361 to 0.9398)
20 Months	0.9444 (0.8917 to 0.9718)	0.8890 (0.8210 to 0.9322)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
22 Months	0.9444 (0.8917 to 0.9718)	0.8890 (0.8210 to 0.9322)
24 Months	0.9444 (0.8917 to 0.9718)	0.8890 (0.8210 to 0.9322)
26 Months	0.9444 (0.8917 to 0.9718)	0.8890 (0.8210 to 0.9322)
Number of patients at risk[c]		
2 Months	138	143
4 Months	130	133
6 Months	112	120
8 Months	102	115
10 Months	99	106
12 Months	90	100
14 Months	85	98
16 Months	78	89
18 Months	71	83
20 Months	67	80
22 Months	65	72
24 Months	64	69
26 Months	62	63
Musculoskeletal and connective tissue disorders (days)		

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of events	8 (5.4)	14 (9.2)
Number (%) of patients censored	141 (94.6)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2793
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.6102 (0.6739 to 3.8478)
P-value	-	0.2838
Events probability (95% CI)[c]		
2 Months	0.9523 (0.9025 to 0.9770)	0.9669 (0.9224 to 0.9861)
4 Months	0.9523 (0.9025 to 0.9770)	0.9602 (0.9136 to 0.9819)
6 Months	0.9523 (0.9025 to 0.9770)	0.9459 (0.8946 to 0.9726)
8 Months	0.9434 (0.8895 to 0.9714)	0.9459 (0.8946 to 0.9726)
10 Months	0.9434 (0.8895 to 0.9714)	0.9377 (0.8835 to 0.9672)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	0.9434 (0.8895 to 0.9714)	0.9292 (0.8719 to 0.9614)
14 Months	0.9434 (0.8895 to 0.9714)	0.9292 (0.8719 to 0.9614)
16 Months	0.9434 (0.8895 to 0.9714)	0.9107 (0.8471 to 0.9486)
18 Months	0.9434 (0.8895 to 0.9714)	0.9107 (0.8471 to 0.9486)
20 Months	0.9434 (0.8895 to 0.9714)	0.9107 (0.8471 to 0.9486)
22 Months	0.9434 (0.8895 to 0.9714)	0.9107 (0.8471 to 0.9486)
24 Months	0.9434 (0.8895 to 0.9714)	0.8987 (0.8298 to 0.9407)
26 Months	0.9434 (0.8895 to 0.9714)	0.8853 (0.8104 to 0.9318)
Number of patients at risk[c]		
2 Months	137	145
4 Months	129	136
6 Months	113	123
8 Months	101	122
10 Months	97	114
12 Months	90	106
14 Months	85	105
16 Months	79	94
18 Months	72	88
20 Months	68	84

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
22 Months	66	76
24 Months	65	72
26 Months	62	65
Nervous system disorders (days)		
Number (%) of events	9 (6.0)	14 (9.2)
Number (%) of patients censored	140 (94.0)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3411
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.4983 (0.6481 to 3.4638)
P-value	-	0.3443
Events probability (95% CI)[c]		

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	0.9592 (0.9115 to 0.9815)	0.9603 (0.9137 to 0.9819)
4 Months	0.9518 (0.9015 to 0.9767)	0.9397 (0.8872 to 0.9682)
6 Months	0.9443 (0.8916 to 0.9718)	0.9397 (0.8872 to 0.9682)
8 Months	0.9443 (0.8916 to 0.9718)	0.9237 (0.8661 to 0.9571)
10 Months	0.9443 (0.8916 to 0.9718)	0.9237 (0.8661 to 0.9571)
12 Months	0.9339 (0.8758 to 0.9654)	0.9147 (0.8541 to 0.9509)
14 Months	0.9339 (0.8758 to 0.9654)	0.9147 (0.8541 to 0.9509)
16 Months	0.9339 (0.8758 to 0.9654)	0.9147 (0.8541 to 0.9509)
18 Months	0.9339 (0.8758 to 0.9654)	0.9147 (0.8541 to 0.9509)
20 Months	0.9339 (0.8758 to 0.9654)	0.9147 (0.8541 to 0.9509)
22 Months	0.9339 (0.8758 to 0.9654)	0.9025 (0.8359 to 0.9430)
24 Months	0.9339 (0.8758 to 0.9654)	0.9025 (0.8359 to 0.9430)
26 Months	0.9339 (0.8758 to 0.9654)	0.9025 (0.8359 to 0.9430)
Number of patients at risk[c]		
2 Months	137	143
4 Months	128	132
6 Months	112	119
8 Months	101	113
10 Months	97	107

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	87	99
14 Months	82	98
16 Months	75	89
18 Months	67	82
20 Months	63	78
22 Months	61	70
24 Months	60	68
26 Months	57	62
Renal and urinary disorders (days)		
Number (%) of events	12 (8.1)	10 (6.6)
Number (%) of patients censored	137 (91.9)	142 (93.4)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4553

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.7268 (0.3134 to 1.6854)
P-value	-	0.4571
Events probability (95% CI)[c]		
2 Months	0.9381 (0.8844 to 0.9673)	0.9802 (0.9398 to 0.9936)
4 Months	0.9310 (0.8756 to 0.9623)	0.9734 (0.9307 to 0.9899)
6 Months	0.9229 (0.8650 to 0.9566)	0.9659 (0.9200 to 0.9857)
8 Months	0.9229 (0.8650 to 0.9566)	0.9659 (0.9200 to 0.9857)
10 Months	0.9229 (0.8650 to 0.9566)	0.9495 (0.8966 to 0.9757)
12 Months	0.9130 (0.8512 to 0.9499)	0.9410 (0.8849 to 0.9702)
14 Months	0.9130 (0.8512 to 0.9499)	0.9319 (0.8725 to 0.9642)
16 Months	0.9130 (0.8512 to 0.9499)	0.9319 (0.8725 to 0.9642)
18 Months	0.9130 (0.8512 to 0.9499)	0.9218 (0.8584 to 0.9575)
20 Months	0.9130 (0.8512 to 0.9499)	0.9218 (0.8584 to 0.9575)
22 Months	0.9130 (0.8512 to 0.9499)	0.9218 (0.8584 to 0.9575)
24 Months	0.9130 (0.8512 to 0.9499)	0.9218 (0.8584 to 0.9575)
26 Months	0.9130 (0.8512 to 0.9499)	0.9218 (0.8584 to 0.9575)
Number of patients at risk[c]		

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	134	147
4 Months	127	138
6 Months	113	126
8 Months	102	121
10 Months	99	112
12 Months	90	105
14 Months	85	103
16 Months	78	93
18 Months	70	86
20 Months	67	83
22 Months	65	76
24 Months	64	73
26 Months	61	67
Respiratory, thoracic and mediastinal disorders (days)		
Number (%) of events	11 (7.4)	14 (9.2)
Number (%) of patients censored	138 (92.6)	138 (90.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6539
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.1981 (0.5431 to 2.6433)
P-value	-	0.6543
Events probability (95% CI)[c]		
2 Months	0.9797 (0.9383 to 0.9934)	0.9603 (0.9138 to 0.9820)
4 Months	0.9797 (0.9383 to 0.9934)	0.9463 (0.8955 to 0.9728)
6 Months	0.9636 (0.9143 to 0.9847)	0.9388 (0.8855 to 0.9677)
8 Months	0.9546 (0.9010 to 0.9795)	0.9148 (0.8545 to 0.9509)
10 Months	0.9356 (0.8743 to 0.9675)	0.9065 (0.8439 to 0.9448)
12 Months	0.9356 (0.8743 to 0.9675)	0.8975 (0.8324 to 0.9383)
14 Months	0.9141 (0.8445 to 0.9534)	0.8975 (0.8324 to 0.9383)
16 Months	0.9141 (0.8445 to 0.9534)	0.8975 (0.8324 to 0.9383)
18 Months	0.9141 (0.8445 to 0.9534)	0.8975 (0.8324 to 0.9383)
20 Months	0.9141 (0.8445 to 0.9534)	0.8975 (0.8324 to 0.9383)

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.11 Treatment emergent severe adverse event including death according to SOC by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
22 Months	0.9141 (0.8445 to 0.9534)	0.8975 (0.8324 to 0.9383)
24 Months	0.9141 (0.8445 to 0.9534)	0.8975 (0.8324 to 0.9383)
26 Months	0.9141 (0.8445 to 0.9534)	0.8975 (0.8324 to 0.9383)
Number of patients at risk[c]		
2 Months	140	143
4 Months	132	133
6 Months	113	121
8 Months	102	113
10 Months	96	105
12 Months	87	97
14 Months	80	96
16 Months	74	87
18 Months	67	80
20 Months	63	76
22 Months	61	69
24 Months	60	66
26 Months	58	61

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345soc_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.12 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Disease progression (days)		
Number (%) of events	9 (6.0)	9 (5.9)
Number (%) of patients censored	140 (94.0)	143 (94.1)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8052
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.8898 (0.3523 to 2.2476)
P-value	-	0.8049
Events probability (95% CI)[c]		
2 Months	0.9794 (0.9375 to 0.9933)	0.9735 (0.9308 to 0.9900)
4 Months	0.9505 (0.8990 to 0.9761)	0.9668 (0.9221 to 0.9860)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.12 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
6 Months	0.9431 (0.8894 to 0.9712)	0.9528 (0.9035 to 0.9772)
8 Months	0.9431 (0.8894 to 0.9712)	0.9452 (0.8932 to 0.9722)
10 Months	0.9431 (0.8894 to 0.9712)	0.9452 (0.8932 to 0.9722)
12 Months	0.9431 (0.8894 to 0.9712)	0.9452 (0.8932 to 0.9722)
14 Months	0.9431 (0.8894 to 0.9712)	0.9452 (0.8932 to 0.9722)
16 Months	0.9431 (0.8894 to 0.9712)	0.9452 (0.8932 to 0.9722)
18 Months	0.9431 (0.8894 to 0.9712)	0.9452 (0.8932 to 0.9722)
20 Months	0.9431 (0.8894 to 0.9712)	0.9345 (0.8767 to 0.9658)
22 Months	0.9431 (0.8894 to 0.9712)	0.9345 (0.8767 to 0.9658)
24 Months	0.9431 (0.8894 to 0.9712)	0.9345 (0.8767 to 0.9658)
26 Months	0.9286 (0.8633 to 0.9633)	0.9345 (0.8767 to 0.9658)
Number of patients at risk[c]		
2 Months	140	146
4 Months	129	140
6 Months	115	127
8 Months	104	123
10 Months	100	116
12 Months	91	109
14 Months	87	108

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.12 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
16 Months	80	98
18 Months	72	91
20 Months	68	87
22 Months	66	78
24 Months	65	75
26 Months	61	69
Febrile neutropenia (days)		
Number (%) of events	5 (3.4)	18 (11.8)
Number (%) of patients censored	144 (96.6)	134 (88.2)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0059
Stratified[a] Hazard ratio (95% CI) vs Pd	-	3.6697 (1.3622 to 9.8861)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.12 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
P-value	-	0.0101
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.2725 (0.1012 to 0.7341)	-
Events probability (95% CI)[c]		
2 Months	0.9860 (0.9452 to 0.9965)	0.9073 (0.8485 to 0.9440)
4 Months	0.9860 (0.9452 to 0.9965)	0.9005 (0.8404 to 0.9388)
6 Months	0.9860 (0.9452 to 0.9965)	0.8865 (0.8238 to 0.9279)
8 Months	0.9860 (0.9452 to 0.9965)	0.8865 (0.8238 to 0.9279)
10 Months	0.9763 (0.9270 to 0.9924)	0.8865 (0.8238 to 0.9279)
12 Months	0.9763 (0.9270 to 0.9924)	0.8777 (0.8126 to 0.9213)
14 Months	0.9653 (0.9083 to 0.9871)	0.8777 (0.8126 to 0.9213)
16 Months	0.9653 (0.9083 to 0.9871)	0.8777 (0.8126 to 0.9213)
18 Months	0.9653 (0.9083 to 0.9871)	0.8777 (0.8126 to 0.9213)
20 Months	0.9511 (0.8826 to 0.9801)	0.8777 (0.8126 to 0.9213)
22 Months	0.9511 (0.8826 to 0.9801)	0.8777 (0.8126 to 0.9213)
24 Months	0.9511 (0.8826 to 0.9801)	0.8777 (0.8126 to 0.9213)
26 Months	0.9511 (0.8826 to 0.9801)	0.8777 (0.8126 to 0.9213)
Number of patients at risk[c]		
2 Months	140	135

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.12 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
4 Months	132	129
6 Months	116	114
8 Months	105	110
10 Months	100	107
12 Months	92	99
14 Months	85	98
16 Months	78	89
18 Months	70	83
20 Months	66	79
22 Months	64	71
24 Months	63	68
26 Months	60	63
Lower respiratory tract infection (days)		
Number (%) of events	4 (2.7)	8 (5.3)
Number (%) of patients censored	145 (97.3)	144 (94.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.12 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4848
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5317 (0.4590 to 5.1112)
P-value	-	0.4880
Events probability (95% CI)[c]		
2 Months	0.9932 (0.9530 to 0.9990)	0.9934 (0.9539 to 0.9991)
4 Months	0.9860 (0.9451 to 0.9965)	0.9863 (0.9462 to 0.9966)
6 Months	0.9775 (0.9315 to 0.9927)	0.9863 (0.9462 to 0.9966)
8 Months	0.9684 (0.9175 to 0.9881)	0.9863 (0.9462 to 0.9966)
10 Months	0.9684 (0.9175 to 0.9881)	0.9613 (0.9092 to 0.9838)
12 Months	0.9684 (0.9175 to 0.9881)	0.9613 (0.9092 to 0.9838)
14 Months	0.9684 (0.9175 to 0.9881)	0.9613 (0.9092 to 0.9838)
16 Months	0.9684 (0.9175 to 0.9881)	0.9613 (0.9092 to 0.9838)
18 Months	0.9684 (0.9175 to 0.9881)	0.9510 (0.8932 to 0.9779)
20 Months	0.9684 (0.9175 to 0.9881)	0.9287 (0.8607 to 0.9642)
22 Months	0.9684 (0.9175 to 0.9881)	0.9287 (0.8607 to 0.9642)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.12 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
24 Months	0.9684 (0.9175 to 0.9881)	0.9287 (0.8607 to 0.9642)
26 Months	0.9684 (0.9175 to 0.9881)	0.9287 (0.8607 to 0.9642)
Number of patients at risk[c]		
2 Months	141	148
4 Months	132	139
6 Months	114	127
8 Months	102	122
10 Months	99	112
12 Months	90	106
14 Months	84	105
16 Months	78	95
18 Months	70	87
20 Months	66	82
22 Months	64	73
24 Months	63	70
26 Months	60	64
Neutropenia (days)		
Number (%) of events	52 (34.9)	76 (50.0)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.12 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Number (%) of patients censored	97 (65.1)	76 (50.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	1.9384 (0.9856 to 4.6653)	0.8542 (0.7556 to 0.9856)
Median (95% CI)	NC (NC to NC)	21.9138 (2.8912 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0121
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5664 (1.1002 to 2.2302)
P-value	-	0.0128
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6384 (0.4484 to 0.9089)	-
Events probability (95% CI)[c]		
2 Months	0.7463 (0.6674 to 0.8092)	0.6157 (0.5331 to 0.6880)
4 Months	0.6958 (0.6136 to 0.7639)	0.5749 (0.4919 to 0.6494)
6 Months	0.6639 (0.5795 to 0.7352)	0.5749 (0.4919 to 0.6494)
8 Months	0.6549 (0.5698 to 0.7273)	0.5585 (0.4748 to 0.6341)
10 Months	0.6549 (0.5698 to 0.7273)	0.5399 (0.4551 to 0.6171)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.12 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	0.6549 (0.5698 to 0.7273)	0.5304 (0.4452 to 0.6085)
14 Months	0.6549 (0.5698 to 0.7273)	0.5206 (0.4348 to 0.5995)
16 Months	0.6549 (0.5698 to 0.7273)	0.5206 (0.4348 to 0.5995)
18 Months	0.6418 (0.5543 to 0.7166)	0.5097 (0.4232 to 0.5897)
20 Months	0.6418 (0.5543 to 0.7166)	0.5097 (0.4232 to 0.5897)
22 Months	0.6272 (0.5367 to 0.7050)	0.4970 (0.4092 to 0.5787)
24 Months	0.6272 (0.5367 to 0.7050)	0.4570 (0.3656 to 0.5436)
26 Months	0.6272 (0.5367 to 0.7050)	0.4570 (0.3656 to 0.5436)
Number of patients at risk[c]		
2 Months	108	92
4 Months	93	81
6 Months	80	71
8 Months	71	66
10 Months	69	57
12 Months	64	54
14 Months	58	53
16 Months	53	51
18 Months	48	46
20 Months	45	46

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.12 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
22 Months	43	39
24 Months	42	33
26 Months	39	30
Pneumonia (days)		
Number (%) of events	31 (20.8)	35 (23.0)
Number (%) of patients censored	118 (79.2)	117 (77.0)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	29.5688 (7.0308 to NC)	24.5749 (8.6078 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8720
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0406 (0.6410 to 1.6894)
P-value	-	0.8721
Events probability (95% CI)[c]		

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.12 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	0.9042 (0.8435 to 0.9421)	0.9207 (0.8646 to 0.9542)
4 Months	0.8536 (0.7842 to 0.9020)	0.8866 (0.8238 to 0.9279)
6 Months	0.8299 (0.7567 to 0.8828)	0.8496 (0.7804 to 0.8984)
8 Months	0.8214 (0.7467 to 0.8758)	0.8262 (0.7533 to 0.8793)
10 Months	0.8214 (0.7467 to 0.8758)	0.8181 (0.7440 to 0.8726)
12 Months	0.8214 (0.7467 to 0.8758)	0.8009 (0.7240 to 0.8584)
14 Months	0.8111 (0.7341 to 0.8677)	0.8009 (0.7240 to 0.8584)
16 Months	0.8000 (0.7204 to 0.8591)	0.8009 (0.7240 to 0.8584)
18 Months	0.8000 (0.7204 to 0.8591)	0.7909 (0.7121 to 0.8504)
20 Months	0.7866 (0.7032 to 0.8491)	0.7698 (0.6870 to 0.8333)
22 Months	0.7723 (0.6848 to 0.8384)	0.7588 (0.6740 to 0.8244)
24 Months	0.7723 (0.6848 to 0.8384)	0.7588 (0.6740 to 0.8244)
26 Months	0.7578 (0.6664 to 0.8273)	0.7324 (0.6417 to 0.8036)
Number of patients at risk[c]		
2 Months	129	137
4 Months	115	126
6 Months	102	110
8 Months	92	104
10 Months	90	99

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.12 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
12 Months	83	92
14 Months	77	91
16 Months	69	83
18 Months	62	76
20 Months	57	70
22 Months	54	62
24 Months	53	59
26 Months	50	52
Thrombocytopenia (days)		
Number (%) of events	18 (12.1)	20 (13.2)
Number (%) of patients censored	131 (87.9)	132 (86.8)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8814

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.12 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0497 (0.5550 to 1.9852)
P-value	-	0.8815
Events probability (95% CI)[c]		
2 Months	0.8904 (0.8273 to 0.9314)	0.9009 (0.8409 to 0.9390)
4 Months	0.8904 (0.8273 to 0.9314)	0.8873 (0.8250 to 0.9284)
6 Months	0.8756 (0.8097 to 0.9198)	0.8873 (0.8250 to 0.9284)
8 Months	0.8756 (0.8097 to 0.9198)	0.8795 (0.8155 to 0.9224)
10 Months	0.8756 (0.8097 to 0.9198)	0.8795 (0.8155 to 0.9224)
12 Months	0.8756 (0.8097 to 0.9198)	0.8795 (0.8155 to 0.9224)
14 Months	0.8756 (0.8097 to 0.9198)	0.8795 (0.8155 to 0.9224)
16 Months	0.8756 (0.8097 to 0.9198)	0.8698 (0.8027 to 0.9152)
18 Months	0.8756 (0.8097 to 0.9198)	0.8698 (0.8027 to 0.9152)
20 Months	0.8756 (0.8097 to 0.9198)	0.8698 (0.8027 to 0.9152)
22 Months	0.8756 (0.8097 to 0.9198)	0.8698 (0.8027 to 0.9152)
24 Months	0.8756 (0.8097 to 0.9198)	0.8698 (0.8027 to 0.9152)
26 Months	0.8756 (0.8097 to 0.9198)	0.8698 (0.8027 to 0.9152)
Number of patients at risk[c]		

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.12 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
2 Months	127	135
4 Months	121	126
6 Months	109	115
8 Months	100	110
10 Months	96	103
12 Months	88	98
14 Months	82	97
16 Months	75	89
18 Months	68	82
20 Months	65	78
22 Months	63	72
24 Months	62	69
26 Months	60	64
Urinary tract infection (days)		
Number (%) of events	2 (1.3)	8 (5.3)
Number (%) of patients censored	147 (98.7)	144 (94.7)
Kaplan-Meier estimates of Events in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.12 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Pd		
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0702
Stratified[a] Hazard ratio (95% CI) vs Pd	-	3.7877 (0.8037 to 17.8493)
P-value	-	0.0922
Events probability (95% CI)[c]		
2 Months	1.0000 (1.0000 to 1.0000)	0.9801 (0.9397 to 0.9935)
4 Months	0.9925 (0.9482 to 0.9989)	0.9667 (0.9217 to 0.9860)
6 Months	0.9925 (0.9482 to 0.9989)	0.9592 (0.9114 to 0.9815)
8 Months	0.9836 (0.9356 to 0.9959)	0.9592 (0.9114 to 0.9815)
10 Months	0.9836 (0.9356 to 0.9959)	0.9592 (0.9114 to 0.9815)
12 Months	0.9836 (0.9356 to 0.9959)	0.9592 (0.9114 to 0.9815)
14 Months	0.9836 (0.9356 to 0.9959)	0.9592 (0.9114 to 0.9815)
16 Months	0.9836 (0.9356 to 0.9959)	0.9592 (0.9114 to 0.9815)
18 Months	0.9836 (0.9356 to 0.9959)	0.9489 (0.8946 to 0.9756)
20 Months	0.9836 (0.9356 to 0.9959)	0.9489 (0.8946 to 0.9756)

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.39 Analysis according to SOC/PT
16.2.7.1.39.12 Treatment emergent severe adverse event including death according to PT by treatment group - Safety population

	Pd (N=149)	**IPd (N=152)**
22 Months	0.9836 (0.9356 to 0.9959)	0.9489 (0.8946 to 0.9756)
24 Months	0.9836 (0.9356 to 0.9959)	0.9489 (0.8946 to 0.9756)
26 Months	0.9836 (0.9356 to 0.9959)	0.9345 (0.8687 to 0.9680)
Number of patients at risk[c]		
2 Months	142	147
4 Months	133	138
6 Months	117	125
8 Months	105	121
10 Months	101	114
12 Months	93	107
14 Months	87	106
16 Months	80	96
18 Months	72	88
20 Months	68	84
22 Months	66	75
24 Months	65	72
26 Months	62	65

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_de_sevae345pt_s_t_x.rtf (16NOV2020 12:58)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
Age	SOC :Blood and lymphatic system disorders	0.5840	0.1804	0.9210	0.5875	NC	1.0000
	SOC :Cardiac disorders	0.7673	0.9874	0.6646	0.9134	NC	1.0000
	SOC :Eye disorders	0.7233	NC	0.9326	NC	NC	1.0000
	SOC :Gastrointestinal disorders	0.8787	0.7110	0.7103	0.6790	NC	NC
	SOC :General disorders and administration site conditions	0.5332	0.6644	0.4853	0.2592	NC	0.8250
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	1.0000
	SOC :Infections and infestations	0.3928	0.6559	0.4556	0.5099	NC	0.7510
	SOC :Injury, poisoning and procedural complications	0.0678	0.9257	0.1604	1.0000	NC	NC
	SOC :Investigations	0.1816	NC	0.2228	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.6131	0.9780	0.9540	0.3313	NC	NC
	SOC :Musculoskeletal and connective tissue disorders	0.9710	0.5157	0.9760	0.2169	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.7292	NC	NC	NC	NC	1.0000
	SOC :Nervous system disorders	0.6029	1.0000	0.6673	0.4041	NC	1.0000
	SOC :Psychiatric disorders	0.2086	NC	0.4066	NC	NC	NC
	SOC :Renal and urinary disorders	0.2933	0.8833	0.1905	0.4141	NC	NC
	SOC :Reproductive system and breast disorders	0.3856	NC	0.4528	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_soc_sr_l_x.rtf (10NOV2020 10:55)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
Number of previous lines of therapy (IRT)	SOC :Respiratory, thoracic and mediastinal disorders	0.6965	0.5829	0.6922	0.7749	NC	NC
	SOC :Skin and subcutaneous tissue disorders	0.0534	NC	0.0425	NC	NC	1.0000
	SOC :Vascular disorders	0.4413	NC	0.4859	NC	NC	NC
	SOC :Blood and lymphatic system disorders	0.1745	0.3800	0.2889	0.1733	NC	0.9938
	SOC :Cardiac disorders	0.4837	0.4712	0.5185	0.9906	NC	1.0000
	SOC :Eye disorders	0.6844	NC	0.4763	NC	NC	0.9993
	SOC :Gastrointestinal disorders	0.3816	0.4886	0.4220	0.9589	NC	NC
	SOC :General disorders and administration site conditions	0.7276	0.1249	0.3753	0.0161	NC	0.9708
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	0.9994
	SOC :Infections and infestations	0.2820	0.1850	0.3090	0.3798	NC	0.0583
	SOC :Injury, poisoning and procedural complications	0.4437	0.2731	0.8895	0.9945	NC	NC
	SOC :Investigations	0.4008	NC	0.6083	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.9315	0.2488	0.6258	0.3222	NC	NC
	SOC :Musculoskeletal and connective tissue disorders	0.5349	0.9696	0.2395	0.1659	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.7171	NC	NC	NC	NC	0.9999
	SOC :Nervous system disorders	0.7227	0.7976	0.3588	0.5726	NC	0.9963

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
	SOC :Psychiatric disorders	0.9544	NC	0.9634	NC	NC	NC
	SOC :Renal and urinary disorders	0.3959	0.2347	0.7629	0.2225	NC	NC
	SOC :Reproductive system and breast disorders	0.5737	NC	0.6789	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.0408	0.2029	0.1968	0.1629	NC	NC
	SOC :Skin and subcutaneous tissue disorders	0.2681	NC	0.2137	NC	NC	0.9991
	SOC :Vascular disorders	0.4854	NC	0.5172	NC	NC	NC
Gender	SOC :Blood and lymphatic system disorders	0.7973	0.7855	0.6381	0.8359	NC	0.9951
	SOC :Cardiac disorders	0.3704	0.9922	0.9939	0.9922	NC	1.0000
	SOC :Eye disorders	0.5532	NC	0.8062	NC	NC	0.9992
	SOC :Gastrointestinal disorders	0.4819	0.9937	0.5435	0.4937	NC	NC
	SOC :General disorders and administration site conditions	0.0649	0.7490	0.0911	0.9248	NC	0.8046
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	0.9991
	SOC :Infections and infestations	0.0728	0.7779	0.0172	0.8601	NC	0.2405
	SOC :Injury, poisoning and procedural complications	0.6797	0.9932	0.5291	0.9926	NC	NC
	SOC :Investigations	0.2648	NC	0.4393	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.9869	0.9591	0.8962	0.8216	NC	NC
	SOC :Musculoskeletal and connective tissue disorders	0.0079	0.1238	0.0118	0.0245	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_soc_sr_l_x.rtf (10NOV2020 10:55)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.6799	NC	NC	NC	NC	0.9989
	SOC :Nervous system disorders	0.2164	0.7070	0.1470	0.5036	NC	0.9967
	SOC :Psychiatric disorders	0.0490	NC	0.0275	NC	NC	NC
	SOC :Renal and urinary disorders	0.9402	0.4939	0.9868	0.2459	NC	NC
	SOC :Reproductive system and breast disorders	0.2025	NC	0.1321	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.5502	0.8039	0.4286	0.7505	NC	NC
	SOC :Skin and subcutaneous tissue disorders	0.0369	NC	0.0438	NC	NC	0.9993
	SOC :Vascular disorders	0.4314	NC	0.8415	NC	NC	NC
Race	SOC :Blood and lymphatic system disorders	0.0612	0.9904	0.9922	0.0837	NC	0.9997
	SOC :Cardiac disorders	0.8057	0.5903	0.9987	0.4313	NC	1.0000
	SOC :Eye disorders	0.6544	NC	0.9342	NC	NC	0.9993
	SOC :Gastrointestinal disorders	0.4263	0.9934	0.4673	0.4851	NC	NC
	SOC :General disorders and administration site conditions	0.2911	0.9896	0.2835	0.2327	NC	0.9957
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	0.9994
	SOC :Infections and infestations	0.1866	0.2789	0.1864	0.2941	NC	0.9930
	SOC :Injury, poisoning and procedural complications	0.1492	0.9908	0.1853	0.9932	NC	NC
	SOC :Investigations	0.9086	NC	0.5833	NC	NC	NC

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
	SOC :Metabolism and nutrition disorders	0.9230	0.9879	0.9203	0.4635	NC	NC
	SOC :Musculoskeletal and connective tissue disorders	0.5345	0.9929	0.6901	0.9888	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.9936	NC	NC	NC	NC	0.9999
	SOC :Nervous system disorders	0.3293	0.9931	0.6891	0.6622	NC	0.9999
	SOC :Psychiatric disorders	0.8856	NC	0.7595	NC	NC	NC
	SOC :Renal and urinary disorders	0.1904	0.9924	0.1895	0.5158	NC	NC
	SOC :Reproductive system and breast disorders	0.9924	NC	0.9926	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.7873	0.9925	0.5997	0.7725	NC	NC
	SOC :Skin and subcutaneous tissue disorders	0.5692	NC	0.5326	NC	NC	0.9994
	SOC :Vascular disorders	0.9881	NC	0.9895	NC	NC	NC
Ethnicity	SOC :Blood and lymphatic system disorders	0.8967	0.9890	0.9897	0.9828	NC	0.9996
	SOC :Cardiac disorders	0.9994	0.9998	0.9995	0.9997	NC	NC
	SOC :Eye disorders	0.3272	NC	0.3632	NC	NC	NC
	SOC :Gastrointestinal disorders	0.9927	0.9998	0.9967	0.9999	NC	NC
	SOC :General disorders and administration site conditions	0.0379	0.3173	0.9359	0.9895	NC	0.9928
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	0.9998
	SOC :Infections and infestations	0.6316	0.9495	0.5059	0.5195	NC	0.9892

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
	SOC :Injury, poisoning and procedural complications	0.3183	0.9930	0.2950	0.9942	NC	NC
	SOC :Investigations	0.9901	NC	0.9912	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.9855	1.0000	0.9904	0.9999	NC	NC
	SOC :Musculoskeletal and connective tissue disorders	0.9341	0.9997	0.9827	0.9889	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.9940	NC	NC	NC	NC	0.9998
	SOC :Nervous system disorders	0.0375	0.9998	0.0555	0.9890	NC	0.9999
	SOC :Psychiatric disorders	1.0000	NC	1.0000	NC	NC	NC
	SOC :Renal and urinary disorders	0.9872	0.9998	0.9896	1.0000	NC	NC
	SOC :Reproductive system and breast disorders	0.9999	NC	0.9999	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.9032	0.9905	0.8004	0.9999	NC	NC
	SOC :Skin and subcutaneous tissue disorders	0.5861	NC	0.6028	NC	NC	0.9997
	SOC :Vascular disorders	0.9878	NC	0.9890	NC	NC	NC
Geographical region	SOC :Blood and lymphatic system disorders	0.6386	0.8115	0.9056	0.6884	NC	1.0000
	SOC :Cardiac disorders	0.7868	0.8139	0.8351	0.9566	NC	1.0000
	SOC :Eye disorders	0.6476	NC	0.4964	NC	NC	1.0000
	SOC :Gastrointestinal disorders	0.7452	1.0000	0.7915	0.9981	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_soc_sr_l_x.rtf (10NOV2020 10:55)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
	SOC :General disorders and administration site conditions	0.7581	0.9778	0.4646	0.8878	NC	1.0000
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	1.0000
	SOC :Infections and infestations	0.1960	0.7735	0.2296	0.7935	NC	0.9978
	SOC :Injury, poisoning and procedural complications	0.5445	1.0000	0.7275	1.0000	NC	NC
	SOC :Investigations	0.9859	NC	0.9699	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.9410	0.9955	0.9920	0.9993	NC	NC
	SOC :Musculoskeletal and connective tissue disorders	0.1173	0.8824	0.2074	0.9603	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.9934	NC	NC	NC	NC	1.0000
	SOC :Nervous system disorders	0.3217	0.6481	0.3690	0.7525	NC	1.0000
	SOC :Psychiatric disorders	0.9686	NC	0.9885	NC	NC	NC
	SOC :Renal and urinary disorders	0.6867	1.0000	0.8887	0.9977	NC	NC
	SOC :Reproductive system and breast disorders	1.0000	NC	1.0000	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.5328	0.9889	0.4312	0.9111	NC	NC
	SOC :Skin and subcutaneous tissue disorders	0.5587	NC	0.4577	NC	NC	1.0000
	SOC :Vascular disorders	0.5803	NC	0.8382	NC	NC	NC
Regulatory region	SOC :Blood and lymphatic system disorders	0.2063	0.4094	0.9897	0.1991	NC	0.9949

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
SOC :Cardiac disorders	0.5572	0.6377	0.9395	0.6559	NC	1.0000
SOC :Eye disorders	0.9541	NC	0.7165	NC	NC	0.9994
SOC :Gastrointestinal disorders	0.1412	0.9925	0.2627	0.9867	NC	NC
SOC :General disorders and administration site conditions	0.8423	0.7043	0.5026	0.2865	NC	0.9934
SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	0.9994
SOC :Infections and infestations	0.2090	0.3667	0.7866	0.4979	NC	0.2501
SOC :Injury, poisoning and procedural complications	0.8661	0.2493	0.6312	0.9940	NC	NC
SOC :Investigations	0.6085	NC	0.5525	NC	NC	NC
SOC :Metabolism and nutrition disorders	0.5106	0.2216	0.1940	0.6403	NC	NC
SOC :Musculoskeletal and connective tissue disorders	0.1178	0.3392	0.2117	0.8150	NC	NC
SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.9903	NC	NC	NC	NC	1.0000
SOC :Nervous system disorders	0.6378	0.0642	0.8915	0.2895	NC	0.9966
SOC :Psychiatric disorders	0.6472	NC	0.8124	NC	NC	NC
SOC :Renal and urinary disorders	0.1002	0.9917	0.4882	0.1654	NC	NC
SOC :Reproductive system and breast disorders	0.9919	NC	0.9929	NC	NC	NC
SOC :Respiratory, thoracic and mediastinal disorders	0.5626	0.5702	0.8289	0.5943	NC	NC

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
	SOC :Skin and subcutaneous tissue disorders	0.3702	NC	0.3124	NC	NC	0.9994
	SOC :Vascular disorders	0.1701	NC	0.4642	NC	NC	NC
ECOG PS	SOC :Blood and lymphatic system disorders	0.4474	0.3045	0.9900	0.3622	NC	0.9947
	SOC :Cardiac disorders	0.9881	0.9929	0.9896	0.9930	NC	1.0000
	SOC :Eye disorders	0.4425	NC	0.7513	NC	NC	0.9995
	SOC :Gastrointestinal disorders	0.8427	0.9934	0.7985	0.9904	NC	NC
	SOC :General disorders and administration site conditions	0.6108	0.8621	0.7935	0.9862	NC	0.9999
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	0.9995
	SOC :Infections and infestations	0.8035	0.0171	0.6119	0.3582	NC	0.2552
	SOC :Injury, poisoning and procedural complications	0.3112	0.9908	0.2520	0.9936	NC	NC
	SOC :Investigations	0.9880	NC	0.9886	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.5222	0.8168	0.7705	0.5926	NC	NC
	SOC :Musculoskeletal and connective tissue disorders	0.7727	0.9907	0.7049	0.6556	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.9928	NC	NC	NC	NC	0.9993
	SOC :Nervous system disorders	0.5393	0.2930	0.5600	0.3218	NC	0.9999
	SOC :Psychiatric disorders	0.3320	NC	0.1891	NC	NC	NC
	SOC :Renal and urinary disorders	0.1474	0.2170	0.2919	0.9176	NC	NC

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
ISS staging at study entry	SOC :Reproductive system and breast disorders	0.9908	NC	0.9931	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.3261	0.9906	0.2303	0.6766	NC	NC
	SOC :Skin and subcutaneous tissue disorders	0.2173	NC	0.2269	NC	NC	0.9995
	SOC :Vascular disorders	0.9846	NC	0.9864	NC	NC	NC
	SOC :Blood and lymphatic system disorders	0.9536	0.6124	0.5108	0.7578	NC	1.0000
	SOC :Cardiac disorders	0.9660	0.9710	0.9984	0.7690	NC	1.0000
	SOC :Eye disorders	0.3182	NC	0.3156	NC	NC	1.0000
	SOC :Gastrointestinal disorders	0.4648	0.5104	0.5123	0.4500	NC	NC
	SOC :General disorders and administration site conditions	0.2552	0.5709	0.4066	0.4966	NC	1.0000
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	1.0000
	SOC :Infections and infestations	0.8661	0.7913	0.8319	0.8382	NC	0.6122
	SOC :Injury, poisoning and procedural complications	0.2731	0.9244	0.1515	1.0000	NC	NC
	SOC :Investigations	0.6612	NC	0.6426	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.9803	0.6983	0.9807	0.7495	NC	NC
	SOC :Musculoskeletal and connective tissue disorders	0.3694	0.1832	0.5440	0.7553	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.7755	NC	NC	NC	NC	1.0000

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
	SOC :Nervous system disorders	0.1950	0.3825	0.3301	0.5767	NC	1.0000
	SOC :Psychiatric disorders	0.1227	NC	0.0449	NC	NC	NC
	SOC :Renal and urinary disorders	0.8385	0.9291	0.5437	0.9722	NC	NC
	SOC :Reproductive system and breast disorders	0.5756	NC	0.4325	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.0754	0.5285	0.1468	0.1472	NC	NC
	SOC :Skin and subcutaneous tissue disorders	0.3827	NC	0.3811	NC	NC	1.0000
	SOC :Vascular disorders	0.4435	NC	0.7310	NC	NC	NC
R-ISS staging	SOC :Blood and lymphatic system disorders	0.3502	0.7646	0.4800	0.2055	NC	1.0000
	SOC :Cardiac disorders	0.4984	0.7774	0.7569	0.9957	NC	1.0000
	SOC :Eye disorders	0.9839	NC	0.9214	NC	NC	1.0000
	SOC :Gastrointestinal disorders	0.3025	1.0000	0.3280	0.8211	NC	NC
	SOC :General disorders and administration site conditions	0.5095	0.7463	0.5186	0.8653	NC	1.0000
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	1.0000
	SOC :Infections and infestations	0.3670	0.2964	0.6339	0.5093	NC	1.0000
	SOC :Injury, poisoning and procedural complications	0.8645	0.9807	0.6342	1.0000	NC	NC
	SOC :Investigations	0.9198	NC	0.8872	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.5437	0.4472	0.9779	0.4572	NC	NC

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
	SOC :Musculoskeletal and connective tissue disorders	0.8518	0.6322	0.8599	0.9379	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.9585	NC	NC	NC	NC	1.0000
	SOC :Nervous system disorders	0.1133	0.5941	0.0776	0.6967	NC	1.0000
	SOC :Psychiatric disorders	0.1251	NC	0.1362	NC	NC	NC
	SOC :Renal and urinary disorders	0.2975	0.9978	0.1566	0.9999	NC	NC
	SOC :Reproductive system and breast disorders	0.8038	NC	0.8910	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.3067	0.8710	0.4451	0.9958	NC	NC
	SOC :Skin and subcutaneous tissue disorders	0.4713	NC	0.5081	NC	NC	1.0000
	SOC :Vascular disorders	0.3358	NC	0.9900	NC	NC	NC
Cytogenetic abnormality	SOC :Blood and lymphatic system disorders	0.7395	0.8867	0.7493	0.9474	NC	0.9954
	SOC :Cardiac disorders	0.9892	0.9999	0.9906	0.9999	NC	NC
	SOC :Eye disorders	0.9863	NC	0.9881	NC	NC	NC
	SOC :Gastrointestinal disorders	0.1848	0.9931	0.2746	0.9915	NC	NC
	SOC :General disorders and administration site conditions	0.0620	0.0606	0.0656	0.2797	NC	0.9945
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	0.9993
	SOC :Infections and infestations	0.9118	0.4553	0.9999	0.6623	NC	0.2567

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
	SOC :Injury, poisoning and procedural complications	0.5730	0.9169	0.5694	0.9927	NC	NC
	SOC :Investigations	0.9138	NC	0.9898	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.5575	0.5609	0.5711	0.7609	NC	NC
	SOC :Musculoskeletal and connective tissue disorders	0.6354	0.9916	0.5932	0.8561	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.9929	NC	NC	NC	NC	0.9993
	SOC :Nervous system disorders	0.7500	0.9932	0.7037	0.9582	NC	0.9986
	SOC :Psychiatric disorders	0.3926	NC	0.6536	NC	NC	NC
	SOC :Renal and urinary disorders	0.1911	0.1154	0.2987	0.9689	NC	NC
	SOC :Reproductive system and breast disorders	0.9920	NC	0.9921	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.0193	0.9900	0.0392	0.0808	NC	NC
	SOC :Skin and subcutaneous tissue disorders	0.8128	NC	0.7719	NC	NC	0.9993
	SOC :Vascular disorders	0.4610	NC	0.9767	NC	NC	NC
Cytogenetic abnormality del(17p)	SOC :Blood and lymphatic system disorders	0.2976	0.8145	0.6555	0.3785	NC	0.9951
	SOC :Cardiac disorders	0.9870	0.9999	0.9890	0.9999	NC	NC
	SOC :Eye disorders	0.9895	NC	0.9861	NC	NC	NC
	SOC :Gastrointestinal disorders	0.8862	0.9997	0.8537	0.9916	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_soc_sr_l_x.rtf (10NOV2020 10:55)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
	SOC :General disorders and administration site conditions	0.3171	0.2025	0.3340	0.7015	NC	0.9936
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	0.9995
	SOC :Infections and infestations	0.5826	0.5809	0.3839	0.2974	NC	0.2859
	SOC :Injury, poisoning and procedural complications	0.8129	0.9932	0.7891	0.9930	NC	NC
	SOC :Investigations	0.9932	NC	0.9919	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.9402	0.5398	0.4992	0.7860	NC	NC
	SOC :Musculoskeletal and connective tissue disorders	0.8004	0.9937	0.8700	0.4499	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.9939	NC	NC	NC	NC	0.9993
	SOC :Nervous system disorders	0.4411	0.9999	0.6010	0.4867	NC	1.0000
	SOC :Psychiatric disorders	0.1592	NC	0.2316	NC	NC	NC
	SOC :Renal and urinary disorders	0.7047	0.7013	0.6361	0.9910	NC	NC
	SOC :Reproductive system and breast disorders	0.9905	NC	0.9907	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.3043	0.9926	0.6011	0.9918	NC	NC
	SOC :Skin and subcutaneous tissue disorders	0.9322	NC	0.8990	NC	NC	0.9994
	SOC :Vascular disorders	0.1664	NC	0.5065	NC	NC	NC
Previous	SOC :Blood and lymphatic system disorders	0.5343	0.2843	0.4328	0.4883	NC	0.9923

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
autologous stem-cell transplantation	SOC :Cardiac disorders	0.2009	0.7010	0.2149	0.4921	NC	0.9967
	SOC :Eye disorders	0.8920	NC	0.2148	NC	NC	0.9992
	SOC :Gastrointestinal disorders	0.9998	0.1861	0.7401	0.2038	NC	NC
	SOC :General disorders and administration site conditions	0.5526	0.3436	0.3583	0.3261	NC	0.8458
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	0.9991
	SOC :Infections and infestations	0.7537	0.9899	0.7732	0.3293	NC	0.8348
	SOC :Injury, poisoning and procedural complications	0.8355	0.5982	0.4900	0.9947	NC	NC
	SOC :Investigations	0.8482	NC	0.7618	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.7090	0.7069	0.6932	0.3006	NC	NC
	SOC :Musculoskeletal and connective tissue disorders	0.0624	0.3324	0.0490	0.4151	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.5021	NC	NC	NC	NC	1.0000
	SOC :Nervous system disorders	0.5615	0.4791	0.6538	0.8269	NC	0.9965
	SOC :Psychiatric disorders	0.0445	NC	0.0762	NC	NC	NC
	SOC :Renal and urinary disorders	0.1982	0.7502	0.0668	0.7970	NC	NC
	SOC :Reproductive system and breast disorders	0.9896	NC	0.9898	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.4614	0.2210	0.4463	0.0915	NC	NC

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
Previous allogenic transplantation	SOC :Skin and subcutaneous tissue disorders	0.0400	NC	0.0508	NC	NC	0.9991
	SOC :Vascular disorders	0.0108	NC	0.0719	NC	NC	NC
	SOC :Blood and lymphatic system disorders	0.9808	0.9998	1.0000	0.9814	NC	0.9997
	SOC :Cardiac disorders	0.9994	0.9999	0.9994	0.9998	NC	1.0000
	SOC :Eye disorders	0.8859	NC	0.9072	NC	NC	0.9998
	SOC :Gastrointestinal disorders	0.5513	0.9998	0.5658	0.9998	NC	NC
	SOC :General disorders and administration site conditions	0.9790	0.9899	0.9804	0.9897	NC	0.9999
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	0.9998
	SOC :Infections and infestations	0.2755	0.8963	0.1595	0.7559	NC	1.0000
	SOC :Injury, poisoning and procedural complications	0.9837	0.9997	0.9844	0.9996	NC	NC
	SOC :Investigations	0.9898	NC	0.9875	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.9843	0.9999	0.9848	0.9998	NC	NC
	SOC :Musculoskeletal and connective tissue disorders	0.2785	0.9997	0.2694	0.9923	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.9998	NC	NC	NC	NC	0.9997
	SOC :Nervous system disorders	0.9769	0.9927	0.9781	0.9999	NC	0.9999
	SOC :Psychiatric disorders	0.9821	NC	0.9873	NC	NC	NC
	SOC :Renal and urinary disorders	0.9999	0.9999	1.0000	0.9999	NC	NC

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
	SOC :Reproductive system and breast disorders	0.9899	NC	0.9900	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.3023	1.0000	0.2467	0.9999	NC	NC
	SOC :Skin and subcutaneous tissue disorders	0.9798	NC	0.9799	NC	NC	0.9998
	SOC :Vascular disorders	0.9852	NC	0.9871	NC	NC	NC
MM type	SOC :Blood and lymphatic system disorders	0.7136	0.9867	0.5040	0.8959	NC	0.9937
	SOC :Cardiac disorders	0.4455	0.3970	0.3858	0.6184	NC	1.0000
	SOC :Eye disorders	0.5640	NC	0.7818	NC	NC	0.9993
	SOC :Gastrointestinal disorders	0.3992	0.7679	0.5247	0.8969	NC	NC
	SOC :General disorders and administration site conditions	0.3968	0.3954	0.3027	0.9114	NC	0.5687
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	0.9992
	SOC :Infections and infestations	0.0053	0.0447	0.0040	0.1314	NC	0.2428
	SOC :Injury, poisoning and procedural complications	0.0325	0.7482	0.0399	0.9932	NC	NC
	SOC :Investigations	0.7103	NC	0.8144	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.4809	0.9440	0.7333	0.1697	NC	NC
	SOC :Musculoskeletal and connective tissue disorders	0.1590	0.1514	0.3805	0.0669	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.6957	NC	NC	NC	NC	0.9989

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
Existing plasmacytoma	SOC :Nervous system disorders	0.1117	0.2875	0.1780	0.9880	NC	0.9999
	SOC :Psychiatric disorders	0.0313	NC	0.0250	NC	NC	NC
	SOC :Renal and urinary disorders	0.4428	0.7567	0.2222	0.4576	NC	NC
	SOC :Reproductive system and breast disorders	0.5459	NC	0.4594	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.0732	0.5488	0.0785	0.9725	NC	NC
	SOC :Skin and subcutaneous tissue disorders	0.7680	NC	0.7113	NC	NC	0.9992
	SOC :Vascular disorders	0.4586	NC	0.5493	NC	NC	NC
	SOC :Blood and lymphatic system disorders	0.8078	0.9450	0.7307	0.8969	NC	0.9997
	SOC :Cardiac disorders	0.9892	0.9999	0.9904	0.9998	NC	1.0000
	SOC :Eye disorders	0.9852	NC	1.0000	NC	NC	0.9996
	SOC :Gastrointestinal disorders	0.2286	0.9939	0.2517	0.9923	NC	NC
	SOC :General disorders and administration site conditions	0.4973	0.9867	0.5929	0.9887	NC	0.9950
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	0.9995
	SOC :Infections and infestations	0.4169	0.7346	0.1330	0.3979	NC	1.0000
	SOC :Injury, poisoning and procedural complications	0.5792	0.9929	0.7174	0.9948	NC	NC
	SOC :Investigations	0.9884	NC	0.9893	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.5618	0.9917	0.5944	0.9995	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_soc_sr_l_x.rtf (10NOV2020 10:55)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
	SOC :Musculoskeletal and connective tissue disorders	0.2979	0.7611	0.1860	0.9886	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.9998	NC	NC	NC	NC	0.9993
	SOC :Nervous system disorders	0.3204	0.6112	0.4923	0.2291	NC	0.9999
	SOC :Psychiatric disorders	0.9550	NC	0.7895	NC	NC	NC
	SOC :Renal and urinary disorders	0.9837	0.9895	0.9872	0.9999	NC	NC
	SOC :Reproductive system and breast disorders	0.9998	NC	0.9998	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.1816	0.8117	0.4753	0.2745	NC	NC
	SOC :Skin and subcutaneous tissue disorders	0.3206	NC	0.3341	NC	NC	0.9995
	SOC :Vascular disorders	0.7633	NC	0.4240	NC	NC	NC
Baseline creatinine clearance	SOC :Blood and lymphatic system disorders	0.8074	0.5218	0.2176	0.6113	NC	0.9935
	SOC :Cardiac disorders	0.0998	0.3708	0.1780	0.6112	NC	0.9971
	SOC :Eye disorders	0.5314	NC	0.8904	NC	NC	0.9993
	SOC :Gastrointestinal disorders	0.3414	0.2831	0.4168	0.6074	NC	NC
	SOC :General disorders and administration site conditions	0.2608	0.0062	0.2185	0.9548	NC	0.9945
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	0.9993
	SOC :Infections and infestations	0.4057	0.8146	0.8382	0.5948	NC	0.4568

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
	SOC :Injury, poisoning and procedural complications	0.8564	0.6231	0.5999	0.9943	NC	NC
	SOC :Investigations	0.9166	NC	0.9492	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.8368	0.3816	0.2350	0.2643	NC	NC
	SOC :Musculoskeletal and connective tissue disorders	0.1674	0.6115	0.0585	0.4930	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.9912	NC	NC	NC	NC	0.9990
	SOC :Nervous system disorders	0.0728	0.5152	0.0510	0.7687	NC	0.9957
	SOC :Psychiatric disorders	0.5018	NC	0.4788	NC	NC	NC
	SOC :Renal and urinary disorders	0.5077	0.5286	0.8980	0.3503	NC	NC
	SOC :Reproductive system and breast disorders	0.6646	NC	0.7872	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.0463	0.4308	0.3564	0.0464	NC	NC
	SOC :Skin and subcutaneous tissue disorders	0.3838	NC	0.4576	NC	NC	0.9993
	SOC :Vascular disorders	0.6206	NC	0.4155	NC	NC	NC
Previous therapy with anti-CD38 mAB	SOC :Blood and lymphatic system disorders	0.9786	0.9998	1.0000	0.9790	NC	0.9951
	SOC :Cardiac disorders	0.9996	0.9999	0.9995	0.9999	NC	NC
	SOC :Eye disorders	1.0000	NC	1.0000	NC	NC	NC
	SOC :Gastrointestinal disorders	0.9719	0.9998	0.9721	0.9998	NC	NC

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
	SOC :General disorders and administration site conditions	0.9885	0.9999	0.9739	0.9845	NC	0.9999
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	0.9998
	SOC :Infections and infestations	0.2795	0.9808	0.9686	0.9808	NC	0.9897
	SOC :Injury, poisoning and procedural complications	0.1584	0.9997	0.1593	0.9996	NC	NC
	SOC :Investigations	0.9899	NC	0.9895	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.9998	0.9999	0.9998	0.9998	NC	NC
	SOC :Musculoskeletal and connective tissue disorders	0.4488	0.9905	0.9771	0.3707	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.9932	NC	NC	NC	NC	NC
	SOC :Nervous system disorders	0.9822	0.9999	0.9835	0.9911	NC	0.9999
	SOC :Psychiatric disorders	0.9999	NC	1.0000	NC	NC	NC
	SOC :Renal and urinary disorders	0.9999	1.0000	1.0000	0.9999	NC	NC
	SOC :Reproductive system and breast disorders	0.9998	NC	0.9998	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.9815	1.0000	0.9824	0.9999	NC	NC
	SOC :Skin and subcutaneous tissue disorders	0.9999	NC	0.9999	NC	NC	0.9998
	SOC :Vascular disorders	0.9999	NC	0.9999	NC	NC	NC
Refractory to PI	SOC :Blood and lymphatic system disorders	0.7099	0.2436	0.6256	0.6778	NC	0.9952

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_soc_sr_l_x.rtf (10NOV2020 10:55)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
	SOC :Cardiac disorders	0.4057	0.8768	0.2178	0.5461	NC	1.0000
	SOC :Eye disorders	0.9489	NC	0.7324	NC	NC	0.9993
	SOC :Gastrointestinal disorders	0.1731	0.9923	0.2844	0.7311	NC	NC
	SOC :General disorders and administration site conditions	0.3631	0.1192	0.2567	0.4960	NC	0.9944
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	0.9993
	SOC :Infections and infestations	0.0239	0.0211	0.0627	0.1399	NC	0.4076
	SOC :Injury, poisoning and procedural complications	0.5371	0.9918	0.7866	0.9939	NC	NC
	SOC :Investigations	0.7973	NC	0.3437	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.2036	0.4705	0.1378	0.5451	NC	NC
	SOC :Musculoskeletal and connective tissue disorders	0.2420	0.1830	0.4610	0.1131	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.9910	NC	NC	NC	NC	0.9999
	SOC :Nervous system disorders	0.1614	0.7420	0.0918	0.6649	NC	0.9999
	SOC :Psychiatric disorders	0.9672	NC	0.8671	NC	NC	NC
	SOC :Renal and urinary disorders	0.2412	0.9896	0.6417	0.3857	NC	NC
	SOC :Reproductive system and breast disorders	0.9915	NC	0.9917	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.4827	0.5732	0.7599	0.4302	NC	NC

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
	SOC :Skin and subcutaneous tissue disorders	0.0936	NC	0.0824	NC	NC	0.9993
	SOC :Vascular disorders	0.8068	NC	0.8114	NC	NC	NC
Refractory to IMiD	SOC :Blood and lymphatic system disorders	0.1668	0.9998	0.1410	0.4965	NC	0.9996
	SOC :Cardiac disorders	0.6480	0.3982	0.7049	0.6994	NC	0.9976
	SOC :Eye disorders	0.1905	NC	0.4278	NC	NC	0.9996
	SOC :Gastrointestinal disorders	0.9944	0.9997	0.6952	0.9882	NC	NC
	SOC :General disorders and administration site conditions	0.4243	0.2705	0.2724	0.3012	NC	0.9999
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	0.9996
	SOC :Infections and infestations	0.3376	0.6176	0.0968	0.8120	NC	1.0000
	SOC :Injury, poisoning and procedural complications	0.4766	0.9896	0.4756	0.9964	NC	NC
	SOC :Investigations	0.4581	NC	0.9903	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.9868	0.9895	0.9894	0.9876	NC	NC
	SOC :Musculoskeletal and connective tissue disorders	0.4540	0.6471	0.8020	0.7032	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.9997	NC	NC	NC	NC	0.9994
	SOC :Nervous system disorders	0.9288	0.9923	0.5097	0.9915	NC	0.9999
	SOC :Psychiatric disorders	0.8904	NC	0.7871	NC	NC	NC
	SOC :Renal and urinary disorders	0.4807	0.9999	0.3597	0.9929	NC	NC

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
Refractory to lenalidomide in last previous regimen	SOC :Reproductive system and breast disorders	0.9896	NC	0.9899	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.8468	0.7953	0.9388	0.7298	NC	NC
	SOC :Skin and subcutaneous tissue disorders	0.8414	NC	0.8652	NC	NC	0.9996
	SOC :Vascular disorders	0.9877	NC	0.9896	NC	NC	NC
	SOC :Blood and lymphatic system disorders	0.6251	0.9200	0.6577	0.6706	NC	0.9919
	SOC :Cardiac disorders	0.4751	0.0863	0.4988	0.2014	NC	0.9966
	SOC :Eye disorders	0.6189	NC	0.9902	NC	NC	0.9993
	SOC :Gastrointestinal disorders	0.6006	0.5453	0.6808	0.2241	NC	NC
	SOC :General disorders and administration site conditions	0.7565	0.5061	0.2643	0.0227	NC	0.9949
	SOC :Hepatobiliary disorders	NC	NC	NC	NC	NC	0.9993
	SOC :Infections and infestations	0.8436	0.5603	0.5408	0.6868	NC	0.6431
	SOC :Injury, poisoning and procedural complications	0.0279	0.1130	0.0951	0.9942	NC	NC
	SOC :Investigations	0.8895	NC	0.6029	NC	NC	NC
	SOC :Metabolism and nutrition disorders	0.4899	0.0263	0.1279	0.3157	NC	NC
	SOC :Musculoskeletal and connective tissue disorders	0.4200	0.4354	0.4555	0.1559	NC	NC
	SOC :Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.6105	NC	NC	NC	NC	0.9989

NA:Not Applicable / Not Calculable

P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.1 Listing of subgroup and SOC interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)		Any treatment emergent AE leading to discontinuation of treatment
	SOC :Nervous system disorders	0.4202	0.6921	0.3153	0.2369	NC	0.9957
	SOC :Psychiatric disorders	0.2269	NC	0.6020	NC	NC	NC
	SOC :Renal and urinary disorders	0.7334	0.4223	0.9266	0.2606	NC	NC
	SOC :Reproductive system and breast disorders	0.6285	NC	0.7350	NC	NC	NC
	SOC :Respiratory, thoracic and mediastinal disorders	0.4164	0.1094	0.8304	0.4443	NC	NC
	SOC :Skin and subcutaneous tissue disorders	0.3136	NC	0.2613	NC	NC	0.9992
	SOC :Vascular disorders	0.4829	NC	0.0962	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_soc_sr_l_x.rtf (10NOV2020 10:55)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
Age	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	1.0000
	PT :Arthralgia	0.4955	NC	0.5904	NC	NC	NC
	PT :Asthenia	0.6822	NC	0.4885	NC	NC	NC
	PT :Atrial fibrillation	0.9948	NC	NC	NC	NC	NC
	PT :Atypical pneumonia	NC	NC	NC	NC	NC	1.0000
	PT :Back pain	0.2094	NC	0.1443	NC	NC	NC
	PT :Bone pain	0.5624	NC	0.8082	NC	NC	NC
	PT :Bronchitis	0.3733	NC	0.3569	NC	NC	NC
	PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	1.0000
	PT :Cataract	0.3852	NC	NC	NC	NC	NC
	PT :Cerebellar infarction	NC	NC	NC	NC	NC	1.0000
	PT :Constipation	0.3898	NC	0.3898	NC	NC	NC
	PT :Cough	0.7162	NC	0.8534	NC	NC	NC
	PT :Death	NC	NC	NC	NC	NC	1.0000
	PT :Decreased appetite	0.7447	NC	0.7447	NC	NC	NC
	PT :Decubitus ulcer	NC	NC	NC	NC	NC	1.0000
	PT :Diarrhoea	0.9754	NC	0.9990	NC	NC	NC
	PT :Disease progression	0.6989	0.5545	NC	NC	0.6989	NC
	PT :Dyspnoea	0.2996	NC	0.2818	NC	NC	NC
	PT :Echinococciasis	NC	NC	NC	NC	NC	1.0000

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Fatigue	0.3152	NC	0.5432	NC	NC	NC
PT :Febrile neutropenia	0.9821	0.9904	NC	0.9821	0.9821	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	1.0000
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	1.0000
PT :Headache	0.4789	NC	0.4789	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	1.0000
PT :Hypertension	0.6644	NC	NC	NC	NC	NC
PT :Influenza	0.5284	NC	NC	NC	NC	NC
PT :Infusion related reaction	0.9638	NC	0.9426	NC	NC	NC
PT :Insomnia	0.3646	NC	0.3903	NC	NC	NC
PT :Lower respiratory tract infection	0.3006	NC	NC	0.9232	0.9232	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	1.0000
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	1.0000
PT :Metastases to liver	NC	NC	NC	NC	NC	1.0000
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	1.0000
PT :Muscle spasms	0.6518	NC	0.6181	NC	NC	NC
PT :Muscular weakness	0.4346	NC	0.3680	NC	NC	NC
PT :Musculoskeletal chest pain	0.9994	NC	0.9994	NC	NC	NC
PT :Myalgia	0.5615	NC	0.5615	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	1.0000

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Myocardial infarction	NC	NC	NC	NC	NC	1.0000
PT :Nasopharyngitis	0.9901	NC	0.9901	NC	NC	NC
PT :Nausea	0.8543	NC	0.8543	NC	NC	NC
PT :Neutropenia	0.5670	NC	NC	0.4656	0.4831	1.0000
PT :Oedema peripheral	0.7171	NC	0.7171	NC	NC	NC
PT :Oropharyngeal pain	0.7234	NC	0.7234	NC	NC	NC
PT :Pain in extremity	0.6155	NC	0.6155	NC	NC	NC
PT :Pathological fracture	0.0612	NC	NC	NC	NC	NC
PT :Peripheral sensory neuropathy	0.6769	NC	0.6731	NC	NC	NC
PT :Pneumonia	0.4477	0.2408	0.9165	0.5440	0.5440	1.0000
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	1.0000
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	1.0000
PT :Pruritus	0.5859	NC	0.5859	NC	NC	NC
PT :Pyoderma	NC	NC	NC	NC	NC	1.0000
PT :Pyrexia	0.5483	NC	0.5036	NC	NC	NC
PT :Rash	0.9828	NC	0.9828	NC	NC	NC
PT :Sepsis	NC	NC	NC	NC	NC	1.0000
PT :Septic shock	NC	NC	NC	NC	NC	1.0000
PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	1.0000
PT :Stomatitis	0.9988	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
Number of previous lines of therapy (IRT)	PT :Sudden death	NC	NC	NC	NC	NC	1.0000
	PT :Thrombocytopenia	0.6585	NC	NC	0.7796	0.7796	1.0000
	PT :Tremor	0.9968	NC	NC	NC	NC	NC
	PT :Upper respiratory tract infection	0.0306	NC	0.0173	NC	NC	NC
	PT :Urinary tract infection	0.0156	NC	0.0384	NC	0.5744	NC
	PT :Vision blurred	NC	NC	NC	NC	NC	1.0000
	PT :Vomiting	0.9060	NC	0.9767	NC	NC	NC
	PT :Weight decreased	1.0000	NC	1.0000	NC	NC	NC
	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	0.9992
	PT :Arthralgia	0.4331	NC	0.6155	NC	NC	NC
	PT :Asthenia	0.1270	NC	0.3004	NC	NC	NC
	PT :Atrial fibrillation	0.9916	NC	NC	NC	NC	NC
	PT :Atypical pneumonia	NC	NC	NC	NC	NC	0.9994
	PT :Back pain	0.9784	NC	0.3903	NC	NC	NC
	PT :Bone pain	0.4056	NC	0.6637	NC	NC	NC
	PT :Bronchitis	0.7364	NC	0.9385	NC	NC	NC
	PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	0.9993
	PT :Cataract	0.9141	NC	NC	NC	NC	NC
	PT :Cerebellar infarction	NC	NC	NC	NC	NC	0.9992
	PT :Constipation	0.3120	NC	0.3120	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Cough	0.8688	NC	0.6649	NC	NC	NC
PT :Death	NC	NC	NC	NC	NC	0.9958
PT :Decreased appetite	0.6334	NC	0.6334	NC	NC	NC
PT :Decubitus ulcer	NC	NC	NC	NC	NC	0.9991
PT :Diarrhoea	0.7686	NC	0.6319	NC	NC	NC
PT :Disease progression	0.3393	0.3230	NC	NC	0.3393	NC
PT :Dyspnoea	0.1283	NC	0.2310	NC	NC	NC
PT :Echinococciasis	NC	NC	NC	NC	NC	0.9993
PT :Fatigue	0.1688	NC	0.3045	NC	NC	NC
PT :Febrile neutropenia	0.9898	0.9917	NC	0.9898	0.9898	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	0.9992
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	0.9994
PT :Headache	0.5080	NC	0.5080	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	0.9994
PT :Hypertension	0.3028	NC	NC	NC	NC	NC
PT :Influenza	0.2746	NC	NC	NC	NC	NC
PT :Infusion related reaction	0.9858	NC	0.9859	NC	NC	NC
PT :Insomnia	0.5977	NC	0.7228	NC	NC	NC
PT :Lower respiratory tract infection	0.3512	NC	NC	0.9935	0.9935	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	0.9992

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	0.9993
PT :Metastases to liver	NC	NC	NC	NC	NC	0.9994
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	0.9994
PT :Muscle spasms	0.0443	NC	0.0588	NC	NC	NC
PT :Muscular weakness	0.4482	NC	0.3925	NC	NC	NC
PT :Musculoskeletal chest pain	0.5060	NC	0.5060	NC	NC	NC
PT :Myalgia	0.9903	NC	0.9903	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	0.9992
PT :Myocardial infarction	NC	NC	NC	NC	NC	0.9992
PT :Nasopharyngitis	0.0594	NC	0.0594	NC	NC	NC
PT :Nausea	0.6576	NC	0.6576	NC	NC	NC
PT :Neutropenia	0.3143	NC	NC	0.2220	0.2427	0.9990
PT :Oedema peripheral	0.4595	NC	0.4595	NC	NC	NC
PT :Oropharyngeal pain	0.1824	NC	0.1824	NC	NC	NC
PT :Pain in extremity	0.5911	NC	0.5911	NC	NC	NC
PT :Pathological fracture	0.4853	NC	NC	NC	NC	NC
PT :Peripheral sensory neuropathy	0.3123	NC	0.3092	NC	NC	NC
PT :Pneumonia	0.9611	0.9722	0.7364	0.7745	0.7745	0.9944
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	0.9994
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	0.9993

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
	PT :Pruritus	0.4399	NC	0.4399	NC	NC	NC
	PT :Pyoderma	NC	NC	NC	NC	NC	0.9992
	PT :Pyrexia	0.8969	NC	0.6141	NC	NC	NC
	PT :Rash	0.4602	NC	0.4602	NC	NC	NC
	PT :Sepsis	NC	NC	NC	NC	NC	0.9992
	PT :Septic shock	NC	NC	NC	NC	NC	0.9990
	PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	0.9992
	PT :Stomatitis	0.1369	NC	NC	NC	NC	NC
	PT :Sudden death	NC	NC	NC	NC	NC	0.9993
	PT :Thrombocytopenia	0.4820	NC	NC	0.6284	0.6284	0.9938
	PT :Tremor	0.8619	NC	NC	NC	NC	NC
	PT :Upper respiratory tract infection	0.4603	NC	0.3357	NC	NC	NC
	PT :Urinary tract infection	0.0995	NC	0.2608	NC	0.4748	NC
	PT :Vision blurred	NC	NC	NC	NC	NC	0.9993
	PT :Vomiting	0.8657	NC	0.7218	NC	NC	NC
	PT :Weight decreased	0.9931	NC	0.9931	NC	NC	NC
Gender	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	0.9992
	PT :Arthralgia	0.0093	NC	0.0247	NC	NC	NC
	PT :Asthenia	0.0382	NC	0.0775	NC	NC	NC
	PT :Atrial fibrillation	0.6179	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Atypical pneumonia	NC	NC	NC	NC	NC	0.9993
PT :Back pain	0.1365	NC	0.2142	NC	NC	NC
PT :Bone pain	0.8133	NC	0.9517	NC	NC	NC
PT :Bronchitis	0.8942	NC	0.9928	NC	NC	NC
PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	0.9993
PT :Cataract	0.7200	NC	NC	NC	NC	NC
PT :Cerebellar infarction	NC	NC	NC	NC	NC	0.9992
PT :Constipation	0.6482	NC	0.6482	NC	NC	NC
PT :Cough	0.3116	NC	0.4264	NC	NC	NC
PT :Death	NC	NC	NC	NC	NC	0.9959
PT :Decreased appetite	0.8936	NC	0.8936	NC	NC	NC
PT :Decubitus ulcer	NC	NC	NC	NC	NC	0.9993
PT :Diarrhoea	0.0336	NC	0.0239	NC	NC	NC
PT :Disease progression	0.9744	0.9664	NC	NC	0.9744	NC
PT :Dyspnoea	0.5574	NC	0.9305	NC	NC	NC
PT :Echinococciasis	NC	NC	NC	NC	NC	0.9991
PT :Fatigue	0.8772	NC	0.7347	NC	NC	NC
PT :Febrile neutropenia	0.8888	0.2544	NC	0.8888	0.8888	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	0.9991
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	0.9992

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Headache	0.0476	NC	0.0476	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	0.9991
PT :Hypertension	0.6401	NC	NC	NC	NC	NC
PT :Influenza	0.1099	NC	NC	NC	NC	NC
PT :Infusion related reaction	0.6491	NC	0.7161	NC	NC	NC
PT :Insomnia	0.1502	NC	0.0982	NC	NC	NC
PT :Lower respiratory tract infection	0.3326	NC	NC	0.5891	0.5891	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	0.9993
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	0.9992
PT :Metastases to liver	NC	NC	NC	NC	NC	0.9992
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	0.9991
PT :Muscle spasms	0.2029	NC	0.2538	NC	NC	NC
PT :Muscular weakness	0.0691	NC	0.0452	NC	NC	NC
PT :Musculoskeletal chest pain	0.2980	NC	0.2980	NC	NC	NC
PT :Myalgia	0.1145	NC	0.1145	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	0.9993
PT :Myocardial infarction	NC	NC	NC	NC	NC	0.9993
PT :Nasopharyngitis	0.5504	NC	0.5504	NC	NC	NC
PT :Nausea	0.9850	NC	0.9850	NC	NC	NC
PT :Neutropenia	0.8164	NC	NC	0.6670	0.7288	0.9991

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Oedema peripheral	0.3778	NC	0.3778	NC	NC	NC
PT :Oropharyngeal pain	0.3925	NC	0.3925	NC	NC	NC
PT :Pain in extremity	0.2918	NC	0.2918	NC	NC	NC
PT :Pathological fracture	0.1104	NC	NC	NC	NC	NC
PT :Peripheral sensory neuropathy	0.8867	NC	0.8728	NC	NC	NC
PT :Pneumonia	0.7735	0.6963	0.5493	0.7324	0.7324	0.9956
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	0.9993
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	0.9993
PT :Pruritus	0.6692	NC	0.6692	NC	NC	NC
PT :Pyoderma	NC	NC	NC	NC	NC	0.9991
PT :Pyrexia	0.0890	NC	0.1233	NC	NC	NC
PT :Rash	0.9863	NC	0.9863	NC	NC	NC
PT :Sepsis	NC	NC	NC	NC	NC	0.9994
PT :Septic shock	NC	NC	NC	NC	NC	0.9988
PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	0.9994
PT :Stomatitis	0.1330	NC	NC	NC	NC	NC
PT :Sudden death	NC	NC	NC	NC	NC	0.9991
PT :Thrombocytopenia	0.2736	NC	NC	0.2254	0.2254	0.9951
PT :Tremor	0.4180	NC	NC	NC	NC	NC
PT :Upper respiratory tract infection	0.8056	NC	0.6148	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
	PT :Urinary tract infection	0.4049	NC	0.3692	NC	0.7684	NC
	PT :Vision blurred	NC	NC	NC	NC	NC	0.9992
	PT :Vomiting	0.3854	NC	0.4720	NC	NC	NC
	PT :Weight decreased	0.9935	NC	0.9935	NC	NC	NC
Race	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	0.9993
	PT :Arthralgia	0.8199	NC	0.9425	NC	NC	NC
	PT :Asthenia	0.1177	NC	0.9884	NC	NC	NC
	PT :Atrial fibrillation	0.9942	NC	NC	NC	NC	NC
	PT :Atypical pneumonia	NC	NC	NC	NC	NC	0.9994
	PT :Back pain	0.2827	NC	0.4406	NC	NC	NC
	PT :Bone pain	0.9915	NC	0.9919	NC	NC	NC
	PT :Bronchitis	0.9878	NC	0.9892	NC	NC	NC
	PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	0.9994
	PT :Cataract	0.9195	NC	NC	NC	NC	NC
	PT :Cerebellar infarction	NC	NC	NC	NC	NC	0.9993
	PT :Constipation	0.9453	NC	0.9453	NC	NC	NC
	PT :Cough	0.6551	NC	0.5691	NC	NC	NC
	PT :Death	NC	NC	NC	NC	NC	0.9999
	PT :Decreased appetite	0.5662	NC	0.5662	NC	NC	NC
	PT :Decubitus ulcer	NC	NC	NC	NC	NC	0.9994

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Diarrhoea	0.5545	NC	0.5132	NC	NC	NC
PT :Disease progression	0.9928	0.9933	NC	NC	0.9928	NC
PT :Dyspnoea	0.9629	NC	0.5383	NC	NC	NC
PT :Echinococciasis	NC	NC	NC	NC	NC	0.9994
PT :Fatigue	0.6957	NC	0.6020	NC	NC	NC
PT :Febrile neutropenia	0.9884	0.9937	NC	0.9884	0.9884	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	0.9993
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	0.9994
PT :Headache	0.7466	NC	0.7466	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	0.9994
PT :Hypertension	0.9916	NC	NC	NC	NC	NC
PT :Influenza	0.7289	NC	NC	NC	NC	NC
PT :Infusion related reaction	0.9864	NC	0.9867	NC	NC	NC
PT :Insomnia	0.8611	NC	0.8076	NC	NC	NC
PT :Lower respiratory tract infection	0.7899	NC	NC	0.5561	0.5561	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	0.9993
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	0.9996
PT :Metastases to liver	NC	NC	NC	NC	NC	0.9993
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	0.9994
PT :Muscle spasms	0.6312	NC	0.3326	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Muscular weakness	0.9762	NC	0.9615	NC	NC	NC
PT :Musculoskeletal chest pain	0.0226	NC	0.0226	NC	NC	NC
PT :Myalgia	0.3385	NC	0.3385	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	0.9995
PT :Myocardial infarction	NC	NC	NC	NC	NC	0.9994
PT :Nasopharyngitis	0.7768	NC	0.7768	NC	NC	NC
PT :Nausea	0.2199	NC	0.2199	NC	NC	NC
PT :Neutropenia	0.0115	NC	NC	0.0196	0.0196	0.9991
PT :Oedema peripheral	0.2567	NC	0.2567	NC	NC	NC
PT :Oropharyngeal pain	0.4853	NC	0.4853	NC	NC	NC
PT :Pain in extremity	0.7066	NC	0.7066	NC	NC	NC
PT :Pathological fracture	0.9890	NC	NC	NC	NC	NC
PT :Peripheral sensory neuropathy	0.9998	NC	0.9998	NC	NC	NC
PT :Pneumonia	0.5062	0.8281	0.4098	0.7572	0.7572	0.9999
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	0.9994
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	0.9994
PT :Pruritus	0.5350	NC	0.5350	NC	NC	NC
PT :Pyoderma	NC	NC	NC	NC	NC	0.9993
PT :Pyrexia	0.7937	NC	0.7719	NC	NC	NC
PT :Rash	0.5160	NC	0.5160	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
	PT :Sepsis	NC	NC	NC	NC	NC	0.9994
	PT :Septic shock	NC	NC	NC	NC	NC	0.9991
	PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	0.9994
	PT :Stomatitis	0.5438	NC	NC	NC	NC	NC
	PT :Sudden death	NC	NC	NC	NC	NC	0.9994
	PT :Thrombocytopenia	0.7930	NC	NC	0.7550	0.7550	0.9997
	PT :Tremor	0.9927	NC	NC	NC	NC	NC
	PT :Upper respiratory tract infection	0.7269	NC	0.7245	NC	NC	NC
	PT :Urinary tract infection	0.9999	NC	1.0000	NC	0.9998	NC
	PT :Vision blurred	NC	NC	NC	NC	NC	0.9993
	PT :Vomiting	0.6317	NC	0.6704	NC	NC	NC
	PT :Weight decreased	0.9995	NC	0.9995	NC	NC	NC
Ethnicity	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	NC
	PT :Arthralgia	0.9896	NC	0.9902	NC	NC	NC
	PT :Asthenia	0.9867	NC	0.9876	NC	NC	NC
	PT :Atrial fibrillation	0.9997	NC	NC	NC	NC	NC
	PT :Atypical pneumonia	NC	NC	NC	NC	NC	0.9997
	PT :Back pain	0.3074	NC	0.9865	NC	NC	NC
	PT :Bone pain	0.9921	NC	0.9933	NC	NC	NC
	PT :Bronchitis	0.9889	NC	0.9890	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	0.9997
PT :Cataract	1.0000	NC	NC	NC	NC	NC
PT :Cerebellar infarction	NC	NC	NC	NC	NC	NC
PT :Constipation	1.0000	NC	1.0000	NC	NC	NC
PT :Cough	0.9999	NC	0.9999	NC	NC	NC
PT :Death	NC	NC	NC	NC	NC	0.9960
PT :Decreased appetite	0.9905	NC	0.9905	NC	NC	NC
PT :Decubitus ulcer	NC	NC	NC	NC	NC	0.9997
PT :Diarrhoea	0.7329	NC	0.7096	NC	NC	NC
PT :Disease progression	1.0000	1.0000	NC	NC	1.0000	NC
PT :Dyspnoea	0.2001	NC	0.1722	NC	NC	NC
PT :Echinococciasis	NC	NC	NC	NC	NC	0.9998
PT :Fatigue	0.9827	NC	0.9834	NC	NC	NC
PT :Febrile neutropenia	0.9918	0.9938	NC	0.9918	0.9918	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	NC
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	NC
PT :Headache	0.1890	NC	0.1890	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	0.9998
PT :Hypertension	1.0000	NC	NC	NC	NC	NC
PT :Influenza	0.9924	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Infusion related reaction	0.9878	NC	0.9879	NC	NC	NC
PT :Insomnia	0.9999	NC	0.9999	NC	NC	NC
PT :Lower respiratory tract infection	1.0000	NC	NC	0.9999	0.9999	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	0.9998
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	NC
PT :Metastases to liver	NC	NC	NC	NC	NC	NC
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	0.9998
PT :Muscle spasms	0.9999	NC	0.9999	NC	NC	NC
PT :Muscular weakness	0.9910	NC	0.9930	NC	NC	NC
PT :Musculoskeletal chest pain	0.9911	NC	0.9911	NC	NC	NC
PT :Myalgia	0.9997	NC	0.9997	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	0.9998
PT :Myocardial infarction	NC	NC	NC	NC	NC	NC
PT :Nasopharyngitis	0.9998	NC	0.9998	NC	NC	NC
PT :Nausea	0.9876	NC	0.9876	NC	NC	NC
PT :Neutropenia	0.7753	NC	NC	0.9850	0.9850	0.9996
PT :Oedema peripheral	0.9890	NC	0.9890	NC	NC	NC
PT :Oropharyngeal pain	0.9920	NC	0.9920	NC	NC	NC
PT :Pain in extremity	0.9936	NC	0.9936	NC	NC	NC
PT :Pathological fracture	0.9920	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Peripheral sensory neuropathy	0.9890	NC	0.9887	NC	NC	NC
PT :Pneumonia	0.9842	0.9857	0.9998	0.9852	0.9852	0.9999
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	0.9998
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	NC
PT :Pruritus	0.9920	NC	0.9920	NC	NC	NC
PT :Pyoderma	NC	NC	NC	NC	NC	NC
PT :Pyrexia	0.6936	NC	0.9865	NC	NC	NC
PT :Rash	0.9998	NC	0.9998	NC	NC	NC
PT :Sepsis	NC	NC	NC	NC	NC	NC
PT :Septic shock	NC	NC	NC	NC	NC	0.9996
PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	0.9998
PT :Stomatitis	0.9998	NC	NC	NC	NC	NC
PT :Sudden death	NC	NC	NC	NC	NC	0.9998
PT :Thrombocytopenia	0.9864	NC	NC	0.9865	0.9865	0.9996
PT :Tremor	0.9998	NC	NC	NC	NC	NC
PT :Upper respiratory tract infection	0.1286	NC	0.1179	NC	NC	NC
PT :Urinary tract infection	1.0000	NC	1.0000	NC	0.9998	NC
PT :Vision blurred	NC	NC	NC	NC	NC	NC
PT :Vomiting	0.9917	NC	0.9919	NC	NC	NC
PT :Weight decreased	1.0000	NC	1.0000	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
Geographical region	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	1.0000
	PT :Arthralgia	0.4984	NC	0.7575	NC	NC	NC
	PT :Asthenia	0.6943	NC	1.0000	NC	NC	NC
	PT :Atrial fibrillation	0.9992	NC	NC	NC	NC	NC
	PT :Atypical pneumonia	NC	NC	NC	NC	NC	1.0000
	PT :Back pain	0.4021	NC	0.3855	NC	NC	NC
	PT :Bone pain	1.0000	NC	1.0000	NC	NC	NC
	PT :Bronchitis	0.9615	NC	0.9046	NC	NC	NC
	PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	1.0000
	PT :Cataract	0.9658	NC	NC	NC	NC	NC
	PT :Cerebellar infarction	NC	NC	NC	NC	NC	1.0000
	PT :Constipation	0.9611	NC	0.9611	NC	NC	NC
	PT :Cough	0.6564	NC	0.7436	NC	NC	NC
	PT :Death	NC	NC	NC	NC	NC	1.0000
	PT :Decreased appetite	0.9943	NC	0.9943	NC	NC	NC
	PT :Decubitus ulcer	NC	NC	NC	NC	NC	1.0000
	PT :Diarrhoea	0.6649	NC	0.8081	NC	NC	NC
	PT :Disease progression	0.9132	0.9993	NC	NC	0.9132	NC
	PT :Dyspnoea	0.4661	NC	0.5210	NC	NC	NC
	PT :Echinococciasis	NC	NC	NC	NC	NC	1.0000

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Fatigue	0.8017	NC	0.5577	NC	NC	NC
PT :Febrile neutropenia	0.6852	0.9882	NC	0.6852	0.6852	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	1.0000
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	1.0000
PT :Headache	0.8605	NC	0.8605	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	1.0000
PT :Hypertension	0.8577	NC	NC	NC	NC	NC
PT :Influenza	0.5539	NC	NC	NC	NC	NC
PT :Infusion related reaction	1.0000	NC	1.0000	NC	NC	NC
PT :Insomnia	0.6303	NC	0.7068	NC	NC	NC
PT :Lower respiratory tract infection	0.6631	NC	NC	1.0000	1.0000	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	1.0000
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	1.0000
PT :Metastases to liver	NC	NC	NC	NC	NC	1.0000
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	1.0000
PT :Muscle spasms	0.8726	NC	0.7923	NC	NC	NC
PT :Muscular weakness	0.9983	NC	0.9958	NC	NC	NC
PT :Musculoskeletal chest pain	0.6347	NC	0.6347	NC	NC	NC
PT :Myalgia	0.9946	NC	0.9946	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	1.0000

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Myocardial infarction	NC	NC	NC	NC	NC	1.0000
PT :Nasopharyngitis	0.9357	NC	0.9357	NC	NC	NC
PT :Nausea	0.4433	NC	0.4433	NC	NC	NC
PT :Neutropenia	0.2523	NC	NC	0.3210	0.3095	1.0000
PT :Oedema peripheral	0.5333	NC	0.5333	NC	NC	NC
PT :Oropharyngeal pain	0.9984	NC	0.9984	NC	NC	NC
PT :Pain in extremity	0.5059	NC	0.5059	NC	NC	NC
PT :Pathological fracture	1.0000	NC	NC	NC	NC	NC
PT :Peripheral sensory neuropathy	0.9755	NC	0.9747	NC	NC	NC
PT :Pneumonia	0.9218	0.8282	0.7669	0.9607	0.9607	0.9963
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	1.0000
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	1.0000
PT :Pruritus	0.9972	NC	0.9972	NC	NC	NC
PT :Pyoderma	NC	NC	NC	NC	NC	1.0000
PT :Pyrexia	0.9923	NC	0.9825	NC	NC	NC
PT :Rash	0.4884	NC	0.4884	NC	NC	NC
PT :Sepsis	NC	NC	NC	NC	NC	1.0000
PT :Septic shock	NC	NC	NC	NC	NC	1.0000
PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	1.0000
PT :Stomatitis	0.9903	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
	PT :Sudden death	NC	NC	NC	NC	NC	1.0000
	PT :Thrombocytopenia	0.9952	NC	NC	0.9873	0.9873	1.0000
	PT :Tremor	0.8429	NC	NC	NC	NC	NC
	PT :Upper respiratory tract infection	0.5157	NC	0.7997	NC	NC	NC
	PT :Urinary tract infection	0.1517	NC	0.1599	NC	1.0000	NC
	PT :Vision blurred	NC	NC	NC	NC	NC	1.0000
	PT :Vomiting	0.9578	NC	0.9582	NC	NC	NC
	PT :Weight decreased	1.0000	NC	1.0000	NC	NC	NC
Regulatory region	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	0.9993
	PT :Arthralgia	0.1927	NC	0.1775	NC	NC	NC
	PT :Asthenia	0.3376	NC	0.3580	NC	NC	NC
	PT :Atrial fibrillation	0.9906	NC	NC	NC	NC	NC
	PT :Atypical pneumonia	NC	NC	NC	NC	NC	0.9994
	PT :Back pain	0.2200	NC	0.1799	NC	NC	NC
	PT :Bone pain	0.8471	NC	0.9610	NC	NC	NC
	PT :Bronchitis	0.7036	NC	0.6740	NC	NC	NC
	PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	0.9994
	PT :Cataract	0.3761	NC	NC	NC	NC	NC
	PT :Cerebellar infarction	NC	NC	NC	NC	NC	0.9993
	PT :Constipation	0.4292	NC	0.4292	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Cough	0.3682	NC	0.4372	NC	NC	NC
PT :Death	NC	NC	NC	NC	NC	0.9963
PT :Decreased appetite	0.1968	NC	0.1968	NC	NC	NC
PT :Decubitus ulcer	NC	NC	NC	NC	NC	0.9994
PT :Diarrhoea	0.0837	NC	0.1240	NC	NC	NC
PT :Disease progression	0.1465	0.3323	NC	NC	0.1465	NC
PT :Dyspnoea	0.2365	NC	0.4429	NC	NC	NC
PT :Echinococciasis	NC	NC	NC	NC	NC	0.9994
PT :Fatigue	0.5684	NC	0.4485	NC	NC	NC
PT :Febrile neutropenia	0.2604	0.2455	NC	0.2604	0.2604	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	0.9993
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	0.9994
PT :Headache	0.7543	NC	0.7543	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	0.9994
PT :Hypertension	0.4735	NC	NC	NC	NC	NC
PT :Influenza	0.1989	NC	NC	NC	NC	NC
PT :Infusion related reaction	0.9845	NC	0.9848	NC	NC	NC
PT :Insomnia	0.3645	NC	0.4079	NC	NC	NC
PT :Lower respiratory tract infection	0.9945	NC	NC	0.9998	0.9998	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	0.9993

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	0.9993
PT :Metastases to liver	NC	NC	NC	NC	NC	0.9993
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	0.9994
PT :Muscle spasms	0.2832	NC	0.1758	NC	NC	NC
PT :Muscular weakness	0.1067	NC	0.0761	NC	NC	NC
PT :Musculoskeletal chest pain	0.2257	NC	0.2257	NC	NC	NC
PT :Myalgia	0.5497	NC	0.5497	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	0.9993
PT :Myocardial infarction	NC	NC	NC	NC	NC	0.9993
PT :Nasopharyngitis	0.6302	NC	0.6302	NC	NC	NC
PT :Nausea	0.4343	NC	0.4343	NC	NC	NC
PT :Neutropenia	0.3741	NC	NC	0.3579	0.3134	0.9990
PT :Oedema peripheral	0.4903	NC	0.4903	NC	NC	NC
PT :Oropharyngeal pain	0.9896	NC	0.9896	NC	NC	NC
PT :Pain in extremity	0.7500	NC	0.7500	NC	NC	NC
PT :Pathological fracture	0.5393	NC	NC	NC	NC	NC
PT :Peripheral sensory neuropathy	0.7905	NC	0.7866	NC	NC	NC
PT :Pneumonia	0.3611	0.9219	0.2378	0.7578	0.7578	0.9960
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	0.9994
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	0.9993

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
	PT :Pruritus	0.4982	NC	0.4982	NC	NC	NC
	PT :Pyoderma	NC	NC	NC	NC	NC	0.9993
	PT :Pyrexia	0.3716	NC	0.2159	NC	NC	NC
	PT :Rash	0.4202	NC	0.4202	NC	NC	NC
	PT :Sepsis	NC	NC	NC	NC	NC	0.9993
	PT :Septic shock	NC	NC	NC	NC	NC	1.0000
	PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	0.9993
	PT :Stomatitis	0.9926	NC	NC	NC	NC	NC
	PT :Sudden death	NC	NC	NC	NC	NC	0.9993
	PT :Thrombocytopenia	0.6916	NC	NC	0.8597	0.8597	0.9949
	PT :Tremor	0.1891	NC	NC	NC	NC	NC
	PT :Upper respiratory tract infection	0.7469	NC	0.7771	NC	NC	NC
	PT :Urinary tract infection	0.1097	NC	0.2122	NC	0.9933	NC
	PT :Vision blurred	NC	NC	NC	NC	NC	0.9994
	PT :Vomiting	0.8859	NC	0.9655	NC	NC	NC
	PT :Weight decreased	0.9925	NC	0.9925	NC	NC	NC
ECOG PS	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	0.9995
	PT :Arthralgia	0.9831	NC	0.8937	NC	NC	NC
	PT :Asthenia	0.2539	NC	0.2954	NC	NC	NC
	PT :Atrial fibrillation	0.9933	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Atypical pneumonia	NC	NC	NC	NC	NC	0.9995
PT :Back pain	0.3095	NC	0.9842	NC	NC	NC
PT :Bone pain	0.4224	NC	0.2920	NC	NC	NC
PT :Bronchitis	0.4935	NC	0.4495	NC	NC	NC
PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	0.9995
PT :Cataract	0.9253	NC	NC	NC	NC	NC
PT :Cerebellar infarction	NC	NC	NC	NC	NC	0.9995
PT :Constipation	0.8518	NC	0.8518	NC	NC	NC
PT :Cough	0.9891	NC	0.9892	NC	NC	NC
PT :Death	NC	NC	NC	NC	NC	0.9999
PT :Decreased appetite	0.7160	NC	0.7160	NC	NC	NC
PT :Decubitus ulcer	NC	NC	NC	NC	NC	0.9995
PT :Diarrhoea	0.3237	NC	0.3003	NC	NC	NC
PT :Disease progression	0.9908	0.9913	NC	NC	0.9908	NC
PT :Dyspnoea	0.1143	NC	0.2042	NC	NC	NC
PT :Echinococciasis	NC	NC	NC	NC	NC	0.9996
PT :Fatigue	0.9732	NC	0.9150	NC	NC	NC
PT :Febrile neutropenia	0.9907	0.9921	NC	0.9907	0.9907	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	0.9996
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	0.9995

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Headache	0.8987	NC	0.8987	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	0.9995
PT :Hypertension	0.9902	NC	NC	NC	NC	NC
PT :Influenza	0.9906	NC	NC	NC	NC	NC
PT :Infusion related reaction	0.9885	NC	0.9888	NC	NC	NC
PT :Insomnia	0.9883	NC	1.0000	NC	NC	NC
PT :Lower respiratory tract infection	0.9900	NC	NC	0.9999	0.9999	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	0.9995
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	0.9995
PT :Metastases to liver	NC	NC	NC	NC	NC	0.9996
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	0.9995
PT :Muscle spasms	0.9880	NC	0.9882	NC	NC	NC
PT :Muscular weakness	0.9907	NC	0.9909	NC	NC	NC
PT :Musculoskeletal chest pain	0.9394	NC	0.9394	NC	NC	NC
PT :Myalgia	0.9998	NC	0.9998	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	0.9995
PT :Myocardial infarction	NC	NC	NC	NC	NC	0.9996
PT :Nasopharyngitis	0.9998	NC	0.9998	NC	NC	NC
PT :Nausea	0.3651	NC	0.3651	NC	NC	NC
PT :Neutropenia	0.6045	NC	NC	0.4257	0.5677	0.9999

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Oedema peripheral	0.9857	NC	0.9857	NC	NC	NC
PT :Oropharyngeal pain	0.4327	NC	0.4327	NC	NC	NC
PT :Pain in extremity	0.9930	NC	0.9930	NC	NC	NC
PT :Pathological fracture	0.9902	NC	NC	NC	NC	NC
PT :Peripheral sensory neuropathy	0.7913	NC	0.7841	NC	NC	NC
PT :Pneumonia	0.2158	0.0799	0.1754	0.5821	0.5821	0.7419
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	0.9995
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	0.9996
PT :Pruritus	0.9900	NC	0.9900	NC	NC	NC
PT :Pyoderma	NC	NC	NC	NC	NC	0.9995
PT :Pyrexia	0.5285	NC	0.8680	NC	NC	NC
PT :Rash	0.9901	NC	0.9901	NC	NC	NC
PT :Sepsis	NC	NC	NC	NC	NC	0.9995
PT :Septic shock	NC	NC	NC	NC	NC	0.9993
PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	0.9995
PT :Stomatitis	0.9913	NC	NC	NC	NC	NC
PT :Sudden death	NC	NC	NC	NC	NC	0.9995
PT :Thrombocytopenia	0.6892	NC	NC	0.7492	0.7492	0.9947
PT :Tremor	0.9902	NC	NC	NC	NC	NC
PT :Upper respiratory tract infection	0.9819	NC	0.9822	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
	PT :Urinary tract infection	0.1580	NC	0.2975	NC	0.9927	NC
	PT :Vision blurred	NC	NC	NC	NC	NC	0.9995
	PT :Vomiting	0.4014	NC	0.4379	NC	NC	NC
	PT :Weight decreased	0.9938	NC	0.9938	NC	NC	NC
ISS staging at study entry	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	1.0000
	PT :Arthralgia	0.6570	NC	0.5764	NC	NC	NC
	PT :Asthenia	0.9680	NC	0.9013	NC	NC	NC
	PT :Atrial fibrillation	0.9088	NC	NC	NC	NC	NC
	PT :Atypical pneumonia	NC	NC	NC	NC	NC	NC
	PT :Back pain	0.1075	NC	0.1181	NC	NC	NC
	PT :Bone pain	0.1597	NC	0.1745	NC	NC	NC
	PT :Bronchitis	0.1708	NC	0.1317	NC	NC	NC
	PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	1.0000
	PT :Cataract	0.7886	NC	NC	NC	NC	NC
	PT :Cerebellar infarction	NC	NC	NC	NC	NC	1.0000
	PT :Constipation	0.5608	NC	0.5608	NC	NC	NC
	PT :Cough	0.2393	NC	0.3503	NC	NC	NC
	PT :Death	NC	NC	NC	NC	NC	1.0000
	PT :Decreased appetite	0.8987	NC	0.8987	NC	NC	NC
	PT :Decubitus ulcer	NC	NC	NC	NC	NC	1.0000

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Diarrhoea	0.7735	NC	0.6342	NC	NC	NC
PT :Disease progression	0.5135	0.7872	NC	NC	0.5135	NC
PT :Dyspnoea	0.8229	NC	0.9960	NC	NC	NC
PT :Echinococciasis	NC	NC	NC	NC	NC	1.0000
PT :Fatigue	0.5707	NC	0.5943	NC	NC	NC
PT :Febrile neutropenia	0.9786	0.8057	NC	0.9786	0.9786	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	1.0000
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	1.0000
PT :Headache	0.4518	NC	0.4518	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	1.0000
PT :Hypertension	0.4665	NC	NC	NC	NC	NC
PT :Influenza	0.4332	NC	NC	NC	NC	NC
PT :Infusion related reaction	0.8236	NC	0.8406	NC	NC	NC
PT :Insomnia	0.3323	NC	0.4306	NC	NC	NC
PT :Lower respiratory tract infection	0.3079	NC	NC	0.7517	0.7517	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	1.0000
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	1.0000
PT :Metastases to liver	NC	NC	NC	NC	NC	1.0000
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	1.0000
PT :Muscle spasms	0.9983	NC	0.9837	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Muscular weakness	0.9121	NC	0.7321	NC	NC	NC
PT :Musculoskeletal chest pain	0.8010	NC	0.8010	NC	NC	NC
PT :Myalgia	0.9620	NC	0.9620	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	1.0000
PT :Myocardial infarction	NC	NC	NC	NC	NC	1.0000
PT :Nasopharyngitis	0.7517	NC	0.7517	NC	NC	NC
PT :Nausea	0.9314	NC	0.9314	NC	NC	NC
PT :Neutropenia	0.3400	NC	NC	0.3282	0.3026	1.0000
PT :Oedema peripheral	0.4253	NC	0.4253	NC	NC	NC
PT :Oropharyngeal pain	0.9863	NC	0.9863	NC	NC	NC
PT :Pain in extremity	0.9036	NC	0.9036	NC	NC	NC
PT :Pathological fracture	0.2450	NC	NC	NC	NC	NC
PT :Peripheral sensory neuropathy	0.5834	NC	0.5939	NC	NC	NC
PT :Pneumonia	0.3313	0.4763	0.4915	0.3481	0.3481	1.0000
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	1.0000
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	1.0000
PT :Pruritus	0.9978	NC	0.9978	NC	NC	NC
PT :Pyoderma	NC	NC	NC	NC	NC	1.0000
PT :Pyrexia	0.8485	NC	0.5903	NC	NC	NC
PT :Rash	0.9999	NC	0.9999	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
	PT :Sepsis	NC	NC	NC	NC	NC	NC
	PT :Septic shock	NC	NC	NC	NC	NC	1.0000
	PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	1.0000
	PT :Stomatitis	0.7984	NC	NC	NC	NC	NC
	PT :Sudden death	NC	NC	NC	NC	NC	1.0000
	PT :Thrombocytopenia	0.6781	NC	NC	0.8241	0.8241	1.0000
	PT :Tremor	0.9590	NC	NC	NC	NC	NC
	PT :Upper respiratory tract infection	0.4649	NC	0.3959	NC	NC	NC
	PT :Urinary tract infection	0.4167	NC	0.3122	NC	0.8114	NC
	PT :Vision blurred	NC	NC	NC	NC	NC	1.0000
	PT :Vomiting	0.8547	NC	0.9352	NC	NC	NC
	PT :Weight decreased	1.0000	NC	1.0000	NC	NC	NC
R-ISS staging	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	NC
	PT :Arthralgia	0.7669	NC	0.5938	NC	NC	NC
	PT :Asthenia	0.1519	NC	0.4053	NC	NC	NC
	PT :Atrial fibrillation	0.9868	NC	NC	NC	NC	NC
	PT :Atypical pneumonia	NC	NC	NC	NC	NC	NC
	PT :Back pain	0.5077	NC	0.3737	NC	NC	NC
	PT :Bone pain	0.2031	NC	0.2481	NC	NC	NC
	PT :Bronchitis	0.1893	NC	0.1725	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	1.0000
PT :Cataract	0.8526	NC	NC	NC	NC	NC
PT :Cerebellar infarction	NC	NC	NC	NC	NC	1.0000
PT :Constipation	0.3551	NC	0.3551	NC	NC	NC
PT :Cough	0.5315	NC	0.7716	NC	NC	NC
PT :Death	NC	NC	NC	NC	NC	1.0000
PT :Decreased appetite	0.9682	NC	0.9682	NC	NC	NC
PT :Decubitus ulcer	NC	NC	NC	NC	NC	1.0000
PT :Diarrhoea	0.8655	NC	0.8655	NC	NC	NC
PT :Disease progression	0.8719	0.8764	NC	NC	0.8719	NC
PT :Dyspnoea	0.7906	NC	0.8731	NC	NC	NC
PT :Echinococciasis	NC	NC	NC	NC	NC	1.0000
PT :Fatigue	0.0316	NC	0.0164	NC	NC	NC
PT :Febrile neutropenia	0.9996	0.9304	NC	0.9996	0.9996	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	1.0000
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	NC
PT :Headache	0.9205	NC	0.9205	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	1.0000
PT :Hypertension	0.9879	NC	NC	NC	NC	NC
PT :Influenza	0.2237	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Infusion related reaction	0.8944	NC	0.8941	NC	NC	NC
PT :Insomnia	0.6397	NC	0.7958	NC	NC	NC
PT :Lower respiratory tract infection	0.9956	NC	NC	0.9990	0.9990	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	NC
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	1.0000
PT :Metastases to liver	NC	NC	NC	NC	NC	1.0000
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	1.0000
PT :Muscle spasms	0.9973	NC	0.9776	NC	NC	NC
PT :Muscular weakness	0.9605	NC	0.9999	NC	NC	NC
PT :Musculoskeletal chest pain	0.8712	NC	0.8712	NC	NC	NC
PT :Myalgia	0.3113	NC	0.3113	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	1.0000
PT :Myocardial infarction	NC	NC	NC	NC	NC	1.0000
PT :Nasopharyngitis	0.9234	NC	0.9234	NC	NC	NC
PT :Nausea	0.7587	NC	0.7587	NC	NC	NC
PT :Neutropenia	0.4720	NC	NC	0.4758	0.4631	1.0000
PT :Oedema peripheral	0.4471	NC	0.4471	NC	NC	NC
PT :Oropharyngeal pain	0.4248	NC	0.4248	NC	NC	NC
PT :Pain in extremity	0.7490	NC	0.7490	NC	NC	NC
PT :Pathological fracture	0.6670	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Peripheral sensory neuropathy	0.6741	NC	0.6806	NC	NC	NC
PT :Pneumonia	0.4230	0.3348	0.4982	0.6042	0.6042	1.0000
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	1.0000
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	1.0000
PT :Pruritus	0.9095	NC	0.9095	NC	NC	NC
PT :Pyoderma	NC	NC	NC	NC	NC	1.0000
PT :Pyrexia	0.8725	NC	0.8582	NC	NC	NC
PT :Rash	0.9999	NC	0.9999	NC	NC	NC
PT :Sepsis	NC	NC	NC	NC	NC	NC
PT :Septic shock	NC	NC	NC	NC	NC	1.0000
PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	1.0000
PT :Stomatitis	0.7724	NC	NC	NC	NC	NC
PT :Sudden death	NC	NC	NC	NC	NC	1.0000
PT :Thrombocytopenia	0.0674	NC	NC	0.0889	0.0889	1.0000
PT :Tremor	0.9555	NC	NC	NC	NC	NC
PT :Upper respiratory tract infection	0.1480	NC	0.1257	NC	NC	NC
PT :Urinary tract infection	0.2744	NC	0.1637	NC	1.0000	NC
PT :Vision blurred	NC	NC	NC	NC	NC	1.0000
PT :Vomiting	0.6265	NC	0.6863	NC	NC	NC
PT :Weight decreased	1.0000	NC	1.0000	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
Cytogenetic abnormality	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	NC
	PT :Arthralgia	0.3425	NC	0.4673	NC	NC	NC
	PT :Asthenia	0.3819	NC	0.4641	NC	NC	NC
	PT :Atrial fibrillation	0.9935	NC	NC	NC	NC	NC
	PT :Atypical pneumonia	NC	NC	NC	NC	NC	0.9993
	PT :Back pain	0.2972	NC	0.2904	NC	NC	NC
	PT :Bone pain	0.4453	NC	0.7349	NC	NC	NC
	PT :Bronchitis	0.4214	NC	0.5423	NC	NC	NC
	PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	0.9993
	PT :Cataract	0.9903	NC	NC	NC	NC	NC
	PT :Cerebellar infarction	NC	NC	NC	NC	NC	0.9993
	PT :Constipation	0.9222	NC	0.9222	NC	NC	NC
	PT :Cough	0.0303	NC	0.0449	NC	NC	NC
	PT :Death	NC	NC	NC	NC	NC	0.9954
	PT :Decreased appetite	0.5445	NC	0.5445	NC	NC	NC
	PT :Decubitus ulcer	NC	NC	NC	NC	NC	0.9993
	PT :Diarrhoea	0.8702	NC	0.8702	NC	NC	NC
	PT :Disease progression	0.2463	0.0910	NC	NC	0.2463	NC
	PT :Dyspnoea	0.1879	NC	0.2303	NC	NC	NC
	PT :Echinococciasis	NC	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Fatigue	0.4385	NC	0.3399	NC	NC	NC
PT :Febrile neutropenia	0.9902	0.9999	NC	0.9902	0.9902	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	0.9993
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	NC
PT :Headache	0.8209	NC	0.8209	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	0.9993
PT :Hypertension	0.4317	NC	NC	NC	NC	NC
PT :Influenza	0.6886	NC	NC	NC	NC	NC
PT :Infusion related reaction	0.5398	NC	0.4241	NC	NC	NC
PT :Insomnia	0.9054	NC	0.7924	NC	NC	NC
PT :Lower respiratory tract infection	0.6494	NC	NC	0.9925	0.9925	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	NC
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	0.9993
PT :Metastases to liver	NC	NC	NC	NC	NC	0.9993
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	0.9993
PT :Muscle spasms	0.2083	NC	0.2410	NC	NC	NC
PT :Muscular weakness	0.9911	NC	0.9914	NC	NC	NC
PT :Musculoskeletal chest pain	0.9906	NC	0.9906	NC	NC	NC
PT :Myalgia	0.9934	NC	0.9934	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Myocardial infarction	NC	NC	NC	NC	NC	NC
PT :Nasopharyngitis	0.6324	NC	0.6324	NC	NC	NC
PT :Nausea	0.0775	NC	0.0775	NC	NC	NC
PT :Neutropenia	0.9339	NC	NC	0.7666	0.6194	NC
PT :Oedema peripheral	0.7322	NC	0.7322	NC	NC	NC
PT :Oropharyngeal pain	0.7656	NC	0.7656	NC	NC	NC
PT :Pain in extremity	0.9937	NC	0.9937	NC	NC	NC
PT :Pathological fracture	0.9999	NC	NC	NC	NC	NC
PT :Peripheral sensory neuropathy	0.8529	NC	0.8272	NC	NC	NC
PT :Pneumonia	0.7202	0.8775	0.9911	0.5189	0.5189	0.9965
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	0.9993
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	0.9993
PT :Pruritus	0.2987	NC	0.2987	NC	NC	NC
PT :Pyoderma	NC	NC	NC	NC	NC	0.9993
PT :Pyrexia	0.3277	NC	0.3315	NC	NC	NC
PT :Rash	0.8980	NC	0.8980	NC	NC	NC
PT :Sepsis	NC	NC	NC	NC	NC	NC
PT :Septic shock	NC	NC	NC	NC	NC	0.9989
PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	0.9994
PT :Stomatitis	0.9931	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
	PT :Sudden death	NC	NC	NC	NC	NC	0.9994
	PT :Thrombocytopenia	0.5189	NC	NC	0.5941	0.5941	0.9954
	PT :Tremor	0.4593	NC	NC	NC	NC	NC
	PT :Upper respiratory tract infection	0.9509	NC	0.6736	NC	NC	NC
	PT :Urinary tract infection	0.4142	NC	0.3860	NC	0.9786	NC
	PT :Vision blurred	NC	NC	NC	NC	NC	NC
	PT :Vomiting	0.3431	NC	0.4576	NC	NC	NC
	PT :Weight decreased	0.9939	NC	0.9939	NC	NC	NC
Cytogenetic abnormality del(17p)	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	NC
	PT :Arthralgia	0.4125	NC	0.7656	NC	NC	NC
	PT :Asthenia	0.5975	NC	0.7920	NC	NC	NC
	PT :Atrial fibrillation	0.9924	NC	NC	NC	NC	NC
	PT :Atypical pneumonia	NC	NC	NC	NC	NC	0.9995
	PT :Back pain	0.9375	NC	0.5893	NC	NC	NC
	PT :Bone pain	0.9902	NC	1.0000	NC	NC	NC
	PT :Bronchitis	0.9275	NC	0.9385	NC	NC	NC
	PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	0.9994
	PT :Cataract	0.9890	NC	NC	NC	NC	NC
	PT :Cerebellar infarction	NC	NC	NC	NC	NC	0.9994
	PT :Constipation	0.2122	NC	0.2122	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Cough	0.3907	NC	0.4689	NC	NC	NC
PT :Death	NC	NC	NC	NC	NC	0.9951
PT :Decreased appetite	0.7193	NC	0.7193	NC	NC	NC
PT :Decubitus ulcer	NC	NC	NC	NC	NC	0.9994
PT :Diarrhoea	0.7376	NC	0.7376	NC	NC	NC
PT :Disease progression	0.4878	0.2061	NC	NC	0.4878	NC
PT :Dyspnoea	0.9898	NC	0.9903	NC	NC	NC
PT :Echinococciasis	NC	NC	NC	NC	NC	NC
PT :Fatigue	0.8544	NC	0.9520	NC	NC	NC
PT :Febrile neutropenia	0.9926	0.9999	NC	0.9926	0.9926	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	0.9995
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	NC
PT :Headache	0.6394	NC	0.6394	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	0.9995
PT :Hypertension	0.3682	NC	NC	NC	NC	NC
PT :Influenza	0.9906	NC	NC	NC	NC	NC
PT :Infusion related reaction	0.9900	NC	0.9906	NC	NC	NC
PT :Insomnia	0.7436	NC	0.6794	NC	NC	NC
PT :Lower respiratory tract infection	0.7599	NC	NC	0.9913	0.9913	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	0.9995

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	0.9994
PT :Metastases to liver	NC	NC	NC	NC	NC	0.9995
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	0.9995
PT :Muscle spasms	0.6976	NC	0.7531	NC	NC	NC
PT :Muscular weakness	0.9935	NC	0.9936	NC	NC	NC
PT :Musculoskeletal chest pain	0.9931	NC	0.9931	NC	NC	NC
PT :Myalgia	0.9922	NC	0.9922	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	0.9995
PT :Myocardial infarction	NC	NC	NC	NC	NC	NC
PT :Nasopharyngitis	0.9873	NC	0.9873	NC	NC	NC
PT :Nausea	0.9897	NC	0.9897	NC	NC	NC
PT :Neutropenia	0.5631	NC	NC	0.5351	0.7480	NC
PT :Oedema peripheral	0.7564	NC	0.7564	NC	NC	NC
PT :Oropharyngeal pain	0.9914	NC	0.9914	NC	NC	NC
PT :Pain in extremity	0.9997	NC	0.9997	NC	NC	NC
PT :Pathological fracture	0.9999	NC	NC	NC	NC	NC
PT :Peripheral sensory neuropathy	0.7707	NC	0.8018	NC	NC	NC
PT :Pneumonia	0.5125	0.3573	0.9892	0.7227	0.7227	0.9950
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	0.9999
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	0.9995

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
	PT :Pruritus	1.0000	NC	1.0000	NC	NC	NC
	PT :Pyoderma	NC	NC	NC	NC	NC	0.9995
	PT :Pyrexia	0.8591	NC	0.9137	NC	NC	NC
	PT :Rash	0.9592	NC	0.9592	NC	NC	NC
	PT :Sepsis	NC	NC	NC	NC	NC	0.9995
	PT :Septic shock	NC	NC	NC	NC	NC	0.9992
	PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	0.9995
	PT :Stomatitis	0.9946	NC	NC	NC	NC	NC
	PT :Sudden death	NC	NC	NC	NC	NC	0.9995
	PT :Thrombocytopenia	0.9877	NC	NC	0.9458	0.9458	0.9951
	PT :Tremor	0.9910	NC	NC	NC	NC	NC
	PT :Upper respiratory tract infection	0.6087	NC	0.3039	NC	NC	NC
	PT :Urinary tract infection	0.2081	NC	0.2706	NC	0.9522	NC
	PT :Vision blurred	NC	NC	NC	NC	NC	NC
	PT :Vomiting	0.9527	NC	0.9999	NC	NC	NC
	PT :Weight decreased	0.9927	NC	0.9927	NC	NC	NC
Previous autologous stem-cell transplantation	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	0.9994
	PT :Arthralgia	0.1238	NC	0.1808	NC	NC	NC
	PT :Asthenia	0.8976	NC	0.7055	NC	NC	NC
	PT :Atrial fibrillation	0.9906	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Atypical pneumonia	NC	NC	NC	NC	NC	0.9993
PT :Back pain	0.3864	NC	0.6708	NC	NC	NC
PT :Bone pain	0.5796	NC	0.5749	NC	NC	NC
PT :Bronchitis	0.4718	NC	0.5283	NC	NC	NC
PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	0.9991
PT :Cataract	0.5819	NC	NC	NC	NC	NC
PT :Cerebellar infarction	NC	NC	NC	NC	NC	0.9993
PT :Constipation	0.5675	NC	0.5675	NC	NC	NC
PT :Cough	0.3312	NC	0.4142	NC	NC	NC
PT :Death	NC	NC	NC	NC	NC	0.9957
PT :Decreased appetite	0.3279	NC	0.3279	NC	NC	NC
PT :Decubitus ulcer	NC	NC	NC	NC	NC	0.9991
PT :Diarrhoea	0.5507	NC	0.7220	NC	NC	NC
PT :Disease progression	0.4021	0.7012	NC	NC	0.4021	NC
PT :Dyspnoea	0.3537	NC	0.0946	NC	NC	NC
PT :Echinococciasis	NC	NC	NC	NC	NC	0.9993
PT :Fatigue	0.8713	NC	0.7705	NC	NC	NC
PT :Febrile neutropenia	0.4975	0.6265	NC	0.4975	0.4975	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	0.9994
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	0.9992

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Headache	0.1128	NC	0.1128	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	0.9991
PT :Hypertension	0.0622	NC	NC	NC	NC	NC
PT :Influenza	0.8597	NC	NC	NC	NC	NC
PT :Infusion related reaction	0.9836	NC	0.9840	NC	NC	NC
PT :Insomnia	0.2874	NC	0.3388	NC	NC	NC
PT :Lower respiratory tract infection	0.7198	NC	NC	0.5772	0.5772	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	0.9994
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	0.9993
PT :Metastases to liver	NC	NC	NC	NC	NC	0.9994
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	0.9991
PT :Muscle spasms	0.5061	NC	0.6260	NC	NC	NC
PT :Muscular weakness	0.9106	NC	0.9080	NC	NC	NC
PT :Musculoskeletal chest pain	0.1362	NC	0.1362	NC	NC	NC
PT :Myalgia	0.8979	NC	0.8979	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	0.9993
PT :Myocardial infarction	NC	NC	NC	NC	NC	0.9994
PT :Nasopharyngitis	0.4785	NC	0.4785	NC	NC	NC
PT :Nausea	0.2236	NC	0.2236	NC	NC	NC
PT :Neutropenia	0.9595	NC	NC	0.9565	0.9795	1.0000

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Oedema peripheral	0.1402	NC	0.1402	NC	NC	NC
PT :Oropharyngeal pain	0.9896	NC	0.9896	NC	NC	NC
PT :Pain in extremity	0.3181	NC	0.3181	NC	NC	NC
PT :Pathological fracture	0.9575	NC	NC	NC	NC	NC
PT :Peripheral sensory neuropathy	0.6630	NC	0.6584	NC	NC	NC
PT :Pneumonia	0.7103	0.9077	0.4801	0.6305	0.6305	0.9952
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	0.9993
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	0.9993
PT :Pruritus	0.2765	NC	0.2765	NC	NC	NC
PT :Pyoderma	NC	NC	NC	NC	NC	0.9994
PT :Pyrexia	0.3837	NC	0.8540	NC	NC	NC
PT :Rash	0.3516	NC	0.3516	NC	NC	NC
PT :Sepsis	NC	NC	NC	NC	NC	0.9993
PT :Septic shock	NC	NC	NC	NC	NC	0.9990
PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	0.9993
PT :Stomatitis	0.5579	NC	NC	NC	NC	NC
PT :Sudden death	NC	NC	NC	NC	NC	0.9993
PT :Thrombocytopenia	0.6396	NC	NC	0.7698	0.7698	0.9923
PT :Tremor	0.0768	NC	NC	NC	NC	NC
PT :Upper respiratory tract infection	0.6420	NC	0.7782	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
	PT :Urinary tract infection	0.2547	NC	0.1376	NC	0.8013	NC
	PT :Vision blurred	NC	NC	NC	NC	NC	0.9992
	PT :Vomiting	0.3174	NC	0.2765	NC	NC	NC
	PT :Weight decreased	0.9937	NC	0.9937	NC	NC	NC
Previous allogenic transplantation	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	0.9998
	PT :Arthralgia	0.9905	NC	0.9903	NC	NC	NC
	PT :Asthenia	0.9999	NC	0.9999	NC	NC	NC
	PT :Atrial fibrillation	0.9997	NC	NC	NC	NC	NC
	PT :Atypical pneumonia	NC	NC	NC	NC	NC	0.9998
	PT :Back pain	0.9842	NC	1.0000	NC	NC	NC
	PT :Bone pain	1.0000	NC	0.9999	NC	NC	NC
	PT :Bronchitis	0.5051	NC	0.5642	NC	NC	NC
	PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	0.9998
	PT :Cataract	0.9999	NC	NC	NC	NC	NC
	PT :Cerebellar infarction	NC	NC	NC	NC	NC	0.9998
	PT :Constipation	0.9833	NC	0.9833	NC	NC	NC
	PT :Cough	0.9869	NC	0.9868	NC	NC	NC
	PT :Death	NC	NC	NC	NC	NC	0.9999
	PT :Decreased appetite	0.9921	NC	0.9921	NC	NC	NC
	PT :Decubitus ulcer	NC	NC	NC	NC	NC	0.9998

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Diarrhoea	0.7672	NC	0.7838	NC	NC	NC
PT :Disease progression	0.9899	0.9924	NC	NC	0.9899	NC
PT :Dyspnoea	0.9888	NC	0.9893	NC	NC	NC
PT :Echinococciasis	NC	NC	NC	NC	NC	0.9998
PT :Fatigue	0.9999	NC	0.9998	NC	NC	NC
PT :Febrile neutropenia	0.9996	0.9998	NC	0.9996	0.9996	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	0.9998
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	0.9998
PT :Headache	0.9919	NC	0.9919	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	0.9998
PT :Hypertension	0.9999	NC	NC	NC	NC	NC
PT :Influenza	0.9885	NC	NC	NC	NC	NC
PT :Infusion related reaction	0.9900	NC	0.9901	NC	NC	NC
PT :Insomnia	0.9905	NC	0.9907	NC	NC	NC
PT :Lower respiratory tract infection	0.7007	NC	NC	0.4794	0.4794	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	0.9998
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	0.9998
PT :Metastases to liver	NC	NC	NC	NC	NC	0.9998
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	0.9998
PT :Muscle spasms	0.9901	NC	0.9901	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Muscular weakness	0.9923	NC	0.9923	NC	NC	NC
PT :Musculoskeletal chest pain	0.9882	NC	0.9882	NC	NC	NC
PT :Myalgia	0.9998	NC	0.9998	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	0.9998
PT :Myocardial infarction	NC	NC	NC	NC	NC	NC
PT :Nasopharyngitis	0.9997	NC	0.9997	NC	NC	NC
PT :Nausea	0.9998	NC	0.9998	NC	NC	NC
PT :Neutropenia	0.9740	NC	NC	0.9746	0.9745	0.9997
PT :Oedema peripheral	0.9998	NC	0.9998	NC	NC	NC
PT :Oropharyngeal pain	0.9998	NC	0.9998	NC	NC	NC
PT :Pain in extremity	0.9929	NC	0.9929	NC	NC	NC
PT :Pathological fracture	0.6463	NC	NC	NC	NC	NC
PT :Peripheral sensory neuropathy	0.9999	NC	0.9999	NC	NC	NC
PT :Pneumonia	0.9394	0.9821	0.7908	0.9821	0.9821	0.9999
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	0.9998
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	0.9998
PT :Pruritus	0.9914	NC	0.9914	NC	NC	NC
PT :Pyoderma	NC	NC	NC	NC	NC	0.9998
PT :Pyrexia	0.9880	NC	0.9884	NC	NC	NC
PT :Rash	0.9999	NC	0.9999	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
	PT :Sepsis	NC	NC	NC	NC	NC	0.9998
	PT :Septic shock	NC	NC	NC	NC	NC	0.9997
	PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	0.9998
	PT :Stomatitis	0.9998	NC	NC	NC	NC	NC
	PT :Sudden death	NC	NC	NC	NC	NC	0.9998
	PT :Thrombocytopenia	1.0000	NC	NC	1.0000	1.0000	0.9997
	PT :Tremor	0.9998	NC	NC	NC	NC	NC
	PT :Upper respiratory tract infection	0.0071	NC	0.0050	NC	NC	NC
	PT :Urinary tract infection	0.9999	NC	1.0000	NC	0.9997	NC
	PT :Vision blurred	NC	NC	NC	NC	NC	0.9998
	PT :Vomiting	0.9996	NC	0.9996	NC	NC	NC
	PT :Weight decreased	0.9995	NC	0.9995	NC	NC	NC
MM type	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	0.9992
	PT :Arthralgia	0.2402	NC	0.3099	NC	NC	NC
	PT :Asthenia	0.8346	NC	0.8723	NC	NC	NC
	PT :Atrial fibrillation	0.9917	NC	NC	NC	NC	NC
	PT :Atypical pneumonia	NC	NC	NC	NC	NC	0.9992
	PT :Back pain	0.9592	NC	0.8198	NC	NC	NC
	PT :Bone pain	0.6007	NC	0.7969	NC	NC	NC
	PT :Bronchitis	0.9089	NC	0.9317	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	0.9992
PT :Cataract	0.8444	NC	NC	NC	NC	NC
PT :Cerebellar infarction	NC	NC	NC	NC	NC	0.9992
PT :Constipation	0.1008	NC	0.1008	NC	NC	NC
PT :Cough	0.1121	NC	0.0616	NC	NC	NC
PT :Death	NC	NC	NC	NC	NC	0.9964
PT :Decreased appetite	0.9962	NC	0.9962	NC	NC	NC
PT :Decubitus ulcer	NC	NC	NC	NC	NC	0.9992
PT :Diarrhoea	0.5680	NC	0.4932	NC	NC	NC
PT :Disease progression	0.5571	0.9619	NC	NC	0.5571	NC
PT :Dyspnoea	0.1399	NC	0.3760	NC	NC	NC
PT :Echinococciasis	NC	NC	NC	NC	NC	0.9993
PT :Fatigue	0.3337	NC	0.2131	NC	NC	NC
PT :Febrile neutropenia	0.3155	0.5115	NC	0.3155	0.3155	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	0.9992
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	0.9993
PT :Headache	0.9252	NC	0.9252	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	0.9992
PT :Hypertension	0.5225	NC	NC	NC	NC	NC
PT :Influenza	0.4056	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Infusion related reaction	0.9829	NC	0.9835	NC	NC	NC
PT :Insomnia	0.0243	NC	0.0290	NC	NC	NC
PT :Lower respiratory tract infection	0.9929	NC	NC	0.5931	0.5931	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	0.9994
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	0.9992
PT :Metastases to liver	NC	NC	NC	NC	NC	0.9992
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	0.9992
PT :Muscle spasms	0.0426	NC	0.0674	NC	NC	NC
PT :Muscular weakness	0.9088	NC	0.9738	NC	NC	NC
PT :Musculoskeletal chest pain	0.7716	NC	0.7716	NC	NC	NC
PT :Myalgia	0.8091	NC	0.8091	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	0.9992
PT :Myocardial infarction	NC	NC	NC	NC	NC	0.9993
PT :Nasopharyngitis	0.7868	NC	0.7868	NC	NC	NC
PT :Nausea	0.2473	NC	0.2473	NC	NC	NC
PT :Neutropenia	0.5934	NC	NC	0.5931	0.5225	0.9990
PT :Oedema peripheral	0.8880	NC	0.8880	NC	NC	NC
PT :Oropharyngeal pain	0.2523	NC	0.2523	NC	NC	NC
PT :Pain in extremity	0.9354	NC	0.9354	NC	NC	NC
PT :Pathological fracture	0.0496	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Peripheral sensory neuropathy	0.7880	NC	0.7956	NC	NC	NC
PT :Pneumonia	0.1053	0.1137	0.9868	0.2337	0.2337	0.9942
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	0.9992
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	0.9993
PT :Pruritus	0.9623	NC	0.9623	NC	NC	NC
PT :Pyoderma	NC	NC	NC	NC	NC	0.9992
PT :Pyrexia	0.6380	NC	0.6103	NC	NC	NC
PT :Rash	0.3444	NC	0.3444	NC	NC	NC
PT :Sepsis	NC	NC	NC	NC	NC	0.9992
PT :Septic shock	NC	NC	NC	NC	NC	0.9990
PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	0.9993
PT :Stomatitis	0.5057	NC	NC	NC	NC	NC
PT :Sudden death	NC	NC	NC	NC	NC	0.9993
PT :Thrombocytopenia	0.6453	NC	NC	0.5580	0.5580	0.9937
PT :Tremor	0.3132	NC	NC	NC	NC	NC
PT :Upper respiratory tract infection	0.0023	NC	0.0013	NC	NC	NC
PT :Urinary tract infection	0.2097	NC	0.3468	NC	0.9924	NC
PT :Vision blurred	NC	NC	NC	NC	NC	0.9993
PT :Vomiting	0.3093	NC	0.2749	NC	NC	NC
PT :Weight decreased	0.9942	NC	0.9942	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
Existing plasmacytoma	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	0.9995
	PT :Arthralgia	0.7387	NC	0.6132	NC	NC	NC
	PT :Asthenia	0.9847	NC	0.9854	NC	NC	NC
	PT :Atrial fibrillation	0.9998	NC	NC	NC	NC	NC
	PT :Atypical pneumonia	NC	NC	NC	NC	NC	0.9995
	PT :Back pain	0.9027	NC	0.8745	NC	NC	NC
	PT :Bone pain	0.9902	NC	0.9911	NC	NC	NC
	PT :Bronchitis	0.6778	NC	0.7395	NC	NC	NC
	PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	0.9995
	PT :Cataract	0.9885	NC	NC	NC	NC	NC
	PT :Cerebellar infarction	NC	NC	NC	NC	NC	0.9996
	PT :Constipation	0.2724	NC	0.2724	NC	NC	NC
	PT :Cough	0.9881	NC	0.9882	NC	NC	NC
	PT :Death	NC	NC	NC	NC	NC	0.9999
	PT :Decreased appetite	0.4898	NC	0.4898	NC	NC	NC
	PT :Decubitus ulcer	NC	NC	NC	NC	NC	0.9995
	PT :Diarrhoea	0.8262	NC	0.7956	NC	NC	NC
	PT :Disease progression	1.0000	1.0000	NC	NC	1.0000	NC
	PT :Dyspnoea	0.7336	NC	0.9226	NC	NC	NC
	PT :Echinococciasis	NC	NC	NC	NC	NC	0.9995

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Fatigue	0.2429	NC	0.2869	NC	NC	NC
PT :Febrile neutropenia	0.9910	0.9998	NC	0.9910	0.9910	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	0.9996
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	0.9996
PT :Headache	0.9903	NC	0.9903	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	0.9995
PT :Hypertension	0.8108	NC	NC	NC	NC	NC
PT :Influenza	0.9999	NC	NC	NC	NC	NC
PT :Infusion related reaction	0.9881	NC	0.9883	NC	NC	NC
PT :Insomnia	0.6212	NC	0.6672	NC	NC	NC
PT :Lower respiratory tract infection	0.2266	NC	NC	0.4784	0.4784	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	0.9995
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	0.9996
PT :Metastases to liver	NC	NC	NC	NC	NC	0.9996
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	0.9995
PT :Muscle spasms	0.9887	NC	0.9888	NC	NC	NC
PT :Muscular weakness	0.9912	NC	0.9913	NC	NC	NC
PT :Musculoskeletal chest pain	0.9889	NC	0.9889	NC	NC	NC
PT :Myalgia	0.9998	NC	0.9998	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	0.9995

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Myocardial infarction	NC	NC	NC	NC	NC	0.9996
PT :Nasopharyngitis	0.9902	NC	0.9902	NC	NC	NC
PT :Nausea	0.9857	NC	0.9857	NC	NC	NC
PT :Neutropenia	0.6888	NC	NC	0.6793	0.6615	0.9993
PT :Oedema peripheral	0.5076	NC	0.5076	NC	NC	NC
PT :Oropharyngeal pain	0.9928	NC	0.9928	NC	NC	NC
PT :Pain in extremity	0.9928	NC	0.9928	NC	NC	NC
PT :Pathological fracture	0.8837	NC	NC	NC	NC	NC
PT :Peripheral sensory neuropathy	0.9883	NC	0.9883	NC	NC	NC
PT :Pneumonia	0.2530	0.4338	1.0000	0.2551	0.2551	0.9999
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	0.9995
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	0.9995
PT :Pruritus	0.9899	NC	0.9899	NC	NC	NC
PT :Pyoderma	NC	NC	NC	NC	NC	0.9996
PT :Pyrexia	0.1511	NC	0.1427	NC	NC	NC
PT :Rash	0.9999	NC	0.9999	NC	NC	NC
PT :Sepsis	NC	NC	NC	NC	NC	0.9995
PT :Septic shock	NC	NC	NC	NC	NC	0.9993
PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	0.9995
PT :Stomatitis	0.3800	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
	PT :Sudden death	NC	NC	NC	NC	NC	1.0000
	PT :Thrombocytopenia	0.9864	NC	NC	0.9865	0.9865	0.9997
	PT :Tremor	0.9999	NC	NC	NC	NC	NC
	PT :Upper respiratory tract infection	0.0690	NC	0.0673	NC	NC	NC
	PT :Urinary tract infection	0.9889	NC	1.0000	NC	0.9944	NC
	PT :Vision blurred	NC	NC	NC	NC	NC	0.9996
	PT :Vomiting	0.3367	NC	0.3588	NC	NC	NC
	PT :Weight decreased	0.9946	NC	0.9946	NC	NC	NC
Baseline creatinine clearance	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	0.9993
	PT :Arthralgia	0.1812	NC	0.0360	NC	NC	NC
	PT :Asthenia	0.4131	NC	0.6677	NC	NC	NC
	PT :Atrial fibrillation	0.5204	NC	NC	NC	NC	NC
	PT :Atypical pneumonia	NC	NC	NC	NC	NC	0.9993
	PT :Back pain	0.3089	NC	0.5395	NC	NC	NC
	PT :Bone pain	0.3566	NC	0.3870	NC	NC	NC
	PT :Bronchitis	0.1723	NC	0.2986	NC	NC	NC
	PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	0.9993
	PT :Cataract	0.8894	NC	NC	NC	NC	NC
	PT :Cerebellar infarction	NC	NC	NC	NC	NC	0.9993
	PT :Constipation	0.4133	NC	0.4133	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Cough	0.8841	NC	0.9036	NC	NC	NC
PT :Death	NC	NC	NC	NC	NC	0.9959
PT :Decreased appetite	0.4348	NC	0.4348	NC	NC	NC
PT :Decubitus ulcer	NC	NC	NC	NC	NC	0.9993
PT :Diarrhoea	0.2303	NC	0.3121	NC	NC	NC
PT :Disease progression	0.0560	0.0415	NC	NC	0.0560	NC
PT :Dyspnoea	0.2075	NC	0.6698	NC	NC	NC
PT :Echinococciasis	NC	NC	NC	NC	NC	0.9993
PT :Fatigue	0.2840	NC	0.4805	NC	NC	NC
PT :Febrile neutropenia	0.6015	0.5471	NC	0.6015	0.6015	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	0.9993
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	0.9994
PT :Headache	0.7950	NC	0.7950	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	0.9993
PT :Hypertension	0.2897	NC	NC	NC	NC	NC
PT :Influenza	0.9119	NC	NC	NC	NC	NC
PT :Infusion related reaction	0.5118	NC	0.5438	NC	NC	NC
PT :Insomnia	0.8426	NC	0.9825	NC	NC	NC
PT :Lower respiratory tract infection	0.8449	NC	NC	0.8528	0.8528	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	0.9994

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	0.9993
PT :Metastases to liver	NC	NC	NC	NC	NC	0.9993
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	0.9993
PT :Muscle spasms	0.3337	NC	0.2127	NC	NC	NC
PT :Muscular weakness	0.6042	NC	0.7501	NC	NC	NC
PT :Musculoskeletal chest pain	0.7657	NC	0.7657	NC	NC	NC
PT :Myalgia	0.4203	NC	0.4203	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	0.9993
PT :Myocardial infarction	NC	NC	NC	NC	NC	0.9993
PT :Nasopharyngitis	0.6751	NC	0.6751	NC	NC	NC
PT :Nausea	0.0658	NC	0.0658	NC	NC	NC
PT :Neutropenia	0.1845	NC	NC	0.2095	0.2095	0.9999
PT :Oedema peripheral	0.6337	NC	0.6337	NC	NC	NC
PT :Oropharyngeal pain	0.5862	NC	0.5862	NC	NC	NC
PT :Pain in extremity	0.6203	NC	0.6203	NC	NC	NC
PT :Pathological fracture	0.6391	NC	NC	NC	NC	NC
PT :Peripheral sensory neuropathy	0.3573	NC	0.3587	NC	NC	NC
PT :Pneumonia	0.6977	0.6203	0.4085	0.5576	0.5576	0.6101
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	0.9993
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	0.9992

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
	PT :Pruritus	0.5115	NC	0.5115	NC	NC	NC
	PT :Pyoderma	NC	NC	NC	NC	NC	0.9993
	PT :Pyrexia	0.8374	NC	0.3710	NC	NC	NC
	PT :Rash	0.4150	NC	0.4150	NC	NC	NC
	PT :Sepsis	NC	NC	NC	NC	NC	0.9993
	PT :Septic shock	NC	NC	NC	NC	NC	0.9999
	PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	0.9993
	PT :Stomatitis	0.9826	NC	NC	NC	NC	NC
	PT :Sudden death	NC	NC	NC	NC	NC	0.9993
	PT :Thrombocytopenia	0.4303	NC	NC	0.5199	0.5199	0.9935
	PT :Tremor	0.2714	NC	NC	NC	NC	NC
	PT :Upper respiratory tract infection	0.8686	NC	0.7380	NC	NC	NC
	PT :Urinary tract infection	0.0772	NC	0.1350	NC	0.9934	NC
	PT :Vision blurred	NC	NC	NC	NC	NC	0.9993
	PT :Vomiting	0.3028	NC	0.2269	NC	NC	NC
	PT :Weight decreased	0.9941	NC	0.9941	NC	NC	NC
Previous therapy with anti-CD38 mAB	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	NC
	PT :Arthralgia	0.9892	NC	0.9999	NC	NC	NC
	PT :Asthenia	0.9860	NC	0.9863	NC	NC	NC
	PT :Atrial fibrillation	0.9998	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Atypical pneumonia	NC	NC	NC	NC	NC	0.9998
PT :Back pain	0.5945	NC	0.9829	NC	NC	NC
PT :Bone pain	1.0000	NC	0.9999	NC	NC	NC
PT :Bronchitis	0.9880	NC	0.9882	NC	NC	NC
PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	0.9998
PT :Cataract	1.0000	NC	NC	NC	NC	NC
PT :Cerebellar infarction	NC	NC	NC	NC	NC	NC
PT :Constipation	0.9999	NC	0.9999	NC	NC	NC
PT :Cough	1.0000	NC	0.9999	NC	NC	NC
PT :Death	NC	NC	NC	NC	NC	0.9999
PT :Decreased appetite	0.9998	NC	0.9998	NC	NC	NC
PT :Decubitus ulcer	NC	NC	NC	NC	NC	0.9998
PT :Diarrhoea	0.9806	NC	0.9808	NC	NC	NC
PT :Disease progression	1.0000	1.0000	NC	NC	1.0000	NC
PT :Dyspnoea	0.9998	NC	0.9998	NC	NC	NC
PT :Echinococciasis	NC	NC	NC	NC	NC	NC
PT :Fatigue	0.9999	NC	0.9998	NC	NC	NC
PT :Febrile neutropenia	0.9996	0.9998	NC	0.9996	0.9996	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	NC
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Headache	0.9901	NC	0.9901	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	0.9998
PT :Hypertension	0.9999	NC	NC	NC	NC	NC
PT :Influenza	0.9999	NC	NC	NC	NC	NC
PT :Infusion related reaction	0.9985	NC	0.9986	NC	NC	NC
PT :Insomnia	1.0000	NC	1.0000	NC	NC	NC
PT :Lower respiratory tract infection	1.0000	NC	NC	0.9999	0.9999	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	NC
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	NC
PT :Metastases to liver	NC	NC	NC	NC	NC	NC
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	0.9998
PT :Muscle spasms	1.0000	NC	0.9999	NC	NC	NC
PT :Muscular weakness	0.9999	NC	0.9999	NC	NC	NC
PT :Musculoskeletal chest pain	0.9895	NC	0.9895	NC	NC	NC
PT :Myalgia	0.9998	NC	0.9998	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	NC
PT :Myocardial infarction	NC	NC	NC	NC	NC	NC
PT :Nasopharyngitis	0.9998	NC	0.9998	NC	NC	NC
PT :Nausea	0.9998	NC	0.9998	NC	NC	NC
PT :Neutropenia	0.9809	NC	NC	0.9813	0.9812	1.0000

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Oedema peripheral	0.9998	NC	0.9998	NC	NC	NC
PT :Oropharyngeal pain	0.9998	NC	0.9998	NC	NC	NC
PT :Pain in extremity	0.9929	NC	0.9929	NC	NC	NC
PT :Pathological fracture	0.9999	NC	NC	NC	NC	NC
PT :Peripheral sensory neuropathy	0.9999	NC	0.9999	NC	NC	NC
PT :Pneumonia	1.0000	1.0000	1.0000	1.0000	1.0000	0.9999
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	0.9998
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	NC
PT :Pruritus	0.9999	NC	0.9999	NC	NC	NC
PT :Pyoderma	NC	NC	NC	NC	NC	NC
PT :Pyrexia	0.5366	NC	0.9859	NC	NC	NC
PT :Rash	0.9999	NC	0.9999	NC	NC	NC
PT :Sepsis	NC	NC	NC	NC	NC	0.9998
PT :Septic shock	NC	NC	NC	NC	NC	0.9997
PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	0.9998
PT :Stomatitis	0.9998	NC	NC	NC	NC	NC
PT :Sudden death	NC	NC	NC	NC	NC	0.9998
PT :Thrombocytopenia	0.9858	NC	NC	0.9859	0.9859	0.9951
PT :Tremor	0.9999	NC	NC	NC	NC	NC
PT :Upper respiratory tract infection	0.9858	NC	0.9863	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
	PT :Urinary tract infection	0.9999	NC	1.0000	NC	0.9998	NC
	PT :Vision blurred	NC	NC	NC	NC	NC	NC
	PT :Vomiting	0.9997	NC	0.9997	NC	NC	NC
	PT :Weight decreased	0.9952	NC	0.9952	NC	NC	NC
Refractory to PI	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	0.9992
	PT :Arthralgia	0.5842	NC	0.3917	NC	NC	NC
	PT :Asthenia	0.5396	NC	0.4620	NC	NC	NC
	PT :Atrial fibrillation	0.3409	NC	NC	NC	NC	NC
	PT :Atypical pneumonia	NC	NC	NC	NC	NC	0.9993
	PT :Back pain	0.9021	NC	0.8451	NC	NC	NC
	PT :Bone pain	0.9902	NC	0.9907	NC	NC	NC
	PT :Bronchitis	0.4967	NC	0.4216	NC	NC	NC
	PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	0.9993
	PT :Cataract	0.8646	NC	NC	NC	NC	NC
	PT :Cerebellar infarction	NC	NC	NC	NC	NC	0.9992
	PT :Constipation	0.3354	NC	0.3354	NC	NC	NC
	PT :Cough	0.5411	NC	0.5950	NC	NC	NC
	PT :Death	NC	NC	NC	NC	NC	0.9964
	PT :Decreased appetite	0.9884	NC	0.9884	NC	NC	NC
	PT :Decubitus ulcer	NC	NC	NC	NC	NC	0.9993

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Diarrhoea	0.1099	NC	0.1325	NC	NC	NC
PT :Disease progression	0.6428	0.8791	NC	NC	0.6428	NC
PT :Dyspnoea	0.1567	NC	0.1252	NC	NC	NC
PT :Echinococciasis	NC	NC	NC	NC	NC	0.9994
PT :Fatigue	0.6255	NC	0.6483	NC	NC	NC
PT :Febrile neutropenia	0.9898	0.9913	NC	0.9898	0.9898	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	0.9992
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	0.9993
PT :Headache	0.2510	NC	0.2510	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	0.9993
PT :Hypertension	0.9903	NC	NC	NC	NC	NC
PT :Influenza	0.2586	NC	NC	NC	NC	NC
PT :Infusion related reaction	0.9873	NC	0.9875	NC	NC	NC
PT :Insomnia	0.9100	NC	0.9781	NC	NC	NC
PT :Lower respiratory tract infection	0.9242	NC	NC	0.7057	0.7057	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	0.9992
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	0.9992
PT :Metastases to liver	NC	NC	NC	NC	NC	0.9994
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	0.9993
PT :Muscle spasms	0.2755	NC	0.3115	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Muscular weakness	0.0941	NC	0.1146	NC	NC	NC
PT :Musculoskeletal chest pain	0.5757	NC	0.5757	NC	NC	NC
PT :Myalgia	0.8829	NC	0.8829	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	0.9993
PT :Myocardial infarction	NC	NC	NC	NC	NC	0.9993
PT :Nasopharyngitis	0.3894	NC	0.3894	NC	NC	NC
PT :Nausea	0.4358	NC	0.4358	NC	NC	NC
PT :Neutropenia	0.2443	NC	NC	0.3567	0.2842	0.9990
PT :Oedema peripheral	0.8026	NC	0.8026	NC	NC	NC
PT :Oropharyngeal pain	0.9912	NC	0.9912	NC	NC	NC
PT :Pain in extremity	0.9914	NC	0.9914	NC	NC	NC
PT :Pathological fracture	0.8433	NC	NC	NC	NC	NC
PT :Peripheral sensory neuropathy	0.7012	NC	0.7061	NC	NC	NC
PT :Pneumonia	0.9220	0.8158	0.6022	0.8374	0.8374	0.9949
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	0.9993
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	0.9995
PT :Pruritus	0.1572	NC	0.1572	NC	NC	NC
PT :Pyoderma	NC	NC	NC	NC	NC	0.9993
PT :Pyrexia	0.0636	NC	0.0270	NC	NC	NC
PT :Rash	0.6196	NC	0.6196	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
	PT :Sepsis	NC	NC	NC	NC	NC	0.9994
	PT :Septic shock	NC	NC	NC	NC	NC	0.9990
	PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	0.9993
	PT :Stomatitis	0.9314	NC	NC	NC	NC	NC
	PT :Sudden death	NC	NC	NC	NC	NC	0.9993
	PT :Thrombocytopenia	0.3135	NC	NC	0.2661	0.2661	0.9952
	PT :Tremor	0.9898	NC	NC	NC	NC	NC
	PT :Upper respiratory tract infection	0.8426	NC	0.8358	NC	NC	NC
	PT :Urinary tract infection	0.0425	NC	0.0660	NC	0.9934	NC
	PT :Vision blurred	NC	NC	NC	NC	NC	0.9993
	PT :Vomiting	0.2614	NC	0.2318	NC	NC	NC
	PT :Weight decreased	0.9915	NC	0.9915	NC	NC	NC
Refractory to IMiD	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	0.9995
	PT :Arthralgia	0.6762	NC	0.8006	NC	NC	NC
	PT :Asthenia	0.9881	NC	0.9887	NC	NC	NC
	PT :Atrial fibrillation	0.9056	NC	NC	NC	NC	NC
	PT :Atypical pneumonia	NC	NC	NC	NC	NC	0.9996
	PT :Back pain	0.7326	NC	0.6916	NC	NC	NC
	PT :Bone pain	1.0000	NC	0.9999	NC	NC	NC
	PT :Bronchitis	0.9868	NC	0.9995	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	0.9996
PT :Cataract	0.9900	NC	NC	NC	NC	NC
PT :Cerebellar infarction	NC	NC	NC	NC	NC	0.9995
PT :Constipation	0.9859	NC	0.9859	NC	NC	NC
PT :Cough	0.9916	NC	0.9917	NC	NC	NC
PT :Death	NC	NC	NC	NC	NC	0.9999
PT :Decreased appetite	0.9997	NC	0.9997	NC	NC	NC
PT :Decubitus ulcer	NC	NC	NC	NC	NC	0.9996
PT :Diarrhoea	0.5266	NC	0.5010	NC	NC	NC
PT :Disease progression	0.8252	0.8250	NC	NC	0.8252	NC
PT :Dyspnoea	0.5301	NC	0.9283	NC	NC	NC
PT :Echinococciasis	NC	NC	NC	NC	NC	0.9996
PT :Fatigue	0.2547	NC	0.3251	NC	NC	NC
PT :Febrile neutropenia	0.9920	0.9998	NC	0.9920	0.9920	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	0.9995
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	0.9996
PT :Headache	0.7019	NC	0.7019	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	0.9996
PT :Hypertension	0.9920	NC	NC	NC	NC	NC
PT :Influenza	0.9905	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Infusion related reaction	0.9875	NC	0.9876	NC	NC	NC
PT :Insomnia	0.6918	NC	0.6404	NC	NC	NC
PT :Lower respiratory tract infection	0.9908	NC	NC	0.9998	0.9998	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	0.9996
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	0.9995
PT :Metastases to liver	NC	NC	NC	NC	NC	0.9995
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	0.9996
PT :Muscle spasms	0.9902	NC	0.9905	NC	NC	NC
PT :Muscular weakness	0.9915	NC	0.9875	NC	NC	NC
PT :Musculoskeletal chest pain	0.9998	NC	0.9998	NC	NC	NC
PT :Myalgia	0.9930	NC	0.9930	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	0.9996
PT :Myocardial infarction	NC	NC	NC	NC	NC	0.9997
PT :Nasopharyngitis	0.7875	NC	0.7875	NC	NC	NC
PT :Nausea	0.9839	NC	0.9839	NC	NC	NC
PT :Neutropenia	0.5943	NC	NC	0.5840	0.5689	0.9994
PT :Oedema peripheral	0.4289	NC	0.4289	NC	NC	NC
PT :Oropharyngeal pain	0.9929	NC	0.9929	NC	NC	NC
PT :Pain in extremity	0.9927	NC	0.9927	NC	NC	NC
PT :Pathological fracture	0.9999	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Peripheral sensory neuropathy	0.9863	NC	0.9594	NC	NC	NC
PT :Pneumonia	0.8349	0.8060	0.9910	0.7920	0.7920	0.9999
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	0.9996
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	0.9996
PT :Pruritus	0.9890	NC	0.9890	NC	NC	NC
PT :Pyoderma	NC	NC	NC	NC	NC	0.9996
PT :Pyrexia	0.6720	NC	0.6639	NC	NC	NC
PT :Rash	0.9999	NC	0.9999	NC	NC	NC
PT :Sepsis	NC	NC	NC	NC	NC	0.9996
PT :Septic shock	NC	NC	NC	NC	NC	0.9994
PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	0.9996
PT :Stomatitis	0.9997	NC	NC	NC	NC	NC
PT :Sudden death	NC	NC	NC	NC	NC	0.9996
PT :Thrombocytopenia	1.0000	NC	NC	1.0000	1.0000	0.9996
PT :Tremor	0.9886	NC	NC	NC	NC	NC
PT :Upper respiratory tract infection	0.3628	NC	0.3611	NC	NC	NC
PT :Urinary tract infection	0.5543	NC	0.7015	NC	0.9997	NC
PT :Vision blurred	NC	NC	NC	NC	NC	0.9996
PT :Vomiting	0.9913	NC	0.9913	NC	NC	NC
PT :Weight decreased	0.9995	NC	0.9995	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
Refractory to lenalidomide in last previous regimen	PT :Arteriosclerosis coronary artery	NC	NC	NC	NC	NC	0.9992
	PT :Arthralgia	0.6642	NC	0.5680	NC	NC	NC
	PT :Asthenia	0.7328	NC	0.5534	NC	NC	NC
	PT :Atrial fibrillation	0.8784	NC	NC	NC	NC	NC
	PT :Atypical pneumonia	NC	NC	NC	NC	NC	0.9992
	PT :Back pain	0.3996	NC	0.3027	NC	NC	NC
	PT :Bone pain	0.9866	NC	0.9875	NC	NC	NC
	PT :Bronchitis	0.6994	NC	0.6408	NC	NC	NC
	PT :Bronchopulmonary aspergillosis	NC	NC	NC	NC	NC	0.9993
	PT :Cataract	0.1719	NC	NC	NC	NC	NC
	PT :Cerebellar infarction	NC	NC	NC	NC	NC	0.9992
	PT :Constipation	0.7978	NC	0.7978	NC	NC	NC
	PT :Cough	0.7221	NC	0.5589	NC	NC	NC
	PT :Death	NC	NC	NC	NC	NC	0.9964
	PT :Decreased appetite	0.1559	NC	0.1559	NC	NC	NC
	PT :Decubitus ulcer	NC	NC	NC	NC	NC	0.9992
	PT :Diarrhoea	0.0130	NC	0.0190	NC	NC	NC
	PT :Disease progression	0.6412	0.9828	NC	NC	0.6412	NC
	PT :Dyspnoea	0.7442	NC	0.7244	NC	NC	NC
	PT :Echinococciasis	NC	NC	NC	NC	NC	0.9993

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Fatigue	0.1121	NC	0.1254	NC	NC	NC
PT :Febrile neutropenia	0.5839	0.4151	NC	0.5839	0.5839	NC
PT :General physical health deterioration	NC	NC	NC	NC	NC	0.9992
PT :Haemorrhage intracranial	NC	NC	NC	NC	NC	0.9993
PT :Headache	0.5503	NC	0.5503	NC	NC	NC
PT :Hepatic failure	NC	NC	NC	NC	NC	0.9993
PT :Hypertension	0.3957	NC	NC	NC	NC	NC
PT :Influenza	0.0968	NC	NC	NC	NC	NC
PT :Infusion related reaction	0.3290	NC	0.3603	NC	NC	NC
PT :Insomnia	0.8012	NC	0.6276	NC	NC	NC
PT :Lower respiratory tract infection	0.4121	NC	NC	0.6488	0.6488	NC
PT :Medical device site infection	NC	NC	NC	NC	NC	0.9992
PT :Meningitis cryptococcal	NC	NC	NC	NC	NC	0.9992
PT :Metastases to liver	NC	NC	NC	NC	NC	0.9992
PT :Multiple organ dysfunction syndrome	NC	NC	NC	NC	NC	0.9993
PT :Muscle spasms	0.2640	NC	0.1778	NC	NC	NC
PT :Muscular weakness	0.0272	NC	0.0330	NC	NC	NC
PT :Musculoskeletal chest pain	0.9860	NC	0.9860	NC	NC	NC
PT :Myalgia	0.4578	NC	0.4578	NC	NC	NC
PT :Myelodysplastic syndrome	NC	NC	NC	NC	NC	0.9993

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

	Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
PT :Myocardial infarction	NC	NC	NC	NC	NC	0.9992
PT :Nasopharyngitis	0.6355	NC	0.6355	NC	NC	NC
PT :Nausea	0.8427	NC	0.8427	NC	NC	NC
PT :Neutropenia	0.6024	NC	NC	0.6083	0.5649	0.9990
PT :Oedema peripheral	0.6873	NC	0.6873	NC	NC	NC
PT :Oropharyngeal pain	0.6450	NC	0.6450	NC	NC	NC
PT :Pain in extremity	0.3112	NC	0.3112	NC	NC	NC
PT :Pathological fracture	0.9959	NC	NC	NC	NC	NC
PT :Peripheral sensory neuropathy	0.2557	NC	0.2610	NC	NC	NC
PT :Pneumonia	0.5575	0.7016	0.7962	0.7106	0.7106	0.7231
PT :Pneumonia influenzal	NC	NC	NC	NC	NC	0.9992
PT :Pneumonia streptococcal	NC	NC	NC	NC	NC	0.9993
PT :Pruritus	0.3520	NC	0.3520	NC	NC	NC
PT :Pyoderma	NC	NC	NC	NC	NC	0.9992
PT :Pyrexia	0.4196	NC	0.2270	NC	NC	NC
PT :Rash	0.3256	NC	0.3256	NC	NC	NC
PT :Sepsis	NC	NC	NC	NC	NC	0.9993
PT :Septic shock	NC	NC	NC	NC	NC	1.0000
PT :Spinal subdural haematoma	NC	NC	NC	NC	NC	0.9993
PT :Stomatitis	0.2743	NC	NC	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.40 Subgroup analysis
16.2.7.1.40.2 Listing of subgroup and PT interaction p-values for time-to-event analysis - Safety population

		Any treatment emergent AE	Any treatment emergent serious AE	Any treatment emergent AE by severity (Grade 1,2)	Any treatment emergent AE by severity (Grade 3,4)	Any treatment emergent AE by severity (Grade 3,4,5)	Any treatment emergent AE leading to discontinuation of treatment
	PT :Sudden death	NC	NC	NC	NC	NC	0.9993
	PT :Thrombocytopenia	0.2429	NC	NC	0.3394	0.3394	0.9919
	PT :Tremor	0.7245	NC	NC	NC	NC	NC
	PT :Upper respiratory tract infection	0.5398	NC	0.3095	NC	NC	NC
	PT :Urinary tract infection	0.2759	NC	0.3390	NC	0.9924	NC
	PT :Vision blurred	NC	NC	NC	NC	NC	0.9993
	PT :Vomiting	0.3897	NC	0.4587	NC	NC	NC
	PT :Weight decreased	0.9925	NC	0.9925	NC	NC	NC

NA:Not Applicable / Not Calculable
P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_pvalint_sr_l.sas OUT=REPORT/OUTPUT/ae_km_pvalint_pt_sr_l_x.rtf (10NOV2020 10:56)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.1 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
Upper respiratory tract infection (days)							
Number (%) of events	18 (26.5)	13 (24.1)	10 (18.9)	27 (40.9)	1 (3.6)	12 (37.5)	0.0306
Number (%) of patients censored	50 (73.5)	41 (75.9)	43 (81.1)	39 (59.1)	27 (96.4)	20 (62.5)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	8.9363 (2.0370 to NC)	13.0760 (3.2854 to NC)	NC (6.9651 to NC)	6.8994 (3.4168 to 12.5832)	NC (5.2895 to NC)	7.4908 (2.3655 to 16.5257)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.5832 to NC)	NC (NC to NC)	NC (7.7536 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5203		0.0154		0.0050	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_age_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.1 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.7904 (0.3853 to 1.6216)		2.3984 (1.1562 to 4.9752)		10.5172 (1.3644 to 81.0720)	
P-value	-	0.5212		0.0188		0.0239	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.4169 (0.2010 to 0.8649)		0.0951 (0.0123 to 0.7329)		
Events probability (95% CI)[c]							
2 Months	0.8657 (0.7578 to 0.9277)	0.8889 (0.7693 to 0.9485)	0.9034 (0.7831 to 0.9586)	0.9072 (0.8050 to 0.9572)	1.0000 (1.0000 to 1.0000)	0.9688 (0.7982 to 0.9955)	
4 Months	0.8041 (0.6865 to 0.8812)	0.8691 (0.7448 to 0.9354)	0.9034 (0.7831 to 0.9586)	0.8446 (0.7304 to 0.9132)	1.0000 (1.0000 to 1.0000)	0.8011 (0.6082 to 0.9058)	
6 Months	0.8041 (0.6865 to 0.8812)	0.8038 (0.6647 to 0.8897)	0.8823 (0.7564 to 0.9454)	0.7606 (0.6340 to 0.8484)	0.9444 (0.6664 to 0.9920)	0.7629 (0.5639 to 0.8800)	
8 Months	0.7628 (0.6356 to 0.8507)	0.8038 (0.6647 to 0.8897)	0.8585 (0.7248 to 0.9302)	0.7063 (0.5739 to 0.8043)	0.9444 (0.6664 to 0.9920)	0.6826 (0.4750 to 0.8221)	
10 Months	0.7210 (0.5866 to 0.8182)	0.7761 (0.6290 to 0.8705)	0.8585 (0.7248 to 0.9302)	0.7063 (0.5739 to 0.8043)	0.9444 (0.6664 to 0.9920)	0.6425 (0.4337 to 0.7911)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_age_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.1 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	0.7210 (0.5866 to 0.8182)	0.7761 (0.6290 to 0.8705)	0.8585 (0.7248 to 0.9302)	0.6647 (0.5275 to 0.7704)	0.9444 (0.6664 to 0.9920)	0.6425 (0.4337 to 0.7911)	
14 Months	0.7210 (0.5866 to 0.8182)	0.7462 (0.5913 to 0.8495)	0.8065 (0.6581 to 0.8953)	0.6024 (0.4613 to 0.7175)	0.9444 (0.6664 to 0.9920)	0.6425 (0.4337 to 0.7911)	
16 Months	0.7210 (0.5866 to 0.8182)	0.7462 (0.5913 to 0.8495)	0.8065 (0.6581 to 0.8953)	0.5561 (0.4125 to 0.6778)	0.9444 (0.6664 to 0.9920)	0.6425 (0.4337 to 0.7911)	
18 Months	0.7210 (0.5866 to 0.8182)	0.7123 (0.5483 to 0.8257)	0.8065 (0.6581 to 0.8953)	0.5319 (0.3875 to 0.6568)	0.9444 (0.6664 to 0.9920)	0.5300 (0.3102 to 0.7087)	
20 Months	0.6922 (0.5498 to 0.7975)	0.7123 (0.5483 to 0.8257)	0.8065 (0.6581 to 0.8953)	0.5053 (0.3598 to 0.6339)	0.9444 (0.6664 to 0.9920)	0.5300 (0.3102 to 0.7087)	
22 Months	0.6922 (0.5498 to 0.7975)	0.7123 (0.5483 to 0.8257)	0.8065 (0.6581 to 0.8953)	0.5053 (0.3598 to 0.6339)	0.9444 (0.6664 to 0.9920)	0.5300 (0.3102 to 0.7087)	
24 Months	0.6922 (0.5498 to 0.7975)	0.7123 (0.5483 to 0.8257)	0.7681 (0.6025 to 0.8716)	0.5053 (0.3598 to 0.6339)	0.9444 (0.6664 to 0.9920)	0.5300 (0.3102 to 0.7087)	
26 Months	0.6922 (0.5498 to 0.7975)	0.7123 (0.5483 to 0.8257)	0.7681 (0.6025 to 0.8716)	0.5053 (0.3598 to 0.6339)	0.9444 (0.6664 to 0.9920)	0.5300 (0.3102 to 0.7087)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_age_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.1 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
Number of patients at risk[c]							
2 Months	57	47	45	58	26	31	
4 Months	49	43	43	54	24	22	
6 Months	42	35	39	43	17	19	
8 Months	37	31	35	39	15	17	
10 Months	34	28	34	36	14	15	
12 Months	31	26	33	32	12	14	
14 Months	29	25	31	29	10	14	
16 Months	28	24	27	24	9	12	
18 Months	25	20	24	21	7	8	
20 Months	24	20	21	19	6	7	
22 Months	23	19	21	14	5	7	
24 Months	22	19	20	14	5	7	
26 Months	21	17	19	13	5	6	
Urinary tract infection (days)							

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_age_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.1 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	4 (5.9)	7 (13.0)	2 (3.8)	9 (13.6)	8 (28.6)	3 (9.4)	0.0156
Number (%) of patients censored	64 (94.1)	47 (87.0)	51 (96.2)	57 (86.4)	20 (71.4)	29 (90.6)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (20.9610 to NC)	NC (NC to NC)	NC (16.9199 to NC)	3.9425 (0.7885 to NC)	NC (14.4559 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.8337 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1727		0.1047		0.0179	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.3142 (0.6700 to 7.9937)		3.3150 (0.7144 to 15.3830)		0.2190 (0.0560 to 0.8573)	
P-value	-	0.1846		0.1259		0.0292	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.1 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]							
2 Months	0.9851 (0.8987 to 0.9979)	0.9444 (0.8376 to 0.9817)	1.0000 (1.0000 to 1.0000)	0.9692 (0.8825 to 0.9922)	0.8116 (0.6048 to 0.9170)	0.9375 (0.7725 to 0.9840)	
4 Months	0.9851 (0.8987 to 0.9979)	0.9055 (0.7876 to 0.9596)	0.9591 (0.8463 to 0.9896)	0.9077 (0.8060 to 0.9574)	0.7304 (0.5154 to 0.8617)	0.9375 (0.7725 to 0.9840)	
6 Months	0.9675 (0.8755 to 0.9918)	0.9055 (0.7876 to 0.9596)	0.9591 (0.8463 to 0.9896)	0.9077 (0.8060 to 0.9574)	0.7304 (0.5154 to 0.8617)	0.9375 (0.7725 to 0.9840)	
8 Months	0.9280 (0.8181 to 0.9726)	0.9055 (0.7876 to 0.9596)	0.9591 (0.8463 to 0.9896)	0.9077 (0.8060 to 0.9574)	0.6742 (0.4464 to 0.8248)	0.9375 (0.7725 to 0.9840)	
10 Months	0.9280 (0.8181 to 0.9726)	0.9055 (0.7876 to 0.9596)	0.9591 (0.8463 to 0.9896)	0.9077 (0.8060 to 0.9574)	0.6742 (0.4464 to 0.8248)	0.9375 (0.7725 to 0.9840)	
12 Months	0.9280 (0.8181 to 0.9726)	0.9055 (0.7876 to 0.9596)	0.9591 (0.8463 to 0.9896)	0.8888 (0.7801 to 0.9456)	0.6742 (0.4464 to 0.8248)	0.9375 (0.7725 to 0.9840)	
14 Months	0.9280 (0.8181 to 0.9726)	0.9055 (0.7876 to 0.9596)	0.9591 (0.8463 to 0.9896)	0.8888 (0.7801 to 0.9456)	0.6742 (0.4464 to 0.8248)	0.9375 (0.7725 to 0.9840)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.1 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.9280 (0.8181 to 0.9726)	0.9055 (0.7876 to 0.9596)	0.9591 (0.8463 to 0.9896)	0.8888 (0.7801 to 0.9456)	0.6742 (0.4464 to 0.8248)	0.8882 (0.6826 to 0.9638)	
18 Months	0.9280 (0.8181 to 0.9726)	0.9055 (0.7876 to 0.9596)	0.9591 (0.8463 to 0.9896)	0.8671 (0.7497 to 0.9318)	0.6742 (0.4464 to 0.8248)	0.8882 (0.6826 to 0.9638)	
20 Months	0.9280 (0.8181 to 0.9726)	0.9055 (0.7876 to 0.9596)	0.9591 (0.8463 to 0.9896)	0.8671 (0.7497 to 0.9318)	0.6742 (0.4464 to 0.8248)	0.8882 (0.6826 to 0.9638)	
22 Months	0.9280 (0.8181 to 0.9726)	0.8731 (0.7327 to 0.9426)	0.9591 (0.8463 to 0.9896)	0.8671 (0.7497 to 0.9318)	0.6742 (0.4464 to 0.8248)	0.8882 (0.6826 to 0.9638)	
24 Months	0.9280 (0.8181 to 0.9726)	0.8731 (0.7327 to 0.9426)	0.9591 (0.8463 to 0.9896)	0.8382 (0.7054 to 0.9146)	0.6742 (0.4464 to 0.8248)	0.8882 (0.6826 to 0.9638)	
26 Months	0.9280 (0.8181 to 0.9726)	0.8731 (0.7327 to 0.9426)	0.9591 (0.8463 to 0.9896)	0.8382 (0.7054 to 0.9146)	0.6742 (0.4464 to 0.8248)	0.8882 (0.6826 to 0.9638)	
Number of patients at risk[c]							
2 Months	65	50	50	63	21	30	
4 Months	61	45	46	59	18	26	
6 Months	52	41	43	54	13	24	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_age_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.1 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	45	38	39	53	10	24	
10 Months	43	36	38	49	9	23	
12 Months	39	33	37	46	8	21	
14 Months	37	33	35	45	6	21	
16 Months	36	31	30	41	6	16	
18 Months	34	29	28	38	6	14	
20 Months	34	29	25	36	5	13	
22 Months	33	27	25	30	4	12	
24 Months	32	25	25	28	4	12	
26 Months	30	21	24	27	4	11	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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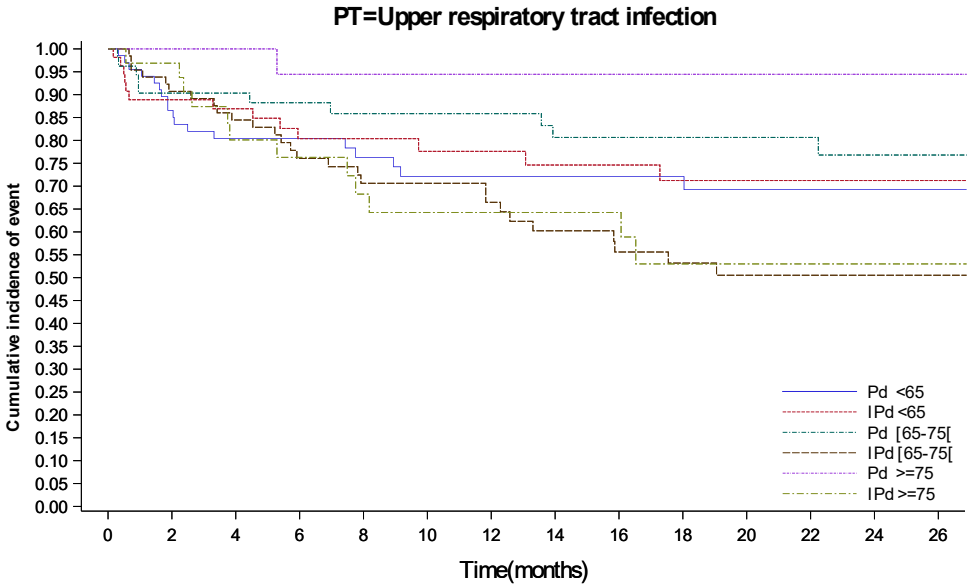
16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to age - Safety population

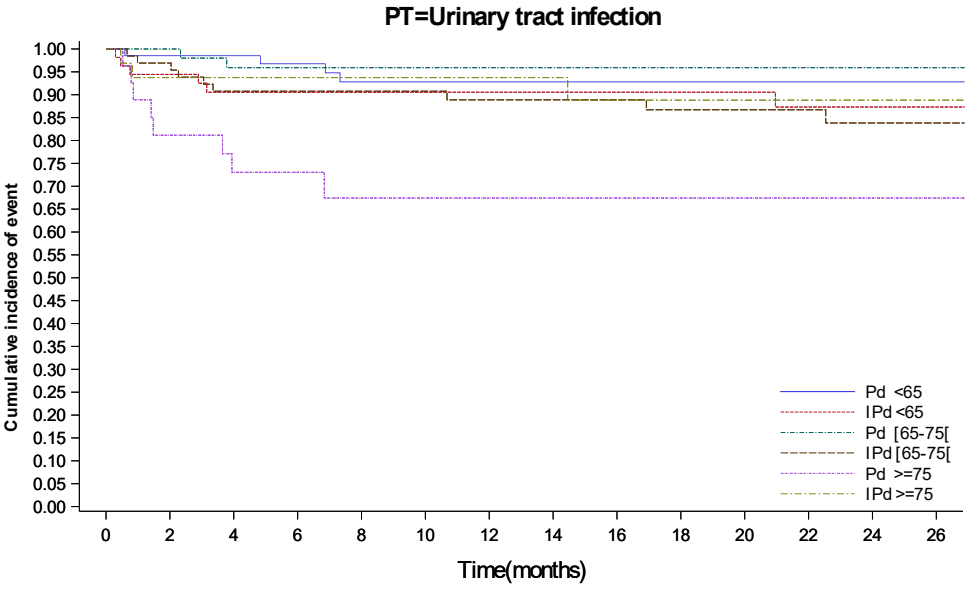


Number at Risk

Pd <65	68	57	49	42	37	34	31	29	28	25	24	23	22	21
IPd <65	54	47	43	35	31	28	26	25	24	20	20	19	19	17
Pd [65-75[	53	45	43	39	35	34	33	31	27	24	21	21	20	19
IPd [65-75[	66	58	54	43	39	36	32	29	24	21	19	14	14	13
Pd >=75	28	26	24	17	15	14	12	10	9	7	6	5	5	5
IPd >=75	32	31	22	19	17	15	14	14	12	8	7	7	7	6

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_teaept_age_s_f_x.rtf (17NOV2020 14:44)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to age - Safety population



Number at Risk

Pd <65	68	65	61	52	45	43	39	37	36	34	34	33	32	30
IPd <65	54	50	45	41	38	36	33	33	31	29	29	27	25	21
Pd [65-75[	53	50	46	43	39	38	37	35	30	28	25	25	25	24
IPd [65-75[	66	63	59	54	53	49	46	45	41	38	36	30	28	27
Pd >=75	28	21	18	13	10	9	8	6	6	6	5	4	4	4
IPd >=75	32	30	26	24	24	23	21	21	16	14	13	12	12	11

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_teaept_age_s_f_x.rtf (17NOV2020 14:44)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.3 Treatment emergent not severe adverse event per SOC by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
Skin and subcutaneous tissue disorders (days)							
Number (%) of events	22 (32.4)	14 (25.9)	12 (22.6)	18 (27.3)	3 (10.7)	14 (43.8)	0.0425
Number (%) of patients censored	46 (67.6)	40 (74.1)	41 (77.4)	48 (72.7)	25 (89.3)	18 (56.3)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	1.0513 (0.3285 to NC)	17.7741 (0.3285 to NC)	12.6160 (3.7125 to NC)	15.0472 (4.5996 to NC)	29.4374 (4.7639 to NC)	2.3984 (0.4271 to 9.2320)	
Median (95% CI)	NC (NC to NC)	NC (27.4004 to NC)	NC (NC to NC)	NC (NC to NC)	NC (29.4374 to NC)	NC (2.9240 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2804		0.6810		0.0081	

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CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.3 Treatment emergent not severe adverse event per SOC by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.6884 (0.3482 to 1.3610)		1.1662 (0.5599 to 2.4289)		4.7375 (1.3418 to 16.7274)	
P-value	-	0.2830		0.6813		0.0157	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd					0.2111 (0.0598 to 0.7453)		
Events probability (95% CI)[c]							
2 Months	0.7475 (0.6257 to 0.8348)	0.8519 (0.7255 to 0.9230)	0.9223 (0.8059 to 0.9701)	0.8775 (0.7699 to 0.9368)	0.9643 (0.7724 to 0.9949)	0.7813 (0.5952 to 0.8892)	
4 Months	0.7164 (0.5920 to 0.8088)	0.8325 (0.7027 to 0.9091)	0.8598 (0.7279 to 0.9307)	0.8619 (0.7512 to 0.9256)	0.9643 (0.7724 to 0.9949)	0.6861 (0.4950 to 0.8172)	
6 Months	0.6970 (0.5698 to 0.7933)	0.8325 (0.7027 to 0.9091)	0.8151 (0.6740 to 0.8995)	0.8459 (0.7324 to 0.9140)	0.9184 (0.7078 to 0.9792)	0.6861 (0.4950 to 0.8172)	
8 Months	0.6771 (0.5472 to 0.7771)	0.8325 (0.7027 to 0.9091)	0.7686 (0.6198 to 0.8651)	0.8106 (0.6901 to 0.8880)	0.9184 (0.7078 to 0.9792)	0.6457 (0.4498 to 0.7870)	
10 Months	0.6546 (0.5211 to 0.7592)	0.8056 (0.6665 to 0.8913)	0.7686 (0.6198 to 0.8651)	0.7724 (0.6447 to 0.8591)	0.9184 (0.7078 to 0.9792)	0.5621 (0.3624 to 0.7212)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.3 Treatment emergent not severe adverse event per SOC by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	0.6546 (0.5211 to 0.7592)	0.7501 (0.5966 to 0.8520)	0.7686 (0.6198 to 0.8651)	0.7724 (0.6447 to 0.8591)	0.9184 (0.7078 to 0.9792)	0.5621 (0.3624 to 0.7212)	
14 Months	0.6546 (0.5211 to 0.7592)	0.7501 (0.5966 to 0.8520)	0.7421 (0.5884 to 0.8455)	0.7521 (0.6208 to 0.8434)	0.9184 (0.7078 to 0.9792)	0.5621 (0.3624 to 0.7212)	
16 Months	0.6546 (0.5211 to 0.7592)	0.7501 (0.5966 to 0.8520)	0.7421 (0.5884 to 0.8455)	0.7300 (0.5946 to 0.8265)	0.9184 (0.7078 to 0.9792)	0.5153 (0.3149 to 0.6835)	
18 Months	0.6546 (0.5211 to 0.7592)	0.7160 (0.5529 to 0.8283)	0.7421 (0.5884 to 0.8455)	0.7300 (0.5946 to 0.8265)	0.9184 (0.7078 to 0.9792)	0.5153 (0.3149 to 0.6835)	
20 Months	0.6546 (0.5211 to 0.7592)	0.7160 (0.5529 to 0.8283)	0.7421 (0.5884 to 0.8455)	0.7300 (0.5946 to 0.8265)	0.9184 (0.7078 to 0.9792)	0.5153 (0.3149 to 0.6835)	
22 Months	0.6546 (0.5211 to 0.7592)	0.7160 (0.5529 to 0.8283)	0.7421 (0.5884 to 0.8455)	0.7300 (0.5946 to 0.8265)	0.9184 (0.7078 to 0.9792)	0.5153 (0.3149 to 0.6835)	
24 Months	0.6546 (0.5211 to 0.7592)	0.7160 (0.5529 to 0.8283)	0.7421 (0.5884 to 0.8455)	0.7008 (0.5571 to 0.8056)	0.9184 (0.7078 to 0.9792)	0.5153 (0.3149 to 0.6835)	
26 Months	0.6546 (0.5211 to 0.7592)	0.7160 (0.5529 to 0.8283)	0.7421 (0.5884 to 0.8455)	0.7008 (0.5571 to 0.8056)	0.9184 (0.7078 to 0.9792)	0.5153 (0.3149 to 0.6835)	

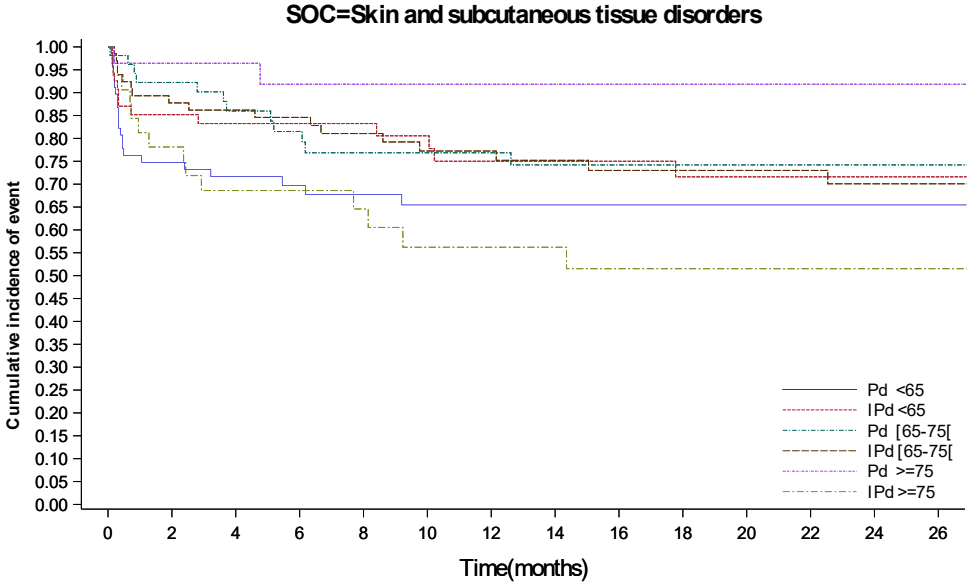
SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12soc_age_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.3 Treatment emergent not severe adverse event per SOC by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
Number of patients at risk[c]							
2 Months	49	45	46	56	25	25	
4 Months	44	41	41	55	23	19	
6 Months	35	36	36	48	16	17	
8 Months	32	32	30	45	14	16	
10 Months	29	29	30	39	13	13	
12 Months	26	25	29	38	11	13	
14 Months	25	25	27	36	10	13	
16 Months	24	24	22	32	10	10	
18 Months	22	21	20	30	8	8	
20 Months	22	21	17	29	7	7	
22 Months	21	20	17	25	6	7	
24 Months	20	18	17	23	6	7	
26 Months	18	14	16	23	6	6	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12soc_age_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.4 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per SOC by treatment group according to age - Safety population



Number at Risk

Pd <65	68	49	44	35	32	29	26	25	24	22	22	21	20	18
IPd <65	54	45	41	36	32	29	25	25	24	21	21	20	18	14
Pd [65-75[	53	46	41	36	30	30	29	27	22	20	17	17	17	16
IPd [65-75[	66	56	55	48	45	39	38	36	32	30	29	25	23	23
Pd >=75	28	25	23	16	14	13	11	10	10	8	7	6	6	6
IPd >=75	32	25	19	17	16	13	13	13	10	8	7	7	7	6

SOC are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12soc_age_s_f_x.rtf (17NOV2020 14:44)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.5 Treatment emergent not severe adverse event per PT by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
Upper respiratory tract infection (days)							
Number (%) of events	18 (26.5)	12 (22.2)	9 (17.0)	27 (40.9)	1 (3.6)	11 (34.4)	0.0173
Number (%) of patients censored	50 (73.5)	42 (77.8)	44 (83.0)	39 (59.1)	27 (96.4)	21 (65.6)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	8.9363 (2.0370 to NC)	17.2813 (4.5339 to NC)	NC (6.9651 to NC)	6.8994 (3.4168 to 12.5832)	NC (5.2895 to NC)	7.4908 (2.6283 to 16.5257)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.5832 to NC)	NC (NC to NC)	NC (7.7536 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3991		0.0062		0.0078	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_age_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.5 Treatment emergent not severe adverse event per PT by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.7295 (0.3494 to 1.5231)		2.7638 (1.2948 to 5.8997)		9.6707 (1.2451 to 75.1102)	
P-value	-	0.4010		0.0086		0.0300	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.3618 (0.1695 to 0.7723)		0.1034 (0.0133 to 0.8031)		
Events probability (95% CI)[c]							
2 Months	0.8657 (0.7578 to 0.9277)	0.8889 (0.7693 to 0.9485)	0.9223 (0.8059 to 0.9701)	0.9072 (0.8050 to 0.9572)	1.0000 (1.0000 to 1.0000)	0.9688 (0.7982 to 0.9955)	
4 Months	0.8041 (0.6865 to 0.8812)	0.8889 (0.7693 to 0.9485)	0.9223 (0.8059 to 0.9701)	0.8446 (0.7304 to 0.9132)	1.0000 (1.0000 to 1.0000)	0.8297 (0.6362 to 0.9259)	
6 Months	0.8041 (0.6865 to 0.8812)	0.8237 (0.6873 to 0.9045)	0.9013 (0.7787 to 0.9577)	0.7606 (0.6340 to 0.8484)	0.9444 (0.6664 to 0.9920)	0.7902 (0.5888 to 0.9006)	
8 Months	0.7628 (0.6356 to 0.8507)	0.8237 (0.6873 to 0.9045)	0.8776 (0.7466 to 0.9433)	0.7063 (0.5739 to 0.8043)	0.9444 (0.6664 to 0.9920)	0.7070 (0.4948 to 0.8430)	
10 Months	0.7210 (0.5866 to 0.8182)	0.7962 (0.6513 to 0.8860)	0.8776 (0.7466 to 0.9433)	0.7063 (0.5739 to 0.8043)	0.9444 (0.6664 to 0.9920)	0.6655 (0.4514 to 0.8118)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_age_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.5 Treatment emergent not severe adverse event per PT by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	0.7210 (0.5866 to 0.8182)	0.7962 (0.6513 to 0.8860)	0.8776 (0.7466 to 0.9433)	0.6647 (0.5275 to 0.7704)	0.9444 (0.6664 to 0.9920)	0.6655 (0.4514 to 0.8118)	
14 Months	0.7210 (0.5866 to 0.8182)	0.7667 (0.6134 to 0.8656)	0.8260 (0.6794 to 0.9098)	0.6024 (0.4613 to 0.7175)	0.9444 (0.6664 to 0.9920)	0.6655 (0.4514 to 0.8118)	
16 Months	0.7210 (0.5866 to 0.8182)	0.7667 (0.6134 to 0.8656)	0.8260 (0.6794 to 0.9098)	0.5561 (0.4125 to 0.6778)	0.9444 (0.6664 to 0.9920)	0.6655 (0.4514 to 0.8118)	
18 Months	0.7210 (0.5866 to 0.8182)	0.7319 (0.5677 to 0.8419)	0.8260 (0.6794 to 0.9098)	0.5319 (0.3875 to 0.6568)	0.9444 (0.6664 to 0.9920)	0.5490 (0.3216 to 0.7283)	
20 Months	0.6922 (0.5498 to 0.7975)	0.7319 (0.5677 to 0.8419)	0.8260 (0.6794 to 0.9098)	0.5053 (0.3598 to 0.6339)	0.9444 (0.6664 to 0.9920)	0.5490 (0.3216 to 0.7283)	
22 Months	0.6922 (0.5498 to 0.7975)	0.7319 (0.5677 to 0.8419)	0.8260 (0.6794 to 0.9098)	0.5053 (0.3598 to 0.6339)	0.9444 (0.6664 to 0.9920)	0.5490 (0.3216 to 0.7283)	
24 Months	0.6922 (0.5498 to 0.7975)	0.7319 (0.5677 to 0.8419)	0.7884 (0.6243 to 0.8870)	0.5053 (0.3598 to 0.6339)	0.9444 (0.6664 to 0.9920)	0.5490 (0.3216 to 0.7283)	
26 Months	0.6922 (0.5498 to 0.7975)	0.7319 (0.5677 to 0.8419)	0.7884 (0.6243 to 0.8870)	0.5053 (0.3598 to 0.6339)	0.9444 (0.6664 to 0.9920)	0.5490 (0.3216 to 0.7283)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_age_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.5 Treatment emergent not severe adverse event per PT by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
Number of patients at risk[c]							
2 Months	57	47	46	58	26	31	
4 Months	49	44	44	54	24	22	
6 Months	42	36	40	43	17	19	
8 Months	37	32	36	39	15	17	
10 Months	34	29	35	36	14	15	
12 Months	31	27	34	32	12	14	
14 Months	29	26	32	29	10	14	
16 Months	28	24	28	24	9	12	
18 Months	25	20	25	21	7	8	
20 Months	24	20	22	19	6	7	
22 Months	23	19	22	14	5	7	
24 Months	22	19	21	14	5	7	
26 Months	21	17	20	13	5	6	
Urinary tract infection (days)							

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_age_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.5 Treatment emergent not severe adverse event per PT by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	4 (5.9)	5 (9.3)	2 (3.8)	7 (10.6)	7 (25.0)	2 (6.3)	0.0384
Number (%) of patients censored	64 (94.1)	49 (90.7)	51 (96.2)	59 (89.4)	21 (75.0)	30 (93.8)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (32.7556 to NC)	NC (NC to NC)	NC (22.5380 to NC)	6.8337 (0.7885 to NC)	NC (14.4559 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.8337 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4384		0.2156		0.0151	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.6820 (0.4453 to 6.3539)		2.6077 (0.5398 to 12.5965)		0.1660 (0.0328 to 0.8396)	
P-value	-	0.4432		0.2330		0.0299	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_age_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.5 Treatment emergent not severe adverse event per PT by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]							
2 Months	0.9851 (0.8987 to 0.9979)	0.9630 (0.8599 to 0.9906)	1.0000 (1.0000 to 1.0000)	0.9846 (0.8958 to 0.9978)	0.8116 (0.6048 to 0.9170)	0.9688 (0.7982 to 0.9955)	
4 Months	0.9851 (0.8987 to 0.9979)	0.9437 (0.8355 to 0.9815)	0.9591 (0.8463 to 0.9896)	0.9221 (0.8229 to 0.9668)	0.7710 (0.5590 to 0.8902)	0.9688 (0.7982 to 0.9955)	
6 Months	0.9675 (0.8755 to 0.9918)	0.9437 (0.8355 to 0.9815)	0.9591 (0.8463 to 0.9896)	0.9221 (0.8229 to 0.9668)	0.7710 (0.5590 to 0.8902)	0.9688 (0.7982 to 0.9955)	
8 Months	0.9477 (0.8454 to 0.9830)	0.9437 (0.8355 to 0.9815)	0.9591 (0.8463 to 0.9896)	0.9221 (0.8229 to 0.9668)	0.7117 (0.4800 to 0.8542)	0.9688 (0.7982 to 0.9955)	
10 Months	0.9262 (0.8133 to 0.9720)	0.9437 (0.8355 to 0.9815)	0.9591 (0.8463 to 0.9896)	0.9221 (0.8229 to 0.9668)	0.7117 (0.4800 to 0.8542)	0.9688 (0.7982 to 0.9955)	
12 Months	0.9262 (0.8133 to 0.9720)	0.9437 (0.8355 to 0.9815)	0.9591 (0.8463 to 0.9896)	0.9029 (0.7958 to 0.9553)	0.7117 (0.4800 to 0.8542)	0.9688 (0.7982 to 0.9955)	
14 Months	0.9262 (0.8133 to 0.9720)	0.9437 (0.8355 to 0.9815)	0.9591 (0.8463 to 0.9896)	0.9029 (0.7958 to 0.9553)	0.7117 (0.4800 to 0.8542)	0.9688 (0.7982 to 0.9955)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_age_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.5 Treatment emergent not severe adverse event per PT by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.9262 (0.8133 to 0.9720)	0.9437 (0.8355 to 0.9815)	0.9591 (0.8463 to 0.9896)	0.9029 (0.7958 to 0.9553)	0.7117 (0.4800 to 0.8542)	0.9178 (0.6981 to 0.9797)	
18 Months	0.9262 (0.8133 to 0.9720)	0.9437 (0.8355 to 0.9815)	0.9591 (0.8463 to 0.9896)	0.9029 (0.7958 to 0.9553)	0.7117 (0.4800 to 0.8542)	0.9178 (0.6981 to 0.9797)	
20 Months	0.9262 (0.8133 to 0.9720)	0.9437 (0.8355 to 0.9815)	0.9591 (0.8463 to 0.9896)	0.9029 (0.7958 to 0.9553)	0.7117 (0.4800 to 0.8542)	0.9178 (0.6981 to 0.9797)	
22 Months	0.9262 (0.8133 to 0.9720)	0.9100 (0.7684 to 0.9668)	0.9591 (0.8463 to 0.9896)	0.9029 (0.7958 to 0.9553)	0.7117 (0.4800 to 0.8542)	0.9178 (0.6981 to 0.9797)	
24 Months	0.9262 (0.8133 to 0.9720)	0.9100 (0.7684 to 0.9668)	0.9591 (0.8463 to 0.9896)	0.8738 (0.7465 to 0.9396)	0.7117 (0.4800 to 0.8542)	0.9178 (0.6981 to 0.9797)	
26 Months	0.9262 (0.8133 to 0.9720)	0.9100 (0.7684 to 0.9668)	0.9591 (0.8463 to 0.9896)	0.8738 (0.7465 to 0.9396)	0.7117 (0.4800 to 0.8542)	0.9178 (0.6981 to 0.9797)	
Number of patients at risk[c]							
2 Months	65	51	50	63	21	31	
4 Months	61	47	46	59	19	26	
6 Months	52	42	43	54	13	24	

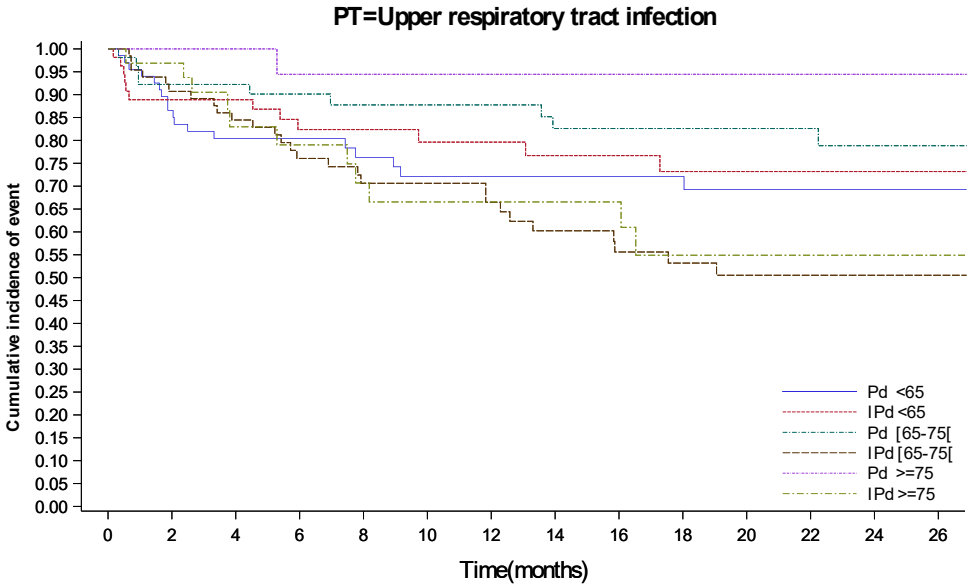
PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_age_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.5 Treatment emergent not severe adverse event per PT by treatment group according to age - Safety population

	<65		[65-75[		>=75		
	Pd (N=68)	**IPd (N=54)**	**Pd (N=53)**	**IPd (N=66)**	**Pd (N=28)**	**IPd (N=32)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	46	38	39	53	10	24	
10 Months	43	36	38	49	9	23	
12 Months	39	33	37	46	8	21	
14 Months	37	33	35	45	6	21	
16 Months	36	31	30	41	6	16	
18 Months	34	29	28	39	6	14	
20 Months	34	29	25	37	5	13	
22 Months	33	27	25	31	4	12	
24 Months	32	25	25	29	4	12	
26 Months	30	21	24	28	4	11	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_age_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.6 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per PT by treatment group according to age - Safety population

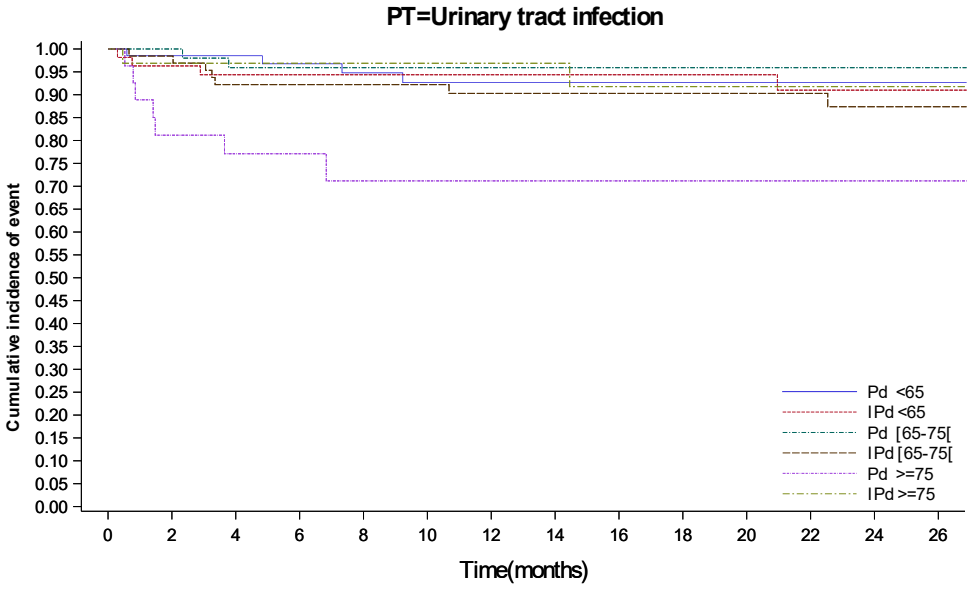


Number at Risk

Pd <65	68	57	49	42	37	34	31	29	28	25	24	23	22	21
IPd <65	54	47	44	36	32	29	27	26	24	20	20	19	19	17
Pd [65-75[	53	46	44	40	36	35	34	32	28	25	22	22	21	20
IPd [65-75[	66	58	54	43	39	36	32	29	24	21	19	14	14	13
Pd >=75	28	26	24	17	15	14	12	10	9	7	6	5	5	5
IPd >=75	32	31	22	19	17	15	14	14	12	8	7	7	7	6

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_age_s_f_x.rtf (17NOV2020 14:44)

16.2.7.1 Safety endpoints
16.2.7.1.41 Subgroup analysis by age
16.2.7.1.41.6 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per PT by treatment group according to age - Safety population



Number at Risk

Pd <65	68	65	61	52	46	43	39	37	36	34	34	33	32	30
IPd <65	54	51	47	42	38	36	33	33	31	29	29	27	25	21
Pd [65-75[	53	50	46	43	39	38	37	35	30	28	25	25	25	24
IPd [65-75[	66	63	59	54	53	49	46	45	41	39	37	31	29	28
Pd >=75	28	21	19	13	10	9	8	6	6	6	5	4	4	4
IPd >=75	32	31	26	24	24	23	21	21	16	14	13	12	12	11

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_age_s_f_x.rtf (17NOV2020 14:44)

16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.1 Treatment emergent adverse event per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population

	2 or 3		>3		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[d]**
Respiratory, thoracic and mediastinal disorders (days)					
Number (%) of events	28 (28.0)	46 (45.5)	23 (46.9)	22 (43.1)	0.0408
Number (%) of patients censored	72 (72.0)	55 (54.5)	26 (53.1)	29 (56.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	5.6838 (1.2813 to NC)	2.7269 (1.3799 to 4.4353)	2.0698 (0.5257 to 8.1807)	4.1068 (1.8398 to 7.3922)	
Median (95% CI)	NC (NC to NC)	24.2793 (7.8522 to NC)	12.1889 (7.2279 to NC)	NC (7.3922 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0231		0.4422	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.7155 (1.0710 to 2.7478)		0.7953 (0.4428 to 1.4283)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.1 Treatment emergent adverse event per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population

	2 or 3		>3		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[d]**
P-value	-	0.0247		0.4432	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.5829 (0.3639 to 0.9337)				
Events probability (95% CI)[c]					
2 Months	0.7951 (0.7006 to 0.8627)	0.7703 (0.6748 to 0.8410)	0.7510 (0.6033 to 0.8502)	0.8418 (0.7084 to 0.9176)	
4 Months	0.7844 (0.6886 to 0.8538)	0.7180 (0.6181 to 0.7960)	0.6637 (0.5103 to 0.7789)	0.7617 (0.6185 to 0.8570)	
6 Months	0.7478 (0.6469 to 0.8236)	0.6395 (0.5348 to 0.7266)	0.6637 (0.5103 to 0.7789)	0.6980 (0.5493 to 0.8059)	
8 Months	0.7349 (0.6324 to 0.8129)	0.6014 (0.4943 to 0.6928)	0.6371 (0.4812 to 0.7574)	0.6289 (0.4759 to 0.7485)	
10 Months	0.7349 (0.6324 to 0.8129)	0.5469 (0.4373 to 0.6438)	0.5223 (0.3609 to 0.6612)	0.6037 (0.4494 to 0.7274)	
12 Months	0.7213 (0.6169 to 0.8017)	0.5325 (0.4224 to 0.6308)	0.5223 (0.3609 to 0.6612)	0.5750 (0.4183 to 0.7037)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.1 Treatment emergent adverse event per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population

	2 or 3		>3		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.6918 (0.5833 to 0.7774)	0.5177 (0.4071 to 0.6173)	0.4897 (0.3276 to 0.6333)	0.5145 (0.3549 to 0.6528)	
16 Months	0.6918 (0.5833 to 0.7774)	0.5177 (0.4071 to 0.6173)	0.4897 (0.3276 to 0.6333)	0.5145 (0.3549 to 0.6528)	
18 Months	0.6918 (0.5833 to 0.7774)	0.5177 (0.4071 to 0.6173)	0.4897 (0.3276 to 0.6333)	0.5145 (0.3549 to 0.6528)	
20 Months	0.6918 (0.5833 to 0.7774)	0.5177 (0.4071 to 0.6173)	0.4897 (0.3276 to 0.6333)	0.5145 (0.3549 to 0.6528)	
22 Months	0.6918 (0.5833 to 0.7774)	0.5177 (0.4071 to 0.6173)	0.4897 (0.3276 to 0.6333)	0.5145 (0.3549 to 0.6528)	
24 Months	0.6918 (0.5833 to 0.7774)	0.5177 (0.4071 to 0.6173)	0.4407 (0.2718 to 0.5973)	0.5145 (0.3549 to 0.6528)	
26 Months	0.6918 (0.5833 to 0.7774)	0.4942 (0.3795 to 0.5988)	0.4407 (0.2718 to 0.5973)	0.5145 (0.3549 to 0.6528)	
Number of patients at risk[c]					
2 Months	75	76	36	42	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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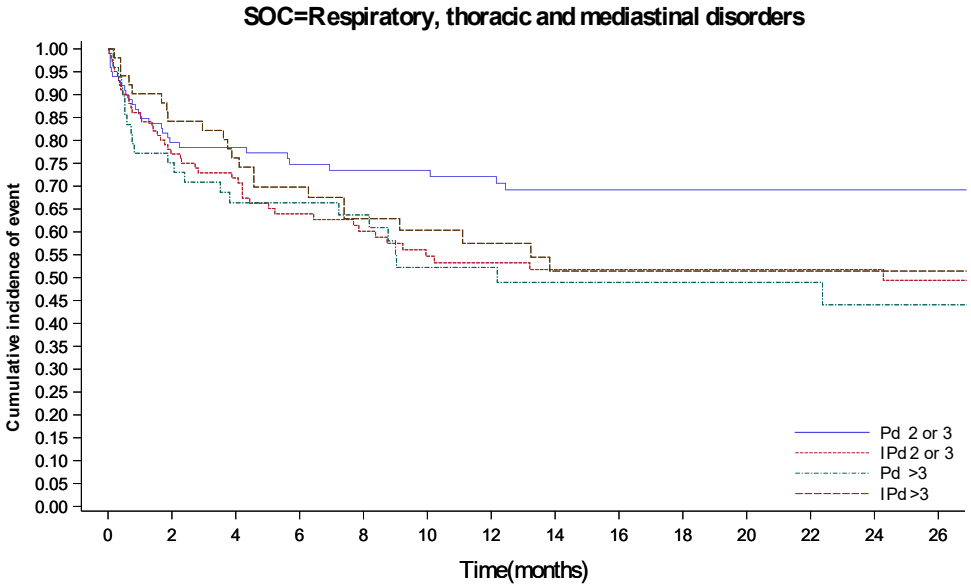
16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.1 Treatment emergent adverse event per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population

	2 or 3		>3		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	70	65	29	38	
6 Months	59	52	26	31	
8 Months	56	47	23	26	
10 Months	55	39	17	23	
12 Months	49	36	16	20	
14 Months	46	35	13	17	
16 Months	42	32	12	15	
18 Months	38	28	11	14	
20 Months	36	27	10	14	
22 Months	34	23	10	13	
24 Months	34	22	8	12	
26 Months	32	21	8	10	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_stratum2_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population



Number at Risk

Pd 2 or 3	100	75	70	59	56	55	49	46	42	38	36	34	34	32
IPd 2 or 3	101	76	65	52	47	39	36	35	32	28	27	23	22	21
Pd >3	49	36	29	26	23	17	16	13	12	11	10	10	8	8
IPd >3	51	42	38	31	26	23	20	17	15	14	14	13	12	10

SOC are presented if at least 10 events in a arm

16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.3 Treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	2 or 3		>3		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[d]**
Muscle spasms (days)					
Number (%) of events	8 (8.0)	13 (12.9)	8 (16.3)	3 (5.9)	0.0443
Number (%) of patients censored	92 (92.0)	88 (87.1)	41 (83.7)	48 (94.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (22.4066 to NC)	NC (4.3696 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3133		0.0755	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5675 (0.6495 to 3.7832)		0.3188 (0.0844 to 1.2049)	
P-value	-	0.3174		0.0919	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.3 Treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	2 or 3		>3		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]					
2 Months	0.9789 (0.9184 to 0.9947)	0.9701 (0.9102 to 0.9903)	0.8958 (0.7677 to 0.9553)	0.9608 (0.8522 to 0.9900)	
4 Months	0.9354 (0.8618 to 0.9705)	0.9276 (0.8539 to 0.9649)	0.8958 (0.7677 to 0.9553)	0.9608 (0.8522 to 0.9900)	
6 Months	0.9228 (0.8445 to 0.9625)	0.9276 (0.8539 to 0.9649)	0.8734 (0.7396 to 0.9411)	0.9384 (0.8206 to 0.9798)	
8 Months	0.9228 (0.8445 to 0.9625)	0.8903 (0.8049 to 0.9397)	0.8734 (0.7396 to 0.9411)	0.9384 (0.8206 to 0.9798)	
10 Months	0.9228 (0.8445 to 0.9625)	0.8774 (0.7886 to 0.9305)	0.8007 (0.6305 to 0.8984)	0.9384 (0.8206 to 0.9798)	
12 Months	0.9228 (0.8445 to 0.9625)	0.8774 (0.7886 to 0.9305)	0.8007 (0.6305 to 0.8984)	0.9384 (0.8206 to 0.9798)	
14 Months	0.9228 (0.8445 to 0.9625)	0.8635 (0.7708 to 0.9206)	0.8007 (0.6305 to 0.8984)	0.9384 (0.8206 to 0.9798)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.3 Treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	2 or 3		>3		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.9039 (0.8136 to 0.9518)	0.8635 (0.7708 to 0.9206)	0.8007 (0.6305 to 0.8984)	0.9384 (0.8206 to 0.9798)	
18 Months	0.9039 (0.8136 to 0.9518)	0.8635 (0.7708 to 0.9206)	0.8007 (0.6305 to 0.8984)	0.9384 (0.8206 to 0.9798)	
20 Months	0.9039 (0.8136 to 0.9518)	0.8635 (0.7708 to 0.9206)	0.8007 (0.6305 to 0.8984)	0.9384 (0.8206 to 0.9798)	
22 Months	0.9039 (0.8136 to 0.9518)	0.8635 (0.7708 to 0.9206)	0.8007 (0.6305 to 0.8984)	0.9384 (0.8206 to 0.9798)	
24 Months	0.9039 (0.8136 to 0.9518)	0.8429 (0.7405 to 0.9074)	0.8007 (0.6305 to 0.8984)	0.9384 (0.8206 to 0.9798)	
26 Months	0.9039 (0.8136 to 0.9518)	0.8429 (0.7405 to 0.9074)	0.8007 (0.6305 to 0.8984)	0.9384 (0.8206 to 0.9798)	
Number of patients at risk[c]					
2 Months	92	96	43	48	
4 Months	83	84	40	48	
6 Months	72	76	32	42	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.3 Treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	2 or 3		>3		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	66	71	27	39	
10 Months	65	65	22	37	
12 Months	57	63	22	33	
14 Months	54	62	19	32	
16 Months	48	55	17	29	
18 Months	42	49	15	28	
20 Months	40	46	13	27	
22 Months	38	42	13	25	
24 Months	38	39	12	24	
26 Months	36	37	11	20	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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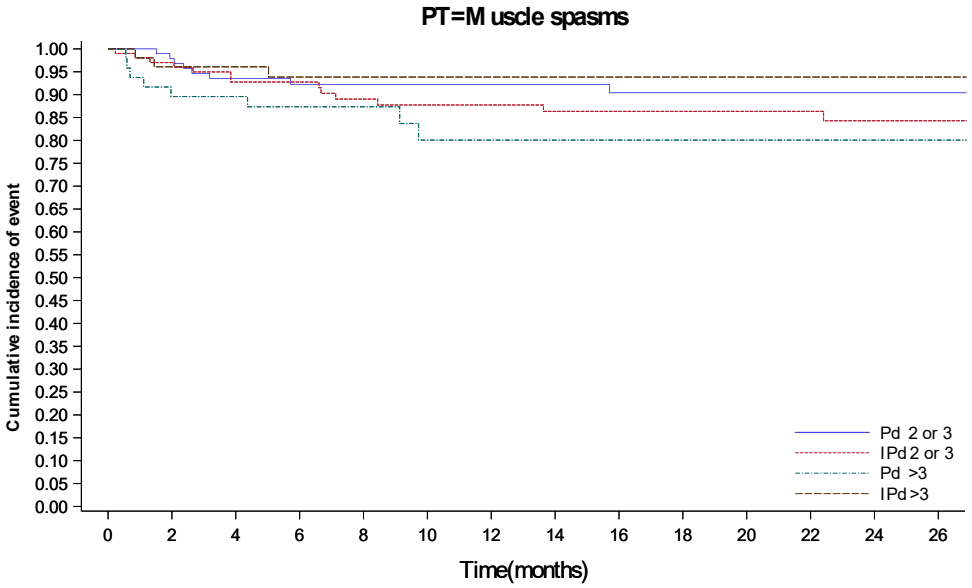
16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population



Number at Risk

Pd 2 or 3	100	92	83	72	66	65	57	54	48	42	40	38	38	36
IPd 2 or 3	101	96	84	76	71	65	63	62	55	49	46	42	39	37
Pd >3	49	43	40	32	27	22	22	19	17	15	13	13	12	11
IPd >3	51	48	48	42	39	37	33	32	29	28	27	25	24	20

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_teaept_stratum2_s_f_x.rtf (17NOV2020 14:44)

16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.5 Treatment emergent severe adverse event per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population

	2 or 3		>3		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[d]**
General disorders and administration site conditions (days)					
Number (%) of events	12 (12.0)	8 (7.9)	3 (6.1)	13 (25.5)	0.0161
Number (%) of patients censored	88 (88.0)	93 (92.1)	46 (93.9)	38 (74.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (31.3758 to NC)	NC (NC to NC)	NC (24.8706 to NC)	22.4723 (4.7967 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2649		0.0215	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.6027 (0.2452 to 1.4815)		3.9185 (1.1155 to 13.7639)	
P-value	-	0.2698		0.0331	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae34soc_stratum2_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.5 Treatment emergent severe adverse event per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population

	2 or 3		>3		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.2552 (0.0727 to 0.8964)		
Events probability (95% CI)[c]					
2 Months	0.9380 (0.8671 to 0.9717)	0.9602 (0.8974 to 0.9849)	1.0000 (1.0000 to 1.0000)	0.9216 (0.8044 to 0.9698)	
4 Months	0.9055 (0.8261 to 0.9497)	0.9501 (0.8842 to 0.9789)	1.0000 (1.0000 to 1.0000)	0.9020 (0.7804 to 0.9580)	
6 Months	0.8936 (0.8110 to 0.9414)	0.9501 (0.8842 to 0.9789)	0.9767 (0.8462 to 0.9967)	0.8618 (0.7318 to 0.9316)	
8 Months	0.8810 (0.7949 to 0.9324)	0.9379 (0.8666 to 0.9717)	0.9767 (0.8462 to 0.9967)	0.8403 (0.7056 to 0.9168)	
10 Months	0.8810 (0.7949 to 0.9324)	0.9379 (0.8666 to 0.9717)	0.9442 (0.7907 to 0.9861)	0.8176 (0.6780 to 0.9009)	
12 Months	0.8810 (0.7949 to 0.9324)	0.9379 (0.8666 to 0.9717)	0.9442 (0.7907 to 0.9861)	0.8176 (0.6780 to 0.9009)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.5 Treatment emergent severe adverse event per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population

	2 or 3		>3		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.8810 (0.7949 to 0.9324)	0.9379 (0.8666 to 0.9717)	0.9442 (0.7907 to 0.9861)	0.8176 (0.6780 to 0.9009)	
16 Months	0.8810 (0.7949 to 0.9324)	0.9379 (0.8666 to 0.9717)	0.9442 (0.7907 to 0.9861)	0.7592 (0.6028 to 0.8607)	
18 Months	0.8810 (0.7949 to 0.9324)	0.9379 (0.8666 to 0.9717)	0.9442 (0.7907 to 0.9861)	0.7592 (0.6028 to 0.8607)	
20 Months	0.8810 (0.7949 to 0.9324)	0.9215 (0.8396 to 0.9624)	0.9442 (0.7907 to 0.9861)	0.7592 (0.6028 to 0.8607)	
22 Months	0.8810 (0.7949 to 0.9324)	0.9215 (0.8396 to 0.9624)	0.9442 (0.7907 to 0.9861)	0.7592 (0.6028 to 0.8607)	
24 Months	0.8810 (0.7949 to 0.9324)	0.9026 (0.8096 to 0.9515)	0.9442 (0.7907 to 0.9861)	0.7262 (0.5614 to 0.8375)	
26 Months	0.8810 (0.7949 to 0.9324)	0.9026 (0.8096 to 0.9515)	0.8917 (0.6820 to 0.9663)	0.7262 (0.5614 to 0.8375)	
Number of patients at risk[c]					
2 Months	89	95	48	47	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.5 Treatment emergent severe adverse event per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population

	2 or 3		>3		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	82	87	45	46	
6 Months	75	80	38	40	
8 Months	68	77	33	39	
10 Months	67	72	29	36	
12 Months	59	70	28	31	
14 Months	58	70	25	31	
16 Months	53	63	23	26	
18 Months	48	58	21	26	
20 Months	46	55	19	25	
22 Months	44	49	19	23	
24 Months	44	46	18	21	
26 Months	42	44	17	17	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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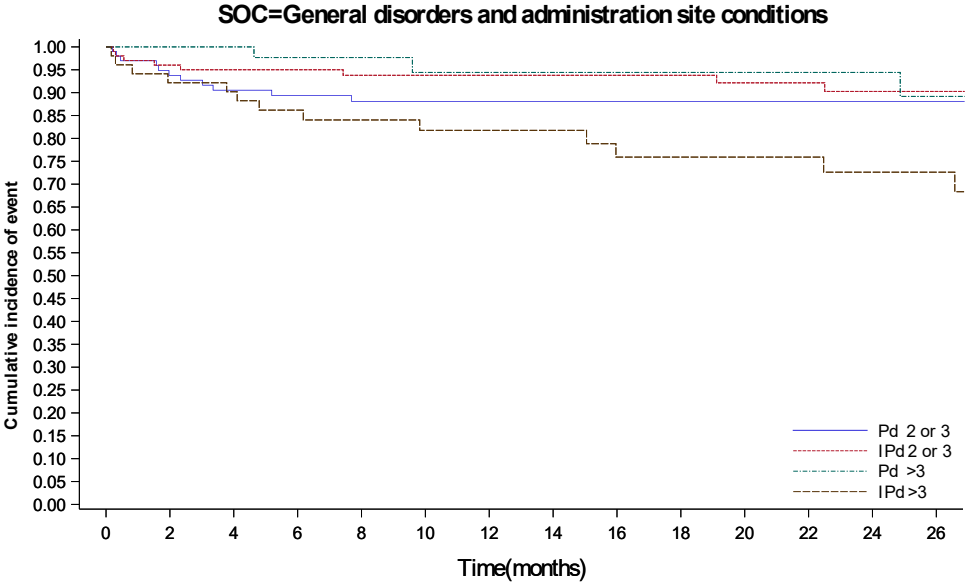
16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.6 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population



Number at Risk

Pd 2 or 3	100	89	82	75	68	67	59	58	53	48	46	44	44	42
IPd 2 or 3	101	95	87	80	77	72	70	70	63	58	55	49	46	44
Pd >3	49	48	45	38	33	29	28	25	23	21	19	19	18	17
IPd >3	51	47	46	40	39	36	31	31	26	26	25	23	21	17

SOC are presented if at least 5% of patients in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae34soc_stratum2_s_f_x.rtf (17NOV2020 14:44)

16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.7 Treatment emergent severe adverse event including death per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population

	2 or 3		>3		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[d]**
General disorders and administration site conditions (days)					
Number (%) of events	15 (15.0)	12 (11.9)	5 (10.2)	15 (29.4)	0.0376
Number (%) of patients censored	85 (85.0)	89 (88.1)	44 (89.8)	36 (70.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (31.3758 to NC)	NC (NC to NC)	NC (24.8706 to NC)	15.9671 (4.3039 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (26.5791 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4290		0.0391	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.7361 (0.3435 to 1.5774)		2.7782 (1.0087 to 7.6521)	
P-value	-	0.4307		0.0481	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.7 Treatment emergent severe adverse event including death per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population

	2 or 3		>3		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.3599 (0.1307 to 0.9914)		
Events probability (95% CI)[c]					
2 Months	0.9280 (0.8548 to 0.9650)	0.9401 (0.8715 to 0.9726)	0.9796 (0.8638 to 0.9971)	0.9216 (0.8044 to 0.9698)	
4 Months	0.8959 (0.8150 to 0.9426)	0.9198 (0.8459 to 0.9590)	0.9583 (0.8433 to 0.9894)	0.9020 (0.7804 to 0.9580)	
6 Months	0.8624 (0.7746 to 0.9178)	0.9198 (0.8459 to 0.9590)	0.9360 (0.8143 to 0.9789)	0.8226 (0.6868 to 0.9035)	
8 Months	0.8502 (0.7598 to 0.9086)	0.9080 (0.8303 to 0.9511)	0.9360 (0.8143 to 0.9789)	0.8021 (0.6632 to 0.8883)	
10 Months	0.8502 (0.7598 to 0.9086)	0.8955 (0.8140 to 0.9426)	0.9048 (0.7617 to 0.9639)	0.7804 (0.6382 to 0.8720)	
12 Months	0.8502 (0.7598 to 0.9086)	0.8955 (0.8140 to 0.9426)	0.9048 (0.7617 to 0.9639)	0.7804 (0.6382 to 0.8720)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.7 Treatment emergent severe adverse event including death per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population

	2 or 3		>3		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.8502 (0.7598 to 0.9086)	0.8955 (0.8140 to 0.9426)	0.9048 (0.7617 to 0.9639)	0.7804 (0.6382 to 0.8720)	
16 Months	0.8502 (0.7598 to 0.9086)	0.8955 (0.8140 to 0.9426)	0.9048 (0.7617 to 0.9639)	0.7246 (0.5698 to 0.8316)	
18 Months	0.8502 (0.7598 to 0.9086)	0.8955 (0.8140 to 0.9426)	0.9048 (0.7617 to 0.9639)	0.7246 (0.5698 to 0.8316)	
20 Months	0.8502 (0.7598 to 0.9086)	0.8798 (0.7916 to 0.9323)	0.9048 (0.7617 to 0.9639)	0.7246 (0.5698 to 0.8316)	
22 Months	0.8502 (0.7598 to 0.9086)	0.8798 (0.7916 to 0.9323)	0.9048 (0.7617 to 0.9639)	0.7246 (0.5698 to 0.8316)	
24 Months	0.8502 (0.7598 to 0.9086)	0.8619 (0.7657 to 0.9205)	0.9048 (0.7617 to 0.9639)	0.6931 (0.5316 to 0.8084)	
26 Months	0.8502 (0.7598 to 0.9086)	0.8619 (0.7657 to 0.9205)	0.8545 (0.6644 to 0.9414)	0.6931 (0.5316 to 0.8084)	
Number of patients at risk[c]					
2 Months	89	93	48	47	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.7 Treatment emergent severe adverse event including death per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population

	2 or 3		>3		
	Pd (N=100)	**IPd (N=101)**	**Pd (N=49)**	**IPd (N=51)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	82	87	44	46	
6 Months	75	80	38	40	
8 Months	68	77	33	39	
10 Months	67	72	29	36	
12 Months	59	70	28	31	
14 Months	58	70	25	31	
16 Months	53	63	23	26	
18 Months	48	58	21	26	
20 Months	46	55	19	25	
22 Months	44	49	19	23	
24 Months	44	46	18	21	
26 Months	42	44	17	17	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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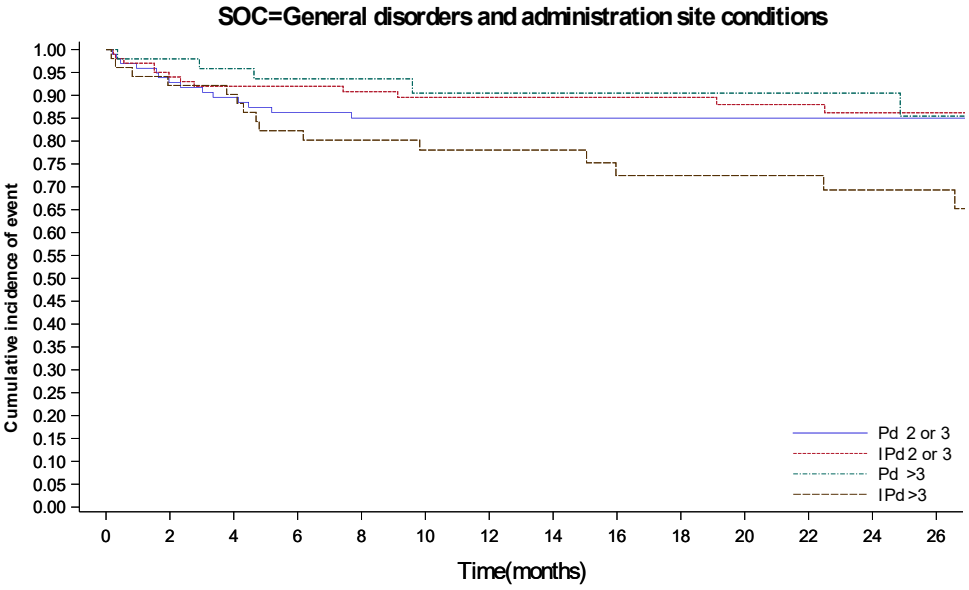
16.2.7.1 Safety endpoints
16.2.7.1.42 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.42.8 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population



Number at Risk

Pd 2 or 3	100	89	82	75	68	67	59	58	53	48	46	44	44	42
IPd 2 or 3	101	93	87	80	77	72	70	70	63	58	55	49	46	44
Pd >3	49	48	44	38	33	29	28	25	23	21	19	19	18	17
IPd >3	51	47	46	40	39	36	31	31	26	26	25	23	21	17

SOC are presented if at least 5% of patients in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae345soc_stratum2_s_f_x.rtf (17NOV2020 14:44)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.1 Treatment emergent adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Musculoskeletal and connective tissue disorders (days)					
Number (%) of events	33 (48.5)	61 (69.3)	45 (55.6)	31 (48.4)	0.0079
Number (%) of patients censored	35 (51.5)	27 (30.7)	36 (44.4)	33 (51.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.7926 (0.8214 to 5.6181)	1.3142 (0.7228 to 2.1027)	1.5770 (0.5585 to 2.8255)	3.7125 (1.4456 to 6.6037)	
Median (95% CI)	10.9733 (5.9138 to NC)	6.6037 (2.7269 to 10.1848)	4.8296 (3.1869 to 27.5647)	15.0801 (6.8008 to NC)	
75% quantile (95% CI)	NC (NC to NC)	26.6448 (12.3860 to NC)	NC (27.5647 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0266		0.0460	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_sex_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.1 Treatment emergent adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.6284 (1.0543 to 2.5151)		0.6221 (0.3888 to 0.9954)	
P-value	-	0.0279		0.0478	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6141 (0.3976 to 0.9485)				
Events probability (95% CI)[c]					
2 Months	0.7746 (0.6541 to 0.8576)	0.7020 (0.5940 to 0.7863)	0.7211 (0.6079 to 0.8067)	0.8275 (0.7102 to 0.9006)	
4 Months	0.7110 (0.5847 to 0.8051)	0.5258 (0.4154 to 0.6248)	0.5706 (0.4517 to 0.6729)	0.7307 (0.6029 to 0.8232)	
6 Months	0.6188 (0.4850 to 0.7274)	0.5013 (0.3915 to 0.6015)	0.4794 (0.3608 to 0.5885)	0.7137 (0.5844 to 0.8091)	
8 Months	0.5795 (0.4439 to 0.6932)	0.4499 (0.3417 to 0.5521)	0.4432 (0.3245 to 0.5552)	0.5638 (0.4269 to 0.6800)	
10 Months	0.5580 (0.4214 to 0.6746)	0.3981 (0.2927 to 0.5013)	0.4199 (0.2999 to 0.5351)	0.5256 (0.3890 to 0.6452)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.1 Treatment emergent adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	0.4883 (0.3494 to 0.6134)	0.3583 (0.2560 to 0.4615)	0.4199 (0.2999 to 0.5351)	0.5256 (0.3890 to 0.6452)	
14 Months	0.4639 (0.3249 to 0.5916)	0.3445 (0.2434 to 0.4477)	0.4199 (0.2999 to 0.5351)	0.5054 (0.3691 to 0.6267)	
16 Months	0.4381 (0.2993 to 0.5686)	0.3132 (0.2142 to 0.4169)	0.4199 (0.2999 to 0.5351)	0.4834 (0.3471 to 0.6069)	
18 Months	0.4381 (0.2993 to 0.5686)	0.3132 (0.2142 to 0.4169)	0.4199 (0.2999 to 0.5351)	0.4834 (0.3471 to 0.6069)	
20 Months	0.4381 (0.2993 to 0.5686)	0.3132 (0.2142 to 0.4169)	0.4199 (0.2999 to 0.5351)	0.4604 (0.3243 to 0.5860)	
22 Months	0.4381 (0.2993 to 0.5686)	0.3132 (0.2142 to 0.4169)	0.3849 (0.2589 to 0.5093)	0.4604 (0.3243 to 0.5860)	
24 Months	0.4381 (0.2993 to 0.5686)	0.2936 (0.1953 to 0.3987)	0.3849 (0.2589 to 0.5093)	0.4604 (0.3243 to 0.5860)	
26 Months	0.4381 (0.2993 to 0.5686)	0.2936 (0.1953 to 0.3987)	0.3849 (0.2589 to 0.5093)	0.4604 (0.3243 to 0.5860)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.1 Treatment emergent adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Number of patients at risk[c]					
2 Months	50	61	56	52	
4 Months	43	44	41	44	
6 Months	32	39	28	39	
8 Months	29	35	19	30	
10 Months	26	30	18	27	
12 Months	20	26	17	26	
14 Months	18	24	15	25	
16 Months	17	20	15	22	
18 Months	17	18	14	21	
20 Months	16	18	12	20	
22 Months	16	16	11	18	
24 Months	15	15	11	18	
26 Months	15	13	10	17	
Psychiatric disorders (days)					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.1 Treatment emergent adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	12 (17.6)	22 (25.0)	20 (24.7)	9 (14.1)	0.0490
Number (%) of patients censored	56 (82.4)	66 (75.0)	61 (75.3)	55 (85.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (6.2423 to NC)	12.2875 (3.8439 to NC)	10.7433 (3.3511 to NC)	NC (24.1478 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3545		0.0814	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.3968 (0.6863 to 2.8427)		0.5015 (0.2273 to 1.1066)	
P-value	-	0.3567		0.0874	
Events probability (95% CI)[c]					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.1 Treatment emergent adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
2 Months	0.8804 (0.7750 to 0.9384)	0.8739 (0.7838 to 0.9281)	0.8996 (0.8091 to 0.9485)	0.9375 (0.8420 to 0.9761)	
4 Months	0.8650 (0.7564 to 0.9274)	0.8383 (0.7421 to 0.9009)	0.8450 (0.7429 to 0.9090)	0.9216 (0.8219 to 0.9666)	
6 Months	0.8650 (0.7564 to 0.9274)	0.7748 (0.6695 to 0.8503)	0.7816 (0.6668 to 0.8608)	0.9042 (0.7989 to 0.9559)	
8 Months	0.8470 (0.7336 to 0.9148)	0.7748 (0.6695 to 0.8503)	0.7620 (0.6427 to 0.8462)	0.9042 (0.7989 to 0.9559)	
10 Months	0.8470 (0.7336 to 0.9148)	0.7593 (0.6511 to 0.8381)	0.7620 (0.6427 to 0.8462)	0.9042 (0.7989 to 0.9559)	
12 Months	0.8470 (0.7336 to 0.9148)	0.7593 (0.6511 to 0.8381)	0.7420 (0.6184 to 0.8308)	0.9042 (0.7989 to 0.9559)	
14 Months	0.8241 (0.7022 to 0.8995)	0.7432 (0.6321 to 0.8253)	0.7420 (0.6184 to 0.8308)	0.9042 (0.7989 to 0.9559)	
16 Months	0.8241 (0.7022 to 0.8995)	0.7267 (0.6129 to 0.8120)	0.7195 (0.5908 to 0.8139)	0.9042 (0.7989 to 0.9559)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.1 Treatment emergent adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
18 Months	0.8241 (0.7022 to 0.8995)	0.7267 (0.6129 to 0.8120)	0.7195 (0.5908 to 0.8139)	0.8798 (0.7610 to 0.9417)	
20 Months	0.8241 (0.7022 to 0.8995)	0.7267 (0.6129 to 0.8120)	0.7195 (0.5908 to 0.8139)	0.8798 (0.7610 to 0.9417)	
22 Months	0.8241 (0.7022 to 0.8995)	0.7267 (0.6129 to 0.8120)	0.7195 (0.5908 to 0.8139)	0.8798 (0.7610 to 0.9417)	
24 Months	0.8241 (0.7022 to 0.8995)	0.7267 (0.6129 to 0.8120)	0.6882 (0.5485 to 0.7926)	0.8798 (0.7610 to 0.9417)	
26 Months	0.8241 (0.7022 to 0.8995)	0.7267 (0.6129 to 0.8120)	0.6882 (0.5485 to 0.7926)	0.8472 (0.7075 to 0.9236)	
Number of patients at risk[c]					
2 Months	57	75	69	59	
4 Months	54	69	60	55	
6 Months	48	58	47	50	
8 Months	46	55	39	48	
10 Months	43	49	39	46	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.1 Treatment emergent adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	37	47	36	43	
14 Months	34	45	34	43	
16 Months	31	41	30	37	
18 Months	28	40	26	33	
20 Months	27	39	23	30	
22 Months	25	35	23	27	
24 Months	24	32	22	27	
26 Months	22	29	21	24	
Skin and subcutaneous tissue disorders (days)					
Number (%) of events	15 (22.1)	34 (38.6)	22 (27.2)	13 (20.3)	0.0369
Number (%) of patients censored	53 (77.9)	54 (61.4)	59 (72.8)	51 (79.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (1.0513 to NC)	6.6694 (1.2813 to 10.2177)	6.0780 (2.3984 to NC)	NC (2.5298 to NC)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.1 Treatment emergent adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Median (95% CI)	NC (NC to NC)	NC (14.3573 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0799		0.2940	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.7181 (0.9308 to 3.1712)		0.6927 (0.3476 to 1.3804)	
P-value	-	0.0835		0.2966	
Events probability (95% CI)[c]					
2 Months	0.8504 (0.7397 to 0.9166)	0.8282 (0.7313 to 0.8927)	0.8505 (0.7516 to 0.9122)	0.8750 (0.7656 to 0.9354)	
4 Months	0.8346 (0.7212 to 0.9049)	0.7812 (0.6786 to 0.8545)	0.7953 (0.6873 to 0.8695)	0.8432 (0.7281 to 0.9124)	
6 Months	0.7975 (0.6758 to 0.8775)	0.7686 (0.6645 to 0.8442)	0.7647 (0.6518 to 0.8453)	0.8432 (0.7281 to 0.9124)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.1 Treatment emergent adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	0.7975 (0.6758 to 0.8775)	0.7264 (0.6166 to 0.8096)	0.7126 (0.5913 to 0.8037)	0.8432 (0.7281 to 0.9124)	
10 Months	0.7765 (0.6499 to 0.8621)	0.6796 (0.5638 to 0.7708)	0.7126 (0.5913 to 0.8037)	0.8035 (0.6786 to 0.8839)	
12 Months	0.7765 (0.6499 to 0.8621)	0.6473 (0.5283 to 0.7434)	0.7126 (0.5913 to 0.8037)	0.8035 (0.6786 to 0.8839)	
14 Months	0.7523 (0.6191 to 0.8445)	0.6311 (0.5109 to 0.7294)	0.7126 (0.5913 to 0.8037)	0.8035 (0.6786 to 0.8839)	
16 Months	0.7523 (0.6191 to 0.8445)	0.5979 (0.4755 to 0.7005)	0.7126 (0.5913 to 0.8037)	0.8035 (0.6786 to 0.8839)	
18 Months	0.7523 (0.6191 to 0.8445)	0.5979 (0.4755 to 0.7005)	0.7126 (0.5913 to 0.8037)	0.7758 (0.6404 to 0.8653)	
20 Months	0.7523 (0.6191 to 0.8445)	0.5979 (0.4755 to 0.7005)	0.7126 (0.5913 to 0.8037)	0.7758 (0.6404 to 0.8653)	
22 Months	0.7523 (0.6191 to 0.8445)	0.5979 (0.4755 to 0.7005)	0.7126 (0.5913 to 0.8037)	0.7758 (0.6404 to 0.8653)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.1 Treatment emergent adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
24 Months	0.7523 (0.6191 to 0.8445)	0.5772 (0.4525 to 0.6833)	0.7126 (0.5913 to 0.8037)	0.7758 (0.6404 to 0.8653)	
26 Months	0.7523 (0.6191 to 0.8445)	0.5772 (0.4525 to 0.6833)	0.7126 (0.5913 to 0.8037)	0.7758 (0.6404 to 0.8653)	
Number of patients at risk[c]					
2 Months	55	71	65	55	
4 Months	51	64	57	50	
6 Months	42	56	45	45	
8 Months	41	50	35	43	
10 Months	37	42	35	39	
12 Months	33	40	33	36	
14 Months	30	38	32	36	
16 Months	27	35	29	31	
18 Months	25	31	25	28	
20 Months	24	31	22	26	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.1 Treatment emergent adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
22 Months	22	29	22	23	
24 Months	21	25	22	23	
26 Months	19	22	21	21	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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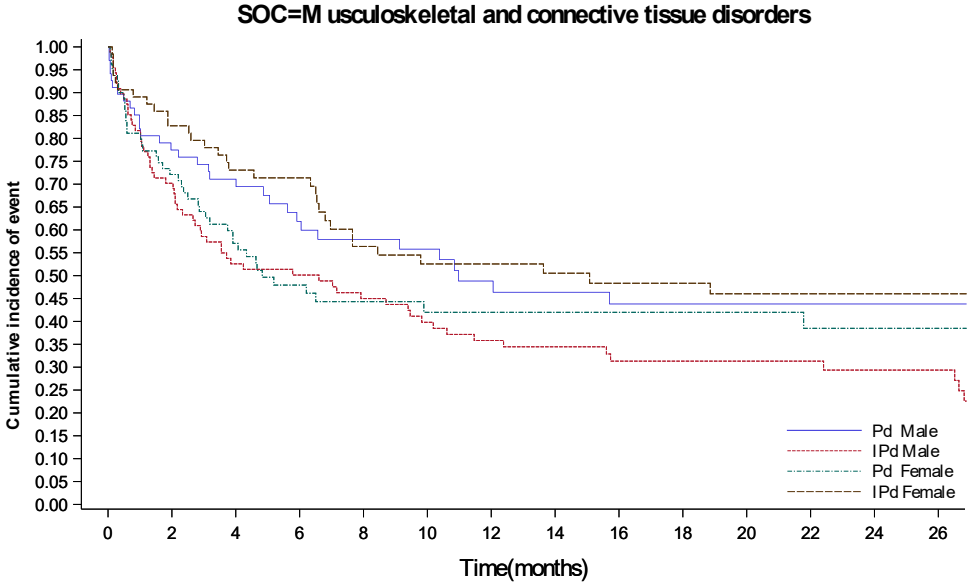
16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per SOC by treatment group according to gender - Safety population

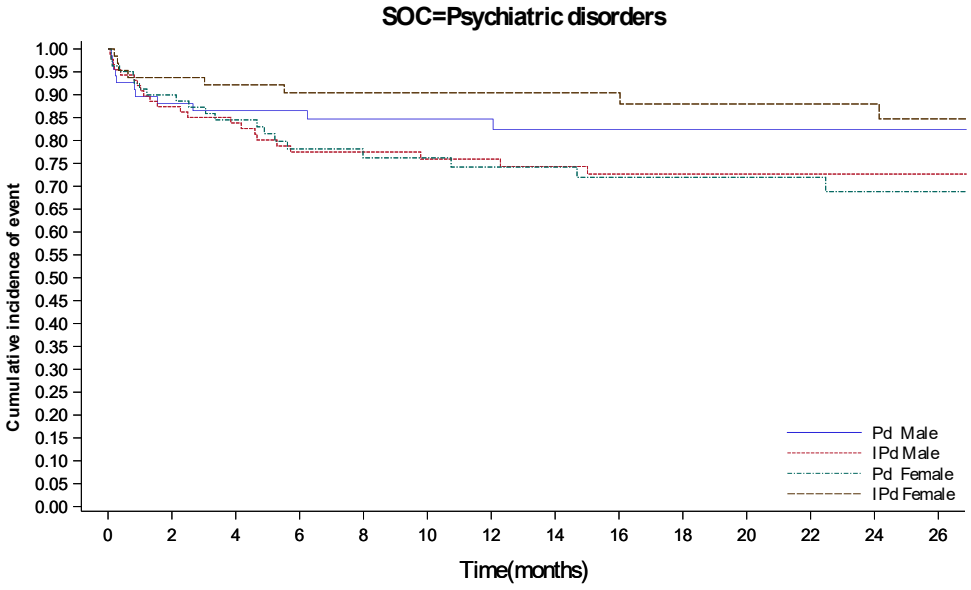


Number at Risk

Pd Male	68	50	43	32	29	26	20	18	17	17	16	16	15	15
IPd Male	88	61	44	39	35	30	26	24	20	18	18	16	15	13
Pd Female	80	56	41	28	19	18	17	15	15	14	12	11	11	10
IPd Female	64	52	44	39	30	27	26	25	22	21	20	18	18	17

SOC are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_sex_s_f_x.rtf (17NOV2020 14:43)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per SOC by treatment group according to gender - Safety population

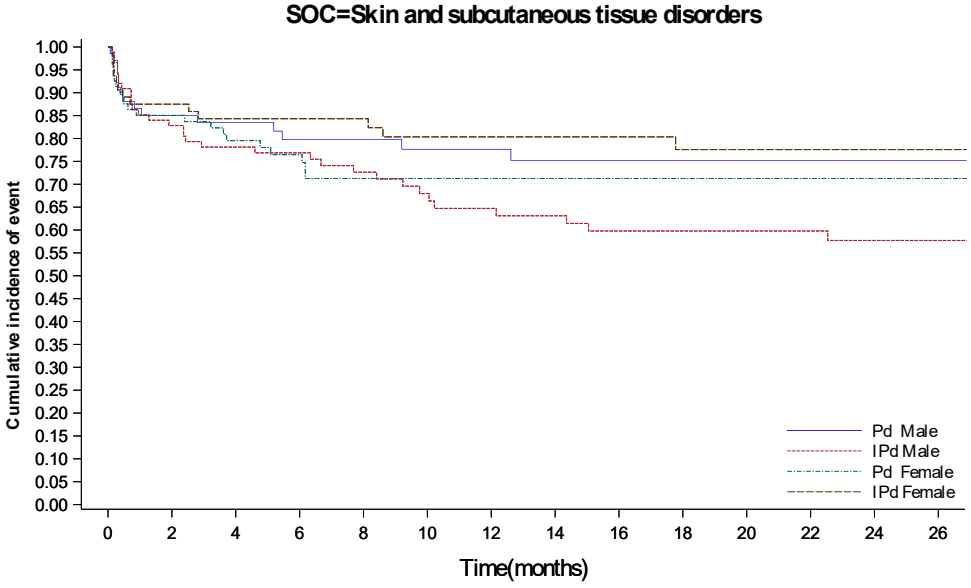


Number at Risk

Pd Male	68	57	54	48	46	43	37	34	31	28	27	25	24	22
IPd Male	88	75	69	58	55	49	47	45	41	40	39	35	32	29
Pd Female	81	69	60	47	39	39	36	34	30	26	23	23	22	21
IPd Female	64	59	55	50	48	46	43	43	37	33	30	27	27	24

SOC are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_sex_s_f_x.rtf (17NOV2020 14:43)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per SOC by treatment group according to gender - Safety population



Number at Risk

Pd Male	68	55	51	42	41	37	33	30	27	25	24	22	21	19
IPd Male	88	71	64	56	50	42	40	38	35	31	31	29	25	22
Pd Female	81	65	57	45	35	35	33	32	29	25	22	22	22	21
IPd Female	64	55	50	45	43	39	36	36	31	28	26	23	23	21

SOC are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_sex_s_f_x.rtf (17NOV2020 14:43)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.3 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Arthralgia (days)					
Number (%) of events	2 (2.9)	12 (13.6)	13 (16.0)	5 (7.8)	0.0093
Number (%) of patients censored	66 (97.1)	76 (86.4)	68 (84.0)	59 (92.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (26.5133 to NC)	NC (7.6222 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0294		0.1358	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	4.5767 (1.0189 to 20.5569)		0.4609 (0.1626 to 1.3065)	
P-value	-	0.0472		0.1451	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_sex_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.3 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.2185 (0.0486 to 0.9814)				
Events probability (95% CI)[c]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9429 (0.8683 to 0.9758)	0.9370 (0.8551 to 0.9733)	0.9688 (0.8808 to 0.9921)	
4 Months	0.9687 (0.8807 to 0.9921)	0.9057 (0.8200 to 0.9517)	0.9098 (0.8199 to 0.9560)	0.9529 (0.8609 to 0.9846)	
6 Months	0.9687 (0.8807 to 0.9921)	0.9057 (0.8200 to 0.9517)	0.8949 (0.8003 to 0.9461)	0.9529 (0.8609 to 0.9846)	
8 Months	0.9687 (0.8807 to 0.9921)	0.9057 (0.8200 to 0.9517)	0.8418 (0.7301 to 0.9101)	0.9148 (0.8062 to 0.9638)	
10 Months	0.9687 (0.8807 to 0.9921)	0.9057 (0.8200 to 0.9517)	0.8418 (0.7301 to 0.9101)	0.9148 (0.8062 to 0.9638)	
12 Months	0.9687 (0.8807 to 0.9921)	0.8745 (0.7777 to 0.9309)	0.8418 (0.7301 to 0.9101)	0.9148 (0.8062 to 0.9638)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.3 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.9687 (0.8807 to 0.9921)	0.8583 (0.7567 to 0.9196)	0.8202 (0.7011 to 0.8953)	0.9148 (0.8062 to 0.9638)	
16 Months	0.9687 (0.8807 to 0.9921)	0.8583 (0.7567 to 0.9196)	0.8202 (0.7011 to 0.8953)	0.9148 (0.8062 to 0.9638)	
18 Months	0.9687 (0.8807 to 0.9921)	0.8583 (0.7567 to 0.9196)	0.7954 (0.6672 to 0.8785)	0.9148 (0.8062 to 0.9638)	
20 Months	0.9687 (0.8807 to 0.9921)	0.8583 (0.7567 to 0.9196)	0.7954 (0.6672 to 0.8785)	0.9148 (0.8062 to 0.9638)	
22 Months	0.9687 (0.8807 to 0.9921)	0.8583 (0.7567 to 0.9196)	0.7954 (0.6672 to 0.8785)	0.9148 (0.8062 to 0.9638)	
24 Months	0.9687 (0.8807 to 0.9921)	0.8583 (0.7567 to 0.9196)	0.7954 (0.6672 to 0.8785)	0.9148 (0.8062 to 0.9638)	
26 Months	0.9687 (0.8807 to 0.9921)	0.8583 (0.7567 to 0.9196)	0.7954 (0.6672 to 0.8785)	0.9148 (0.8062 to 0.9638)	
Number of patients at risk[c]					
2 Months	65	81	72	61	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.3 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	60	73	65	57	
6 Months	53	67	54	52	
8 Months	51	64	43	48	
10 Months	48	59	43	46	
12 Months	42	54	40	43	
14 Months	39	52	36	43	
16 Months	36	48	33	38	
18 Months	32	45	29	35	
20 Months	31	44	27	34	
22 Months	30	40	27	30	
24 Months	29	37	27	30	
26 Months	27	33	26	28	
Asthenia (days)					
Number (%) of events	10 (14.7)	18 (20.5)	18 (22.2)	6 (9.4)	0.0382
Number (%) of patients censored	58 (85.3)	70 (79.5)	63 (77.8)	58 (90.6)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.3 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (5.8809 to NC)	NC (3.9097 to NC)	13.0103 (6.1766 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3975		0.0265	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.3983 (0.6409 to 3.0511)		0.3623 (0.1422 to 0.9228)	
P-value	-	0.3996		0.0333	
Events probability (95% CI)[c]					
2 Months	0.9559 (0.8694 to 0.9856)	0.9087 (0.8257 to 0.9533)	0.8596 (0.7608 to 0.9197)	0.9531 (0.8617 to 0.9846)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_sex_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.3 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	0.9073 (0.8049 to 0.9573)	0.8380 (0.7417 to 0.9008)	0.8596 (0.7608 to 0.9197)	0.9214 (0.8213 to 0.9665)	
6 Months	0.8535 (0.7364 to 0.9213)	0.8257 (0.7274 to 0.8911)	0.8596 (0.7608 to 0.9197)	0.9040 (0.7984 to 0.9557)	
8 Months	0.8535 (0.7364 to 0.9213)	0.7984 (0.6952 to 0.8698)	0.8262 (0.7182 to 0.8957)	0.9040 (0.7984 to 0.9557)	
10 Months	0.8332 (0.7106 to 0.9072)	0.7984 (0.6952 to 0.8698)	0.7887 (0.6710 to 0.8683)	0.9040 (0.7984 to 0.9557)	
12 Months	0.8332 (0.7106 to 0.9072)	0.7821 (0.6752 to 0.8574)	0.7694 (0.6476 to 0.8537)	0.9040 (0.7984 to 0.9557)	
14 Months	0.8332 (0.7106 to 0.9072)	0.7821 (0.6752 to 0.8574)	0.7497 (0.6241 to 0.8386)	0.9040 (0.7984 to 0.9557)	
16 Months	0.8332 (0.7106 to 0.9072)	0.7821 (0.6752 to 0.8574)	0.7497 (0.6241 to 0.8386)	0.9040 (0.7984 to 0.9557)	
18 Months	0.8332 (0.7106 to 0.9072)	0.7821 (0.6752 to 0.8574)	0.7497 (0.6241 to 0.8386)	0.9040 (0.7984 to 0.9557)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_sex_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.3 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
20 Months	0.8332 (0.7106 to 0.9072)	0.7821 (0.6752 to 0.8574)	0.7497 (0.6241 to 0.8386)	0.9040 (0.7984 to 0.9557)	
22 Months	0.8332 (0.7106 to 0.9072)	0.7821 (0.6752 to 0.8574)	0.7497 (0.6241 to 0.8386)	0.9040 (0.7984 to 0.9557)	
24 Months	0.8332 (0.7106 to 0.9072)	0.7821 (0.6752 to 0.8574)	0.7497 (0.6241 to 0.8386)	0.9040 (0.7984 to 0.9557)	
26 Months	0.8332 (0.7106 to 0.9072)	0.7821 (0.6752 to 0.8574)	0.7497 (0.6241 to 0.8386)	0.9040 (0.7984 to 0.9557)	
Number of patients at risk[c]					
2 Months	62	79	66	60	
4 Months	56	68	62	55	
6 Months	47	61	54	50	
8 Months	45	57	45	48	
10 Months	41	52	42	46	
12 Months	36	48	40	42	
14 Months	34	48	36	42	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.3 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	33	45	33	38	
18 Months	30	43	30	35	
20 Months	29	42	27	32	
22 Months	27	38	27	28	
24 Months	26	35	27	28	
26 Months	25	31	26	26	
Diarrhoea (days)					
Number (%) of events	15 (22.1)	35 (39.8)	18 (22.2)	11 (17.2)	0.0336
Number (%) of patients censored	53 (77.9)	53 (60.2)	63 (77.8)	53 (82.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	18.0370 (5.2895 to NC)	6.2423 (1.4456 to 10.6776)	26.9076 (3.0554 to NC)	NC (11.5647 to NC)	
Median (95% CI)	NC (NC to NC)	NC (12.7474 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.3 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0553		0.4172	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.8104 (0.9782 to 3.3507)		0.7327 (0.3446 to 1.5579)	
P-value	-	0.0588		0.4190	
Events probability (95% CI)[c]					
2 Months	0.9242 (0.8273 to 0.9677)	0.8279 (0.7308 to 0.8925)	0.8742 (0.7788 to 0.9303)	0.9219 (0.8224 to 0.9667)	
4 Months	0.8612 (0.7501 to 0.9253)	0.7802 (0.6771 to 0.8538)	0.8202 (0.7151 to 0.8895)	0.8895 (0.7821 to 0.9458)	
6 Months	0.8429 (0.7270 to 0.9124)	0.7550 (0.6491 to 0.8330)	0.8044 (0.6960 to 0.8775)	0.8895 (0.7821 to 0.9458)	
8 Months	0.8237 (0.7032 to 0.8987)	0.7010 (0.5895 to 0.7876)	0.8044 (0.6960 to 0.8775)	0.8710 (0.7580 to 0.9334)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_sex_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.3 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
10 Months	0.8041 (0.6793 to 0.8843)	0.6733 (0.5595 to 0.7637)	0.8044 (0.6960 to 0.8775)	0.8710 (0.7580 to 0.9334)	
12 Months	0.7835 (0.6543 to 0.8690)	0.6270 (0.5093 to 0.7240)	0.8044 (0.6960 to 0.8775)	0.8497 (0.7295 to 0.9194)	
14 Months	0.7835 (0.6543 to 0.8690)	0.6113 (0.4927 to 0.7103)	0.7833 (0.6679 to 0.8626)	0.8497 (0.7295 to 0.9194)	
16 Months	0.7598 (0.6247 to 0.8518)	0.6113 (0.4927 to 0.7103)	0.7833 (0.6679 to 0.8626)	0.8038 (0.6701 to 0.8877)	
18 Months	0.7598 (0.6247 to 0.8518)	0.5939 (0.4737 to 0.6952)	0.7833 (0.6679 to 0.8626)	0.8038 (0.6701 to 0.8877)	
20 Months	0.7316 (0.5884 to 0.8318)	0.5753 (0.4536 to 0.6794)	0.7833 (0.6679 to 0.8626)	0.8038 (0.6701 to 0.8877)	
22 Months	0.7316 (0.5884 to 0.8318)	0.5555 (0.4319 to 0.6625)	0.7833 (0.6679 to 0.8626)	0.8038 (0.6701 to 0.8877)	
24 Months	0.7316 (0.5884 to 0.8318)	0.5555 (0.4319 to 0.6625)	0.7833 (0.6679 to 0.8626)	0.8038 (0.6701 to 0.8877)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_sex_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.3 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
26 Months	0.7316 (0.5884 to 0.8318)	0.5555 (0.4319 to 0.6625)	0.7833 (0.6679 to 0.8626)	0.8038 (0.6701 to 0.8877)	
Number of patients at risk[c]					
2 Months	60	71	67	58	
4 Months	53	64	60	54	
6 Months	45	57	51	49	
8 Months	43	51	42	46	
10 Months	41	44	41	44	
12 Months	36	40	40	40	
14 Months	34	38	37	40	
16 Months	31	36	33	33	
18 Months	27	32	29	31	
20 Months	25	31	26	28	
22 Months	24	27	26	26	
24 Months	23	26	26	26	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.3 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
26 Months	21	23	25	24	
Headache (days)					
Number (%) of events	1 (1.5)	11 (12.5)	8 (9.9)	5 (7.8)	0.0476
Number (%) of patients censored	67 (98.5)	77 (87.5)	73 (90.1)	59 (92.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (12.5503 to NC)	NC (NC to NC)	NC (35.6468 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0121		0.7716	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	8.7915 (1.1324 to 68.2513)		0.8430 (0.2658 to 2.6734)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.3 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
P-value	-	0.0376		0.7718	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.1137 (0.0147 to 0.8831)				
Events probability (95% CI)[c]					
2 Months	0.9848 (0.8973 to 0.9979)	0.9655 (0.8969 to 0.9887)	0.9612 (0.8845 to 0.9873)	0.9841 (0.8926 to 0.9977)	
4 Months	0.9848 (0.8973 to 0.9979)	0.9655 (0.8969 to 0.9887)	0.9612 (0.8845 to 0.9873)	0.9683 (0.8790 to 0.9920)	
6 Months	0.9848 (0.8973 to 0.9979)	0.9266 (0.8435 to 0.9664)	0.9145 (0.8187 to 0.9609)	0.9340 (0.8334 to 0.9747)	
8 Months	0.9848 (0.8973 to 0.9979)	0.9128 (0.8252 to 0.9576)	0.9145 (0.8187 to 0.9609)	0.9340 (0.8334 to 0.9747)	
10 Months	0.9848 (0.8973 to 0.9979)	0.8840 (0.7881 to 0.9382)	0.9145 (0.8187 to 0.9609)	0.9340 (0.8334 to 0.9747)	
12 Months	0.9848 (0.8973 to 0.9979)	0.8690 (0.7692 to 0.9277)	0.9145 (0.8187 to 0.9609)	0.9340 (0.8334 to 0.9747)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.3 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.9848 (0.8973 to 0.9979)	0.8532 (0.7493 to 0.9164)	0.9145 (0.8187 to 0.9609)	0.9340 (0.8334 to 0.9747)	
16 Months	0.9848 (0.8973 to 0.9979)	0.8532 (0.7493 to 0.9164)	0.9145 (0.8187 to 0.9609)	0.9340 (0.8334 to 0.9747)	
18 Months	0.9848 (0.8973 to 0.9979)	0.8532 (0.7493 to 0.9164)	0.9145 (0.8187 to 0.9609)	0.9340 (0.8334 to 0.9747)	
20 Months	0.9848 (0.8973 to 0.9979)	0.8532 (0.7493 to 0.9164)	0.9145 (0.8187 to 0.9609)	0.9340 (0.8334 to 0.9747)	
22 Months	0.9848 (0.8973 to 0.9979)	0.8532 (0.7493 to 0.9164)	0.8860 (0.7666 to 0.9463)	0.9340 (0.8334 to 0.9747)	
24 Months	0.9848 (0.8973 to 0.9979)	0.8532 (0.7493 to 0.9164)	0.8860 (0.7666 to 0.9463)	0.9340 (0.8334 to 0.9747)	
26 Months	0.9848 (0.8973 to 0.9979)	0.8532 (0.7493 to 0.9164)	0.8860 (0.7666 to 0.9463)	0.9340 (0.8334 to 0.9747)	
Number of patients at risk[c]					
2 Months	64	83	73	62	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.3 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	61	79	68	59	
6 Months	54	69	57	52	
8 Months	52	65	49	50	
10 Months	49	59	48	48	
12 Months	43	55	46	44	
14 Months	40	53	43	44	
16 Months	37	50	39	38	
18 Months	33	47	35	35	
20 Months	32	46	32	33	
22 Months	30	41	31	29	
24 Months	29	38	31	29	
26 Months	27	34	30	27	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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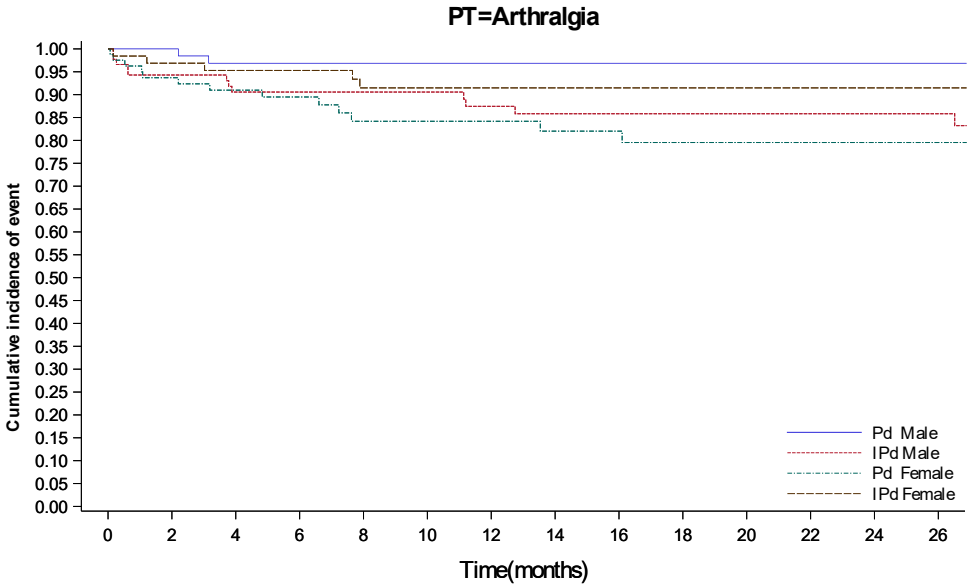
16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to gender - Safety population



Number at Risk

Pd Male	68	65	60	53	51	48	42	39	36	32	31	30	29	27
IPd Male	88	81	73	67	64	59	54	52	48	45	44	40	37	33
Pd Female	81	72	65	54	43	43	40	36	33	29	27	27	27	26
IPd Female	64	61	57	52	48	46	43	43	38	35	34	30	30	28

PT are presented if at least 10 events in a arm
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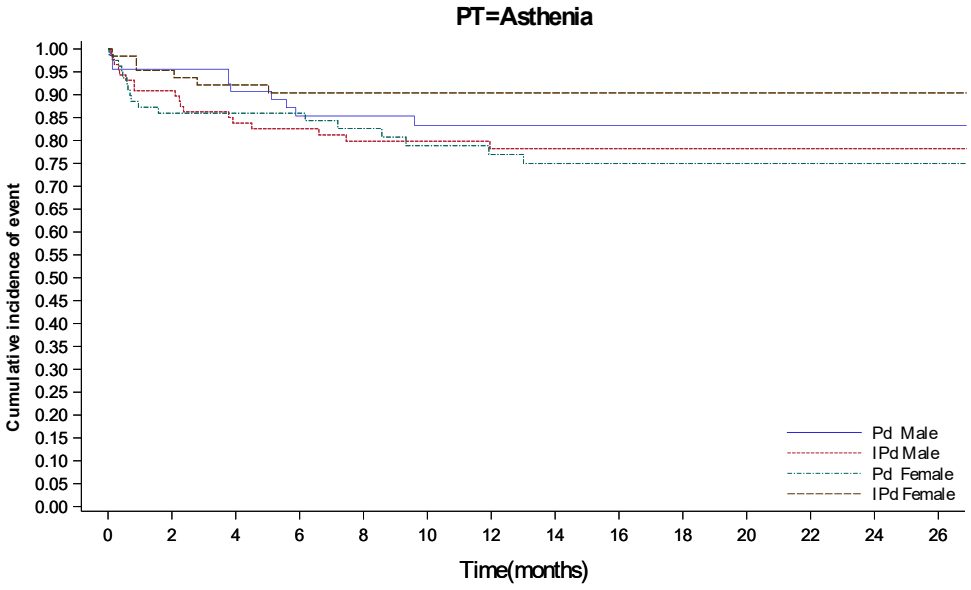
16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to gender - Safety population

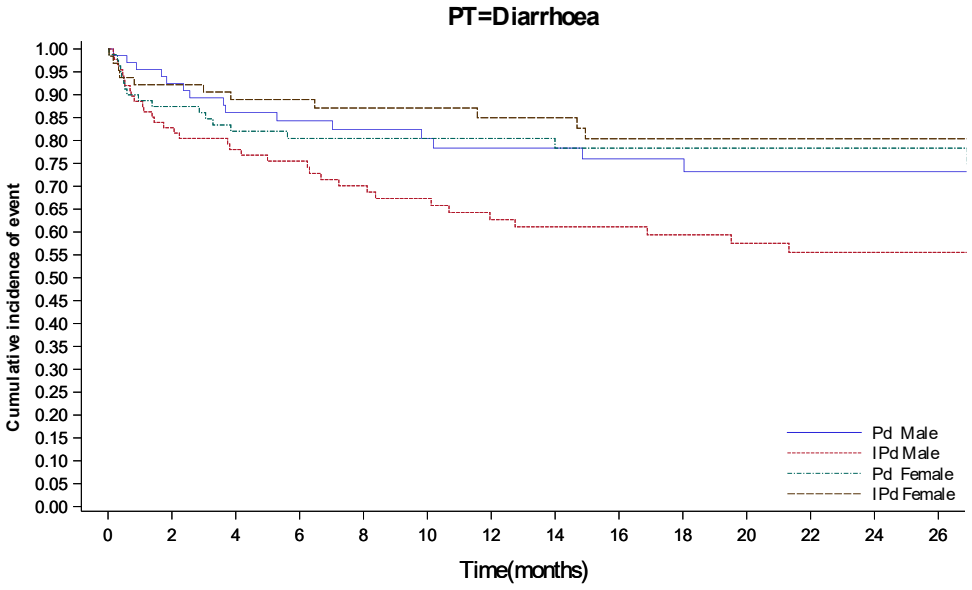


Number at Risk

Pd Male	68	62	56	47	45	41	36	34	33	30	29	27	26	25
IPd Male	88	79	68	61	57	52	48	48	45	43	42	38	35	31
Pd Female	80	66	62	54	45	42	40	36	33	30	27	27	27	26
IPd Female	64	60	55	50	48	46	42	42	38	35	32	28	28	26

PT are presented if at least 10 events in a arm

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to gender - Safety population



Number at Risk

Pd Male	68	60	53	45	43	41	36	34	31	27	25	24	23	21
IPd Male	88	71	64	57	51	44	40	38	36	32	31	27	26	23
Pd Female	81	67	60	51	42	41	40	37	33	29	26	26	26	25
IPd Female	64	58	54	49	46	44	40	40	33	31	28	26	26	24

PT are presented if at least 10 events in a arm
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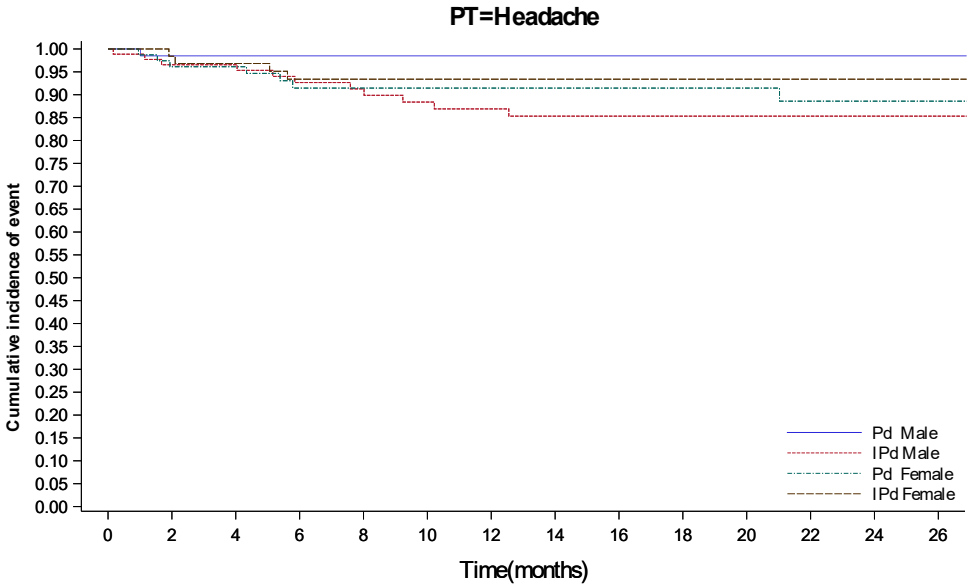
16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to gender - Safety population



Number at Risk

Pd Male	68	64	61	54	52	49	43	40	37	33	32	30	29	27
IPd Male	88	83	79	69	65	59	55	53	50	47	46	41	38	34
Pd Female	80	73	68	57	49	48	46	43	39	35	32	31	31	30
IPd Female	64	62	59	52	50	48	44	44	38	35	33	29	29	27

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_teaept_sex_s_f_x.rtf (17NOV2020 14:43)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.5 Treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Infections and infestations (days)					
Number (%) of events	35 (51.5)	63 (71.6)	51 (63.0)	40 (62.5)	0.0172
Number (%) of patients censored	33 (48.5)	25 (28.4)	30 (37.0)	24 (37.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.9055 (0.9528 to 2.5955)	0.7885 (0.4928 to 1.8070)	1.4784 (0.9528 to 1.8398)	1.7084 (0.7556 to 2.6283)	
Median (95% CI)	9.3306 (3.1211 to NC)	3.3183 (2.1684 to 4.7310)	3.6468 (2.0370 to 7.4251)	4.2382 (2.6612 to 12.0575)	
75% quantile (95% CI)	NC (NC to NC)	11.2690 (5.0924 to NC)	NC (8.9692 to NC)	NC (12.5832 to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0169		0.6106	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12soc_sex_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.5 Treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.6654 (1.0915 to 2.5410)		0.8972 (0.5908 to 1.3624)	
P-value	-	0.0180		0.6108	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6005 (0.3936 to 0.9162)				
Events probability (95% CI)[c]					
2 Months	0.7104 (0.5842 to 0.8045)	0.6204 (0.5097 to 0.7131)	0.6180 (0.5010 to 0.7152)	0.7340 (0.6075 to 0.8255)	
4 Months	0.5833 (0.4535 to 0.6926)	0.4606 (0.3516 to 0.5628)	0.4796 (0.3635 to 0.5864)	0.5066 (0.3770 to 0.6224)	
6 Months	0.5645 (0.4339 to 0.6760)	0.3082 (0.2094 to 0.4123)	0.4486 (0.3333 to 0.5571)	0.4546 (0.3275 to 0.5731)	
8 Months	0.5040 (0.3719 to 0.6222)	0.2620 (0.1684 to 0.3652)	0.3634 (0.2517 to 0.4758)	0.4546 (0.3275 to 0.5731)	
10 Months	0.4821 (0.3496 to 0.6026)	0.2620 (0.1684 to 0.3652)	0.3271 (0.2181 to 0.4403)	0.4151 (0.2895 to 0.5359)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.5 Treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	0.4821 (0.3496 to 0.6026)	0.2418 (0.1498 to 0.3459)	0.3089 (0.2018 to 0.4222)	0.3943 (0.2698 to 0.5163)	
14 Months	0.4580 (0.3249 to 0.5814)	0.2217 (0.1318 to 0.3262)	0.3089 (0.2018 to 0.4222)	0.3528 (0.2316 to 0.4762)	
16 Months	0.4580 (0.3249 to 0.5814)	0.2015 (0.1145 to 0.3060)	0.3089 (0.2018 to 0.4222)	0.3528 (0.2316 to 0.4762)	
18 Months	0.4580 (0.3249 to 0.5814)	0.2015 (0.1145 to 0.3060)	0.3089 (0.2018 to 0.4222)	0.3257 (0.2052 to 0.4517)	
20 Months	0.3969 (0.2605 to 0.5301)	0.2015 (0.1145 to 0.3060)	0.3089 (0.2018 to 0.4222)	0.3257 (0.2052 to 0.4517)	
22 Months	0.3969 (0.2605 to 0.5301)	0.2015 (0.1145 to 0.3060)	0.3089 (0.2018 to 0.4222)	0.3257 (0.2052 to 0.4517)	
24 Months	0.3969 (0.2605 to 0.5301)	0.2015 (0.1145 to 0.3060)	0.3089 (0.2018 to 0.4222)	0.3257 (0.2052 to 0.4517)	
26 Months	0.3969 (0.2605 to 0.5301)	0.2015 (0.1145 to 0.3060)	0.3089 (0.2018 to 0.4222)	0.3257 (0.2052 to 0.4517)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.5 Treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Number of patients at risk[c]					
2 Months	46	53	47	46	
4 Months	35	36	33	30	
6 Months	29	20	28	25	
8 Months	25	17	20	25	
10 Months	22	14	18	21	
12 Months	20	12	17	19	
14 Months	19	11	15	17	
16 Months	16	10	14	14	
18 Months	15	8	13	12	
20 Months	12	8	12	11	
22 Months	10	7	12	9	
24 Months	9	7	12	9	
26 Months	8	6	11	7	
Musculoskeletal and connective tissue disorders (days)					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.5 Treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	32 (47.1)	59 (67.0)	41 (50.6)	29 (45.3)	0.0118
Number (%) of patients censored	36 (52.9)	29 (33.0)	40 (49.4)	35 (54.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	3.1540 (0.9856 to 5.9138)	1.4456 (1.0185 to 2.3326)	2.2998 (1.0185 to 3.7454)	4.5667 (1.4456 to 6.8008)	
Median (95% CI)	12.0575 (6.0452 to NC)	7.0308 (2.9240 to 10.6119)	6.5051 (3.9097 to NC)	18.8583 (6.8008 to NC)	
75% quantile (95% CI)	NC (NC to NC)	27.9261 (15.6057 to NC)	NC (27.5647 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0288		0.0809	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.6316 (1.0480 to 2.5401)		0.6489 (0.3979 to 1.0582)	
P-value	-	0.0302		0.0830	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.5 Treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6129 (0.3937 to 0.9542)				
Events probability (95% CI)[c]					
2 Months	0.7894 (0.6703 to 0.8696)	0.7244 (0.6176 to 0.8060)	0.7695 (0.6592 to 0.8481)	0.8435 (0.7286 to 0.9125)	
4 Months	0.7259 (0.6004 to 0.8178)	0.5456 (0.4342 to 0.6441)	0.6147 (0.4942 to 0.7147)	0.7626 (0.6372 to 0.8496)	
6 Months	0.6342 (0.5005 to 0.7411)	0.5205 (0.4093 to 0.6204)	0.5191 (0.3964 to 0.6284)	0.7283 (0.5994 to 0.8217)	
8 Months	0.5951 (0.4594 to 0.7073)	0.4671 (0.3569 to 0.5699)	0.4813 (0.3577 to 0.5944)	0.5793 (0.4419 to 0.6942)	
10 Months	0.5739 (0.4369 to 0.6890)	0.4266 (0.3181 to 0.5307)	0.4572 (0.3319 to 0.5739)	0.5413 (0.4040 to 0.6598)	
12 Months	0.5021 (0.3616 to 0.6271)	0.3716 (0.2666 to 0.4765)	0.4572 (0.3319 to 0.5739)	0.5413 (0.4040 to 0.6598)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.5 Treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.4770 (0.3361 to 0.6050)	0.3573 (0.2534 to 0.4623)	0.4572 (0.3319 to 0.5739)	0.5212 (0.3841 to 0.6416)	
16 Months	0.4505 (0.3094 to 0.5816)	0.3248 (0.2230 to 0.4306)	0.4572 (0.3319 to 0.5739)	0.5212 (0.3841 to 0.6416)	
18 Months	0.4505 (0.3094 to 0.5816)	0.3248 (0.2230 to 0.4306)	0.4572 (0.3319 to 0.5739)	0.5212 (0.3841 to 0.6416)	
20 Months	0.4505 (0.3094 to 0.5816)	0.3248 (0.2230 to 0.4306)	0.4572 (0.3319 to 0.5739)	0.4964 (0.3581 to 0.6202)	
22 Months	0.4505 (0.3094 to 0.5816)	0.3248 (0.2230 to 0.4306)	0.4191 (0.2854 to 0.5471)	0.4964 (0.3581 to 0.6202)	
24 Months	0.4505 (0.3094 to 0.5816)	0.3248 (0.2230 to 0.4306)	0.4191 (0.2854 to 0.5471)	0.4964 (0.3581 to 0.6202)	
26 Months	0.4505 (0.3094 to 0.5816)	0.3248 (0.2230 to 0.4306)	0.4191 (0.2854 to 0.5471)	0.4964 (0.3581 to 0.6202)	
Number of patients at risk[c]					
2 Months	51	62	58	53	

SOC are presented if at least 10 events in a arm
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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.5 Treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	44	45	43	46	
6 Months	33	39	29	40	
8 Months	30	35	20	31	
10 Months	27	31	19	28	
12 Months	20	26	18	27	
14 Months	18	24	15	26	
16 Months	17	20	15	23	
18 Months	17	18	14	21	
20 Months	16	18	12	20	
22 Months	16	16	11	18	
24 Months	15	16	11	18	
26 Months	15	14	10	17	
Psychiatric disorders (days)					
Number (%) of events	9 (13.2)	21 (23.9)	19 (23.5)	9 (14.1)	0.0275
Number (%) of patients censored	59 (86.8)	67 (76.1)	62 (76.5)	55 (85.9)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.5 Treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (12.0575 to NC)	15.0144 (4.1725 to NC)	14.6858 (4.6653 to NC)	NC (24.1478 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1645		0.1081	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.7363 (0.7899 to 3.8167)		0.5255 (0.2366 to 1.1674)	
P-value	-	0.1698		0.1141	
Events probability (95% CI)[c]					
2 Months	0.9106 (0.8117 to 0.9588)	0.8853 (0.7972 to 0.9366)	0.9122 (0.8247 to 0.9572)	0.9375 (0.8420 to 0.9761)	

SOC are presented if at least 10 events in a arm
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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.5 Treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	0.8949 (0.7920 to 0.9485)	0.8497 (0.7551 to 0.9098)	0.8577 (0.7575 to 0.9187)	0.9216 (0.8219 to 0.9666)	
6 Months	0.8949 (0.7920 to 0.9485)	0.7863 (0.6820 to 0.8599)	0.7945 (0.6809 to 0.8714)	0.9042 (0.7989 to 0.9559)	
8 Months	0.8766 (0.7677 to 0.9365)	0.7863 (0.6820 to 0.8599)	0.7752 (0.6568 to 0.8570)	0.9042 (0.7989 to 0.9559)	
10 Months	0.8766 (0.7677 to 0.9365)	0.7709 (0.6636 to 0.8478)	0.7752 (0.6568 to 0.8570)	0.9042 (0.7989 to 0.9559)	
12 Months	0.8766 (0.7677 to 0.9365)	0.7709 (0.6636 to 0.8478)	0.7553 (0.6326 to 0.8420)	0.9042 (0.7989 to 0.9559)	
14 Months	0.8536 (0.7346 to 0.9219)	0.7548 (0.6446 to 0.8352)	0.7553 (0.6326 to 0.8420)	0.9042 (0.7989 to 0.9559)	
16 Months	0.8536 (0.7346 to 0.9219)	0.7384 (0.6254 to 0.8221)	0.7324 (0.6040 to 0.8250)	0.9042 (0.7989 to 0.9559)	
18 Months	0.8536 (0.7346 to 0.9219)	0.7384 (0.6254 to 0.8221)	0.7324 (0.6040 to 0.8250)	0.8798 (0.7610 to 0.9417)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.5 Treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
20 Months	0.8536 (0.7346 to 0.9219)	0.7384 (0.6254 to 0.8221)	0.7324 (0.6040 to 0.8250)	0.8798 (0.7610 to 0.9417)	
22 Months	0.8536 (0.7346 to 0.9219)	0.7384 (0.6254 to 0.8221)	0.7324 (0.6040 to 0.8250)	0.8798 (0.7610 to 0.9417)	
24 Months	0.8536 (0.7346 to 0.9219)	0.7384 (0.6254 to 0.8221)	0.7006 (0.5602 to 0.8037)	0.8798 (0.7610 to 0.9417)	
26 Months	0.8536 (0.7346 to 0.9219)	0.7384 (0.6254 to 0.8221)	0.7006 (0.5602 to 0.8037)	0.8472 (0.7075 to 0.9236)	
Number of patients at risk[c]					
2 Months	59	76	70	59	
4 Months	55	70	61	55	
6 Months	49	59	48	50	
8 Months	47	56	40	48	
10 Months	44	50	40	46	
12 Months	38	48	37	43	
14 Months	35	46	35	43	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.5 Treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	32	42	30	37	
18 Months	29	41	26	33	
20 Months	28	40	23	30	
22 Months	26	36	23	27	
24 Months	25	33	22	27	
26 Months	23	30	21	24	
Skin and subcutaneous tissue disorders (days)					
Number (%) of events	15 (22.1)	33 (37.5)	22 (27.2)	13 (20.3)	0.0438
Number (%) of patients censored	53 (77.9)	55 (62.5)	59 (72.8)	51 (79.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (1.0513 to NC)	7.6879 (1.2813 to 12.1561)	6.0780 (2.3984 to NC)	NC (2.5298 to NC)	
Median (95% CI)	NC (NC to NC)	NC (15.0472 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.5 Treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0989		0.2940	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.6704 (0.9022 to 3.0924)		0.6927 (0.3476 to 1.3804)	
P-value	-	0.1026		0.2966	
Events probability (95% CI)[c]					
2 Months	0.8504 (0.7397 to 0.9166)	0.8282 (0.7313 to 0.8927)	0.8505 (0.7516 to 0.9122)	0.8750 (0.7656 to 0.9354)	
4 Months	0.8346 (0.7212 to 0.9049)	0.7929 (0.6915 to 0.8642)	0.7953 (0.6873 to 0.8695)	0.8432 (0.7281 to 0.9124)	
6 Months	0.7975 (0.6758 to 0.8775)	0.7803 (0.6773 to 0.8539)	0.7647 (0.6518 to 0.8453)	0.8432 (0.7281 to 0.9124)	
8 Months	0.7975 (0.6758 to 0.8775)	0.7375 (0.6281 to 0.8192)	0.7126 (0.5913 to 0.8037)	0.8432 (0.7281 to 0.9124)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12soc_sex_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.5 Treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
10 Months	0.7765 (0.6499 to 0.8621)	0.6900 (0.5740 to 0.7803)	0.7126 (0.5913 to 0.8037)	0.8035 (0.6786 to 0.8839)	
12 Months	0.7765 (0.6499 to 0.8621)	0.6571 (0.5376 to 0.7527)	0.7126 (0.5913 to 0.8037)	0.8035 (0.6786 to 0.8839)	
14 Months	0.7523 (0.6191 to 0.8445)	0.6407 (0.5198 to 0.7386)	0.7126 (0.5913 to 0.8037)	0.8035 (0.6786 to 0.8839)	
16 Months	0.7523 (0.6191 to 0.8445)	0.6069 (0.4837 to 0.7094)	0.7126 (0.5913 to 0.8037)	0.8035 (0.6786 to 0.8839)	
18 Months	0.7523 (0.6191 to 0.8445)	0.6069 (0.4837 to 0.7094)	0.7126 (0.5913 to 0.8037)	0.7758 (0.6404 to 0.8653)	
20 Months	0.7523 (0.6191 to 0.8445)	0.6069 (0.4837 to 0.7094)	0.7126 (0.5913 to 0.8037)	0.7758 (0.6404 to 0.8653)	
22 Months	0.7523 (0.6191 to 0.8445)	0.6069 (0.4837 to 0.7094)	0.7126 (0.5913 to 0.8037)	0.7758 (0.6404 to 0.8653)	
24 Months	0.7523 (0.6191 to 0.8445)	0.5860 (0.4603 to 0.6921)	0.7126 (0.5913 to 0.8037)	0.7758 (0.6404 to 0.8653)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.5 Treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
26 Months	0.7523 (0.6191 to 0.8445)	0.5860 (0.4603 to 0.6921)	0.7126 (0.5913 to 0.8037)	0.7758 (0.6404 to 0.8653)	
Number of patients at risk[c]					
2 Months	55	71	65	55	
4 Months	51	65	57	50	
6 Months	42	56	45	45	
8 Months	41	50	35	43	
10 Months	37	42	35	39	
12 Months	33	40	33	36	
14 Months	30	38	32	36	
16 Months	27	35	29	31	
18 Months	25	31	25	28	
20 Months	24	31	22	26	
22 Months	22	29	22	23	
24 Months	21	25	22	23	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.5 Treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
26 Months	19	22	21	21	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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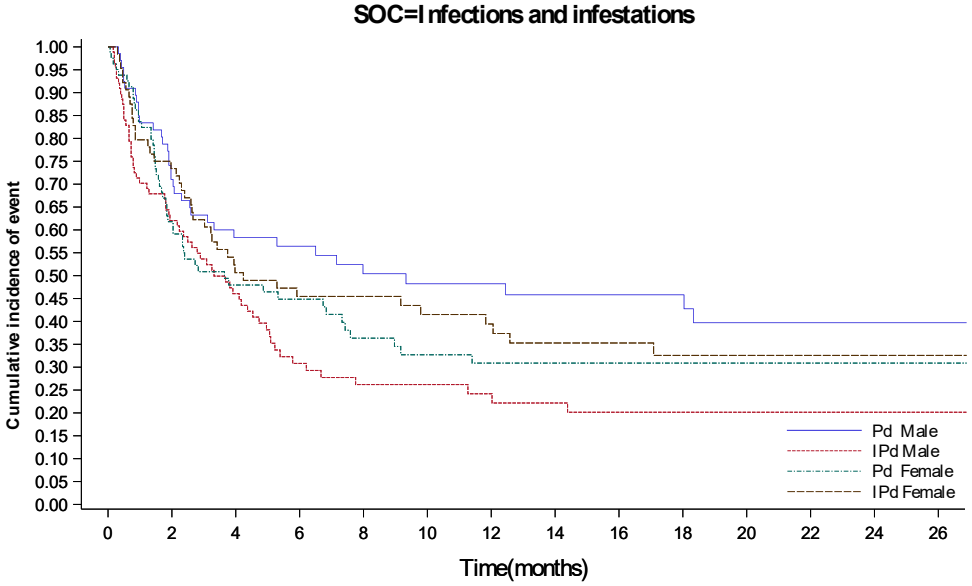
16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.6 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population



Number at Risk

Pd Male	68	46	35	29	25	22	20	19	16	15	12	10	9	8
IPd Male	88	53	36	20	17	14	12	11	10	8	8	7	7	6
Pd Female	81	47	33	28	20	18	17	15	14	13	12	12	12	11
IPd Female	64	46	30	25	25	21	19	17	14	12	11	9	9	7

SOC are presented if at least 10 events in a arm
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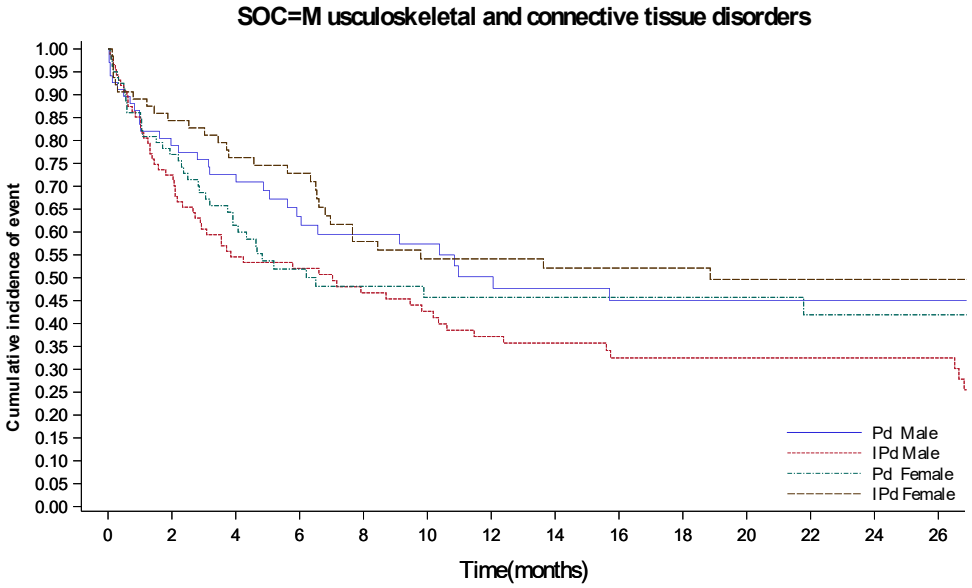
16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.6 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population



Number at Risk

Pd Male	68	51	44	33	30	27	20	18	17	17	16	16	15	15
IPd Male	88	62	45	39	35	31	26	24	20	18	18	16	16	14
Pd Female	80	58	43	29	20	19	18	15	15	14	12	11	11	10
IPd Female	64	53	46	40	31	28	27	26	23	21	20	18	18	17

SOC are presented if at least 10 events in a arm
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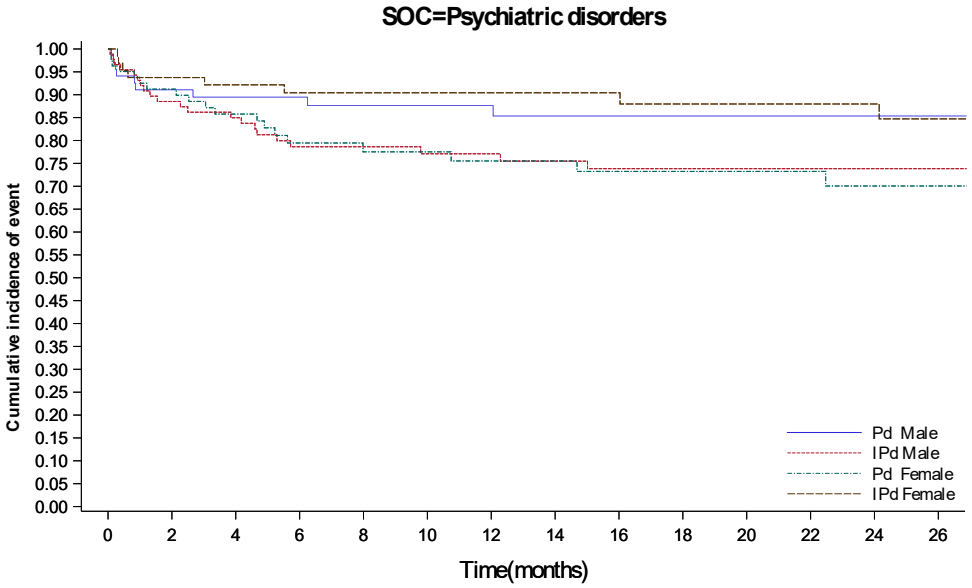
16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.6 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population

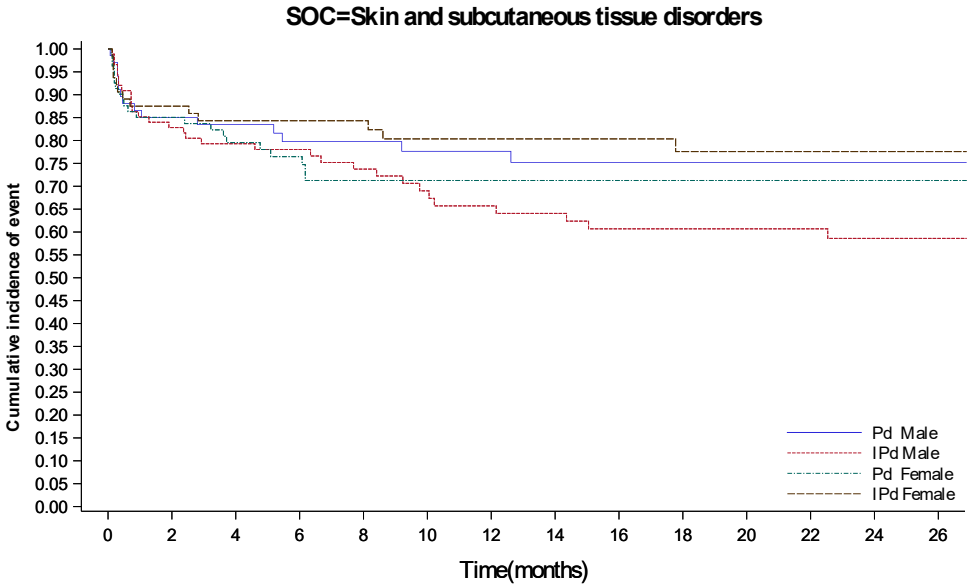


Number at Risk

Pd Male	68	59	55	49	47	44	38	35	32	29	28	26	25	23
IPd Male	88	76	70	59	56	50	48	46	42	41	40	36	33	30
Pd Female	81	70	61	48	40	40	37	35	30	26	23	23	22	21
IPd Female	64	59	55	50	48	46	43	43	37	33	30	27	27	24

SOC are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12soc_sex_s_f_x.rtf (17NOV2020 14:43)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.6 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per SOC by treatment group according to gender - Safety population



Number at Risk

Pd Male	68	55	51	42	41	37	33	30	27	25	24	22	21	19
IPd Male	88	71	65	56	50	42	40	38	35	31	31	29	25	22
Pd Female	81	65	57	45	35	35	33	32	29	25	22	22	22	21
IPd Female	64	55	50	45	43	39	36	36	31	28	26	23	23	21

SOC are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12soc_sex_s_f_x.rtf (17NOV2020 14:43)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.7 Treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Arthralgia (days)					
Number (%) of events	2 (2.9)	9 (10.2)	13 (16.0)	5 (7.8)	0.0247
Number (%) of patients censored	66 (97.1)	79 (89.8)	68 (84.0)	59 (92.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.6222 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0937		0.1358	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	3.4539 (0.7398 to 16.1260)		0.4609 (0.1626 to 1.3065)	
P-value	-	0.1149		0.1451	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.7 Treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9656 (0.8973 to 0.9888)	0.9370 (0.8551 to 0.9733)	0.9688 (0.8808 to 0.9921)	
4 Months	0.9687 (0.8807 to 0.9921)	0.9285 (0.8476 to 0.9673)	0.9098 (0.8199 to 0.9560)	0.9529 (0.8609 to 0.9846)	
6 Months	0.9687 (0.8807 to 0.9921)	0.9285 (0.8476 to 0.9673)	0.8949 (0.8003 to 0.9461)	0.9529 (0.8609 to 0.9846)	
8 Months	0.9687 (0.8807 to 0.9921)	0.9285 (0.8476 to 0.9673)	0.8418 (0.7301 to 0.9101)	0.9148 (0.8062 to 0.9638)	
10 Months	0.9687 (0.8807 to 0.9921)	0.9285 (0.8476 to 0.9673)	0.8418 (0.7301 to 0.9101)	0.9148 (0.8062 to 0.9638)	
12 Months	0.9687 (0.8807 to 0.9921)	0.9125 (0.8240 to 0.9576)	0.8418 (0.7301 to 0.9101)	0.9148 (0.8062 to 0.9638)	
14 Months	0.9687 (0.8807 to 0.9921)	0.8959 (0.8007 to 0.9471)	0.8202 (0.7011 to 0.8953)	0.9148 (0.8062 to 0.9638)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.7 Treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.9687 (0.8807 to 0.9921)	0.8959 (0.8007 to 0.9471)	0.8202 (0.7011 to 0.8953)	0.9148 (0.8062 to 0.9638)	
18 Months	0.9687 (0.8807 to 0.9921)	0.8959 (0.8007 to 0.9471)	0.7954 (0.6672 to 0.8785)	0.9148 (0.8062 to 0.9638)	
20 Months	0.9687 (0.8807 to 0.9921)	0.8959 (0.8007 to 0.9471)	0.7954 (0.6672 to 0.8785)	0.9148 (0.8062 to 0.9638)	
22 Months	0.9687 (0.8807 to 0.9921)	0.8959 (0.8007 to 0.9471)	0.7954 (0.6672 to 0.8785)	0.9148 (0.8062 to 0.9638)	
24 Months	0.9687 (0.8807 to 0.9921)	0.8959 (0.8007 to 0.9471)	0.7954 (0.6672 to 0.8785)	0.9148 (0.8062 to 0.9638)	
26 Months	0.9687 (0.8807 to 0.9921)	0.8959 (0.8007 to 0.9471)	0.7954 (0.6672 to 0.8785)	0.9148 (0.8062 to 0.9638)	
Number of patients at risk[c]					
2 Months	65	83	72	61	
4 Months	60	75	65	57	
6 Months	53	67	54	52	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.7 Treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	51	64	43	48	
10 Months	48	59	43	46	
12 Months	42	55	40	43	
14 Months	39	53	36	43	
16 Months	36	49	33	38	
18 Months	32	46	29	35	
20 Months	31	45	27	34	
22 Months	30	41	27	30	
24 Months	29	38	27	30	
26 Months	27	34	26	28	
Diarrhoea (days)					
Number (%) of events	14 (20.6)	35 (39.8)	18 (22.2)	11 (17.2)	0.0239
Number (%) of patients censored	54 (79.4)	53 (60.2)	63 (77.8)	53 (82.8)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.7 Treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
25% quantile (95% CI)	18.0370 (5.2895 to NC)	6.2423 (1.4456 to 10.6776)	26.9076 (3.0554 to NC)	NC (11.5647 to NC)	
Median (95% CI)	NC (NC to NC)	NC (12.7474 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0310		0.4172	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.9756 (1.0520 to 3.7102)		0.7327 (0.3446 to 1.5579)	
P-value	-	0.0342		0.4190	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.5062 (0.2695 to 0.9506)				
Events probability (95% CI)[c]					
2 Months	0.9242 (0.8273 to 0.9677)	0.8279 (0.7308 to 0.8925)	0.8742 (0.7788 to 0.9303)	0.9219 (0.8224 to 0.9667)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.7 Treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	0.8766 (0.7682 to 0.9364)	0.7802 (0.6771 to 0.8538)	0.8202 (0.7151 to 0.8895)	0.8895 (0.7821 to 0.9458)	
6 Months	0.8584 (0.7449 to 0.9239)	0.7550 (0.6491 to 0.8330)	0.8044 (0.6960 to 0.8775)	0.8895 (0.7821 to 0.9458)	
8 Months	0.8393 (0.7208 to 0.9105)	0.7010 (0.5895 to 0.7876)	0.8044 (0.6960 to 0.8775)	0.8710 (0.7580 to 0.9334)	
10 Months	0.8198 (0.6967 to 0.8965)	0.6733 (0.5595 to 0.7637)	0.8044 (0.6960 to 0.8775)	0.8710 (0.7580 to 0.9334)	
12 Months	0.7993 (0.6716 to 0.8815)	0.6270 (0.5093 to 0.7240)	0.8044 (0.6960 to 0.8775)	0.8497 (0.7295 to 0.9194)	
14 Months	0.7993 (0.6716 to 0.8815)	0.6113 (0.4927 to 0.7103)	0.7833 (0.6679 to 0.8626)	0.8497 (0.7295 to 0.9194)	
16 Months	0.7751 (0.6406 to 0.8643)	0.6113 (0.4927 to 0.7103)	0.7833 (0.6679 to 0.8626)	0.8038 (0.6701 to 0.8877)	
18 Months	0.7751 (0.6406 to 0.8643)	0.5939 (0.4737 to 0.6952)	0.7833 (0.6679 to 0.8626)	0.8038 (0.6701 to 0.8877)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.7 Treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
20 Months	0.7464 (0.6029 to 0.8444)	0.5753 (0.4536 to 0.6794)	0.7833 (0.6679 to 0.8626)	0.8038 (0.6701 to 0.8877)	
22 Months	0.7464 (0.6029 to 0.8444)	0.5555 (0.4319 to 0.6625)	0.7833 (0.6679 to 0.8626)	0.8038 (0.6701 to 0.8877)	
24 Months	0.7464 (0.6029 to 0.8444)	0.5555 (0.4319 to 0.6625)	0.7833 (0.6679 to 0.8626)	0.8038 (0.6701 to 0.8877)	
26 Months	0.7464 (0.6029 to 0.8444)	0.5555 (0.4319 to 0.6625)	0.7833 (0.6679 to 0.8626)	0.8038 (0.6701 to 0.8877)	
Number of patients at risk[c]					
2 Months	60	71	67	58	
4 Months	54	64	60	54	
6 Months	46	57	51	49	
8 Months	44	51	42	46	
10 Months	42	44	41	44	
12 Months	37	40	40	40	
14 Months	34	38	37	40	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.7 Treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	31	36	33	33	
18 Months	27	32	29	31	
20 Months	25	31	26	28	
22 Months	24	27	26	26	
24 Months	23	26	26	26	
26 Months	21	23	25	24	
Headache (days)					
Number (%) of events	1 (1.5)	11 (12.5)	8 (9.9)	5 (7.8)	0.0476
Number (%) of patients censored	67 (98.5)	77 (87.5)	73 (90.1)	59 (92.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (12.5503 to NC)	NC (NC to NC)	NC (35.6468 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.7 Treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0121		0.7716	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	8.7915 (1.1324 to 68.2513)		0.8430 (0.2658 to 2.6734)	
P-value	-	0.0376		0.7718	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.1137 (0.0147 to 0.8831)				
Events probability (95% CI)[c]					
2 Months	0.9848 (0.8973 to 0.9979)	0.9655 (0.8969 to 0.9887)	0.9612 (0.8845 to 0.9873)	0.9841 (0.8926 to 0.9977)	
4 Months	0.9848 (0.8973 to 0.9979)	0.9655 (0.8969 to 0.9887)	0.9612 (0.8845 to 0.9873)	0.9683 (0.8790 to 0.9920)	
6 Months	0.9848 (0.8973 to 0.9979)	0.9266 (0.8435 to 0.9664)	0.9145 (0.8187 to 0.9609)	0.9340 (0.8334 to 0.9747)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.7 Treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	0.9848 (0.8973 to 0.9979)	0.9128 (0.8252 to 0.9576)	0.9145 (0.8187 to 0.9609)	0.9340 (0.8334 to 0.9747)	
10 Months	0.9848 (0.8973 to 0.9979)	0.8840 (0.7881 to 0.9382)	0.9145 (0.8187 to 0.9609)	0.9340 (0.8334 to 0.9747)	
12 Months	0.9848 (0.8973 to 0.9979)	0.8690 (0.7692 to 0.9277)	0.9145 (0.8187 to 0.9609)	0.9340 (0.8334 to 0.9747)	
14 Months	0.9848 (0.8973 to 0.9979)	0.8532 (0.7493 to 0.9164)	0.9145 (0.8187 to 0.9609)	0.9340 (0.8334 to 0.9747)	
16 Months	0.9848 (0.8973 to 0.9979)	0.8532 (0.7493 to 0.9164)	0.9145 (0.8187 to 0.9609)	0.9340 (0.8334 to 0.9747)	
18 Months	0.9848 (0.8973 to 0.9979)	0.8532 (0.7493 to 0.9164)	0.9145 (0.8187 to 0.9609)	0.9340 (0.8334 to 0.9747)	
20 Months	0.9848 (0.8973 to 0.9979)	0.8532 (0.7493 to 0.9164)	0.9145 (0.8187 to 0.9609)	0.9340 (0.8334 to 0.9747)	
22 Months	0.9848 (0.8973 to 0.9979)	0.8532 (0.7493 to 0.9164)	0.8860 (0.7666 to 0.9463)	0.9340 (0.8334 to 0.9747)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.7 Treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
24 Months	0.9848 (0.8973 to 0.9979)	0.8532 (0.7493 to 0.9164)	0.8860 (0.7666 to 0.9463)	0.9340 (0.8334 to 0.9747)	
26 Months	0.9848 (0.8973 to 0.9979)	0.8532 (0.7493 to 0.9164)	0.8860 (0.7666 to 0.9463)	0.9340 (0.8334 to 0.9747)	
Number of patients at risk[c]					
2 Months	64	83	73	62	
4 Months	61	79	68	59	
6 Months	54	69	57	52	
8 Months	52	65	49	50	
10 Months	49	59	48	48	
12 Months	43	55	46	44	
14 Months	40	53	43	44	
16 Months	37	50	39	38	
18 Months	33	47	35	35	
20 Months	32	46	32	33	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.7 Treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
22 Months	30	41	31	29	
24 Months	29	38	31	29	
26 Months	27	34	30	27	
Muscular weakness (days)					
Number (%) of events	1 (1.5)	9 (10.2)	6 (7.4)	3 (4.7)	0.0452
Number (%) of patients censored	67 (98.5)	79 (89.8)	75 (92.6)	61 (95.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0376		0.3630	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.7 Treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	6.6932 (0.8445 to 53.0461)		0.5294 (0.1315 to 2.1318)	
P-value	-	0.0719		0.3709	
Events probability (95% CI)[c]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9769 (0.9107 to 0.9942)	0.9753 (0.9049 to 0.9938)	1.0000 (1.0000 to 1.0000)	
4 Months	1.0000 (1.0000 to 1.0000)	0.9536 (0.8811 to 0.9823)	0.9343 (0.8490 to 0.9722)	1.0000 (1.0000 to 1.0000)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9536 (0.8811 to 0.9823)	0.9199 (0.8300 to 0.9633)	0.9652 (0.8680 to 0.9912)	
8 Months	1.0000 (1.0000 to 1.0000)	0.9536 (0.8811 to 0.9823)	0.9199 (0.8300 to 0.9633)	0.9466 (0.8435 to 0.9825)	
10 Months	1.0000 (1.0000 to 1.0000)	0.9536 (0.8811 to 0.9823)	0.9199 (0.8300 to 0.9633)	0.9466 (0.8435 to 0.9825)	
12 Months	0.9787 (0.8584 to 0.9970)	0.9385 (0.8575 to 0.9741)	0.9199 (0.8300 to 0.9633)	0.9466 (0.8435 to 0.9825)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.7 Treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.9787 (0.8584 to 0.9970)	0.9385 (0.8575 to 0.9741)	0.9199 (0.8300 to 0.9633)	0.9466 (0.8435 to 0.9825)	
16 Months	0.9787 (0.8584 to 0.9970)	0.8881 (0.7860 to 0.9432)	0.9199 (0.8300 to 0.9633)	0.9466 (0.8435 to 0.9825)	
18 Months	0.9787 (0.8584 to 0.9970)	0.8881 (0.7860 to 0.9432)	0.9199 (0.8300 to 0.9633)	0.9466 (0.8435 to 0.9825)	
20 Months	0.9787 (0.8584 to 0.9970)	0.8881 (0.7860 to 0.9432)	0.9199 (0.8300 to 0.9633)	0.9466 (0.8435 to 0.9825)	
22 Months	0.9787 (0.8584 to 0.9970)	0.8881 (0.7860 to 0.9432)	0.9199 (0.8300 to 0.9633)	0.9466 (0.8435 to 0.9825)	
24 Months	0.9787 (0.8584 to 0.9970)	0.8665 (0.7544 to 0.9297)	0.9199 (0.8300 to 0.9633)	0.9466 (0.8435 to 0.9825)	
26 Months	0.9787 (0.8584 to 0.9970)	0.8665 (0.7544 to 0.9297)	0.9199 (0.8300 to 0.9633)	0.9466 (0.8435 to 0.9825)	
Number of patients at risk[c]					
2 Months	65	84	75	63	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.7 Treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	62	78	67	60	
6 Months	55	71	56	53	
8 Months	53	68	47	51	
10 Months	50	63	46	49	
12 Months	43	59	43	45	
14 Months	40	58	40	45	
16 Months	37	51	36	40	
18 Months	33	47	32	37	
20 Months	32	46	29	34	
22 Months	31	41	29	30	
24 Months	30	38	29	30	
26 Months	28	34	28	28	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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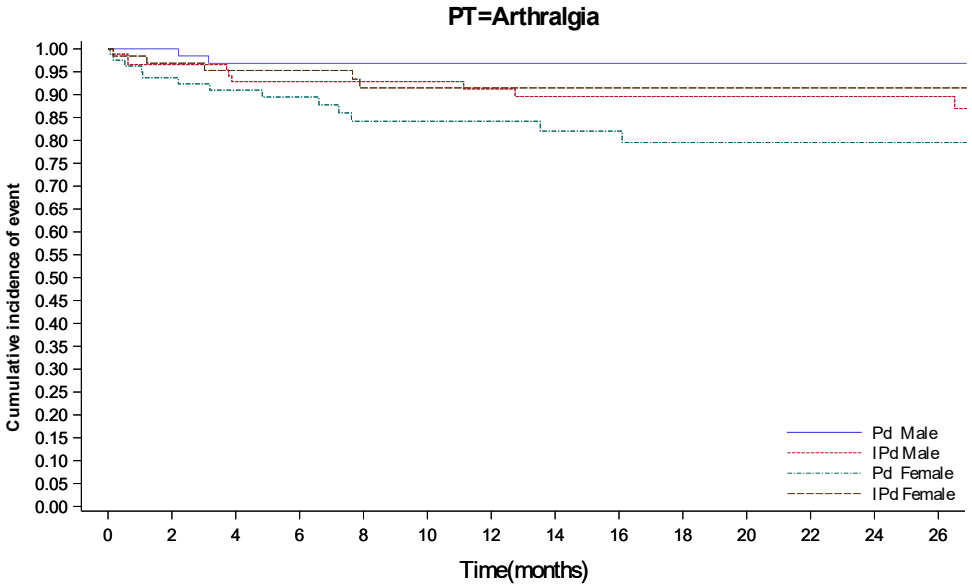
16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.8 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population

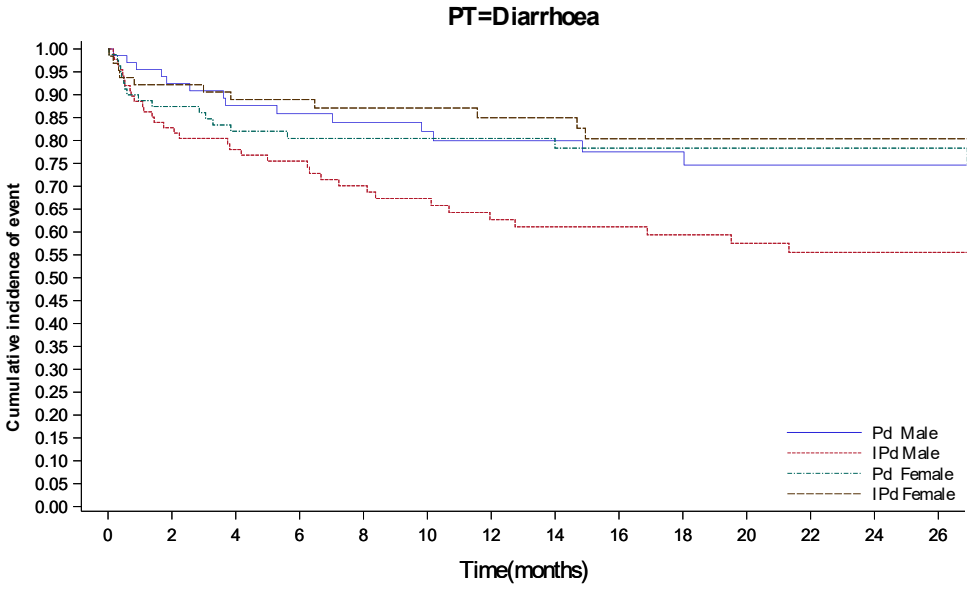


Number at Risk

Pd Male	68	65	60	53	51	48	42	39	36	32	31	30	29	27
IPd Male	88	83	75	67	64	59	55	53	49	46	45	41	38	34
Pd Female	81	72	65	54	43	43	40	36	33	29	27	27	27	26
IPd Female	64	61	57	52	48	46	43	43	38	35	34	30	30	28

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_sex_s_f_x.rtf (17NOV2020 14:43)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.8 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population

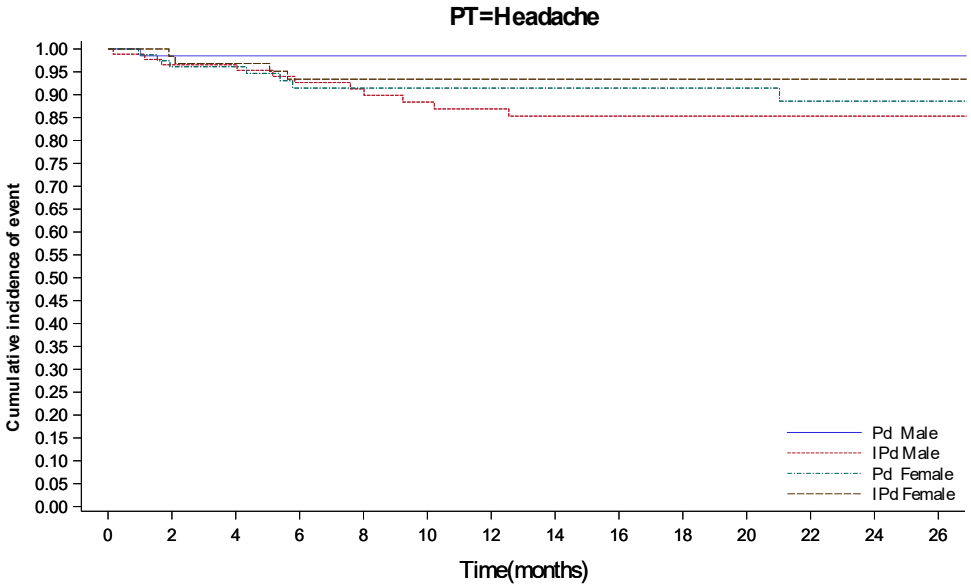


Number at Risk

Pd Male	68	60	54	46	44	42	37	34	31	27	25	24	23	21
IPd Male	88	71	64	57	51	44	40	38	36	32	31	27	26	23
Pd Female	81	67	60	51	42	41	40	37	33	29	26	26	26	25
IPd Female	64	58	54	49	46	44	40	40	33	31	28	26	26	24

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_sex_s_f_x.rtf (17NOV2020 14:43)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.8 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population

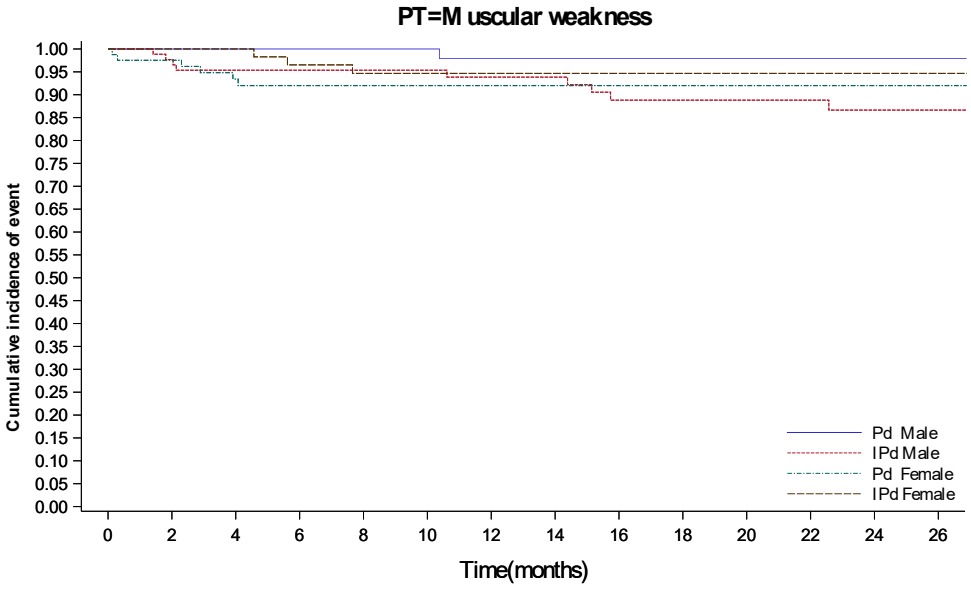


Number at Risk

Pd Male	68	64	61	54	52	49	43	40	37	33	32	30	29	27
IPd Male	88	83	79	69	65	59	55	53	50	47	46	41	38	34
Pd Female	80	73	68	57	49	48	46	43	39	35	32	31	31	30
IPd Female	64	62	59	52	50	48	44	44	38	35	33	29	29	27

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_sex_s_f_x.rtf (17NOV2020 14:43)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.8 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per PT by treatment group according to gender - Safety population



Number at Risk

Pd Male	68	65	62	55	53	50	43	40	37	33	32	31	30	28
IPd Male	88	84	78	71	68	63	59	58	51	47	46	41	38	34
Pd Female	81	75	67	56	47	46	43	40	36	32	29	29	29	28
IPd Female	64	63	60	53	51	49	45	45	40	37	34	30	30	28

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_sex_s_f_x.rtf (17NOV2020 14:43)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.9 Treatment emergent severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Musculoskeletal and connective tissue disorders (days)					
Number (%) of events	1 (1.5)	11 (12.5)	7 (8.6)	3 (4.7)	0.0245
Number (%) of patients censored	67 (98.5)	77 (87.5)	74 (91.4)	61 (95.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (25.6920 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0214		0.3146	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	7.7068 (0.9902 to 59.9816)		0.5050 (0.1300 to 1.9626)	
P-value	-	0.0511		0.3239	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae34soc_sex_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.9 Treatment emergent severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]					
2 Months	0.9853 (0.9002 to 0.9979)	0.9543 (0.8827 to 0.9826)	0.9250 (0.8405 to 0.9656)	0.9841 (0.8926 to 0.9977)	
4 Months	0.9853 (0.9002 to 0.9979)	0.9543 (0.8827 to 0.9826)	0.9250 (0.8405 to 0.9656)	0.9683 (0.8790 to 0.9920)	
6 Months	0.9853 (0.9002 to 0.9979)	0.9295 (0.8496 to 0.9677)	0.9250 (0.8405 to 0.9656)	0.9683 (0.8790 to 0.9920)	
8 Months	0.9853 (0.9002 to 0.9979)	0.9295 (0.8496 to 0.9677)	0.9081 (0.8158 to 0.9554)	0.9683 (0.8790 to 0.9920)	
10 Months	0.9853 (0.9002 to 0.9979)	0.9154 (0.8302 to 0.9589)	0.9081 (0.8158 to 0.9554)	0.9683 (0.8790 to 0.9920)	
12 Months	0.9853 (0.9002 to 0.9979)	0.9009 (0.8107 to 0.9494)	0.9081 (0.8158 to 0.9554)	0.9683 (0.8790 to 0.9920)	
14 Months	0.9853 (0.9002 to 0.9979)	0.9009 (0.8107 to 0.9494)	0.9081 (0.8158 to 0.9554)	0.9683 (0.8790 to 0.9920)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae34soc_sex_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.9 Treatment emergent severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.9853 (0.9002 to 0.9979)	0.8853 (0.7899 to 0.9390)	0.9081 (0.8158 to 0.9554)	0.9452 (0.8364 to 0.9824)	
18 Months	0.9853 (0.9002 to 0.9979)	0.8853 (0.7899 to 0.9390)	0.9081 (0.8158 to 0.9554)	0.9452 (0.8364 to 0.9824)	
20 Months	0.9853 (0.9002 to 0.9979)	0.8853 (0.7899 to 0.9390)	0.9081 (0.8158 to 0.9554)	0.9452 (0.8364 to 0.9824)	
22 Months	0.9853 (0.9002 to 0.9979)	0.8853 (0.7899 to 0.9390)	0.9081 (0.8158 to 0.9554)	0.9452 (0.8364 to 0.9824)	
24 Months	0.9853 (0.9002 to 0.9979)	0.8657 (0.7615 to 0.9265)	0.9081 (0.8158 to 0.9554)	0.9452 (0.8364 to 0.9824)	
26 Months	0.9853 (0.9002 to 0.9979)	0.8429 (0.7283 to 0.9120)	0.9081 (0.8158 to 0.9554)	0.9452 (0.8364 to 0.9824)	
Number of patients at risk[c]					
2 Months	64	83	73	62	
4 Months	61	78	68	58	
6 Months	54	70	59	53	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae34soc_sex_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.9 Treatment emergent severe adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	52	70	49	52	
10 Months	49	64	48	50	
12 Months	44	60	46	46	
14 Months	41	59	44	46	
16 Months	38	54	41	40	
18 Months	34	50	38	38	
20 Months	33	49	35	35	
22 Months	31	45	35	31	
24 Months	30	41	35	31	
26 Months	28	36	34	29	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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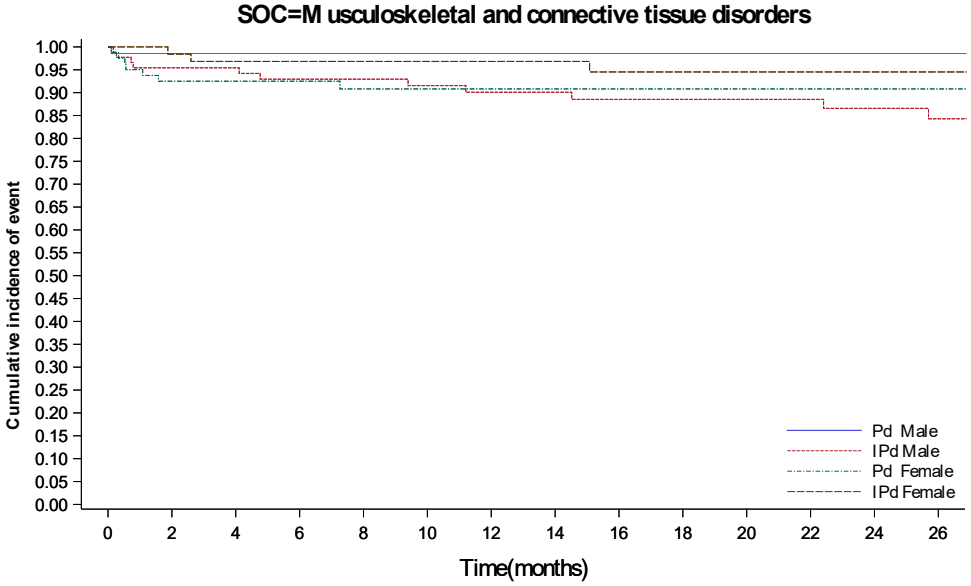
16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.10 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event per SOC by treatment group according to gender - Safety population



Number at Risk

Pd Male	68	64	61	54	52	49	44	41	38	34	33	31	30	28
IPd Male	88	83	78	70	70	64	60	59	54	50	49	45	41	36
Pd Female	81	73	68	59	49	48	46	44	41	38	35	35	35	34
IPd Female	64	62	58	53	52	50	46	46	40	38	35	31	31	29

SOC are presented if at least 5% of patients in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae34soc_sex_s_f_x.rtf (17NOV2020 14:43)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.11 Treatment emergent severe adverse event including death per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Musculoskeletal and connective tissue disorders (days)					
Number (%) of events	1 (1.5)	11 (12.5)	7 (8.6)	3 (4.7)	0.0245
Number (%) of patients censored	67 (98.5)	77 (87.5)	74 (91.4)	61 (95.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (25.6920 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0214		0.3146	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	7.7068 (0.9902 to 59.9816)		0.5050 (0.1300 to 1.9626)	
P-value	-	0.0511		0.3239	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.11 Treatment emergent severe adverse event including death per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]					
2 Months	0.9853 (0.9002 to 0.9979)	0.9543 (0.8827 to 0.9826)	0.9250 (0.8405 to 0.9656)	0.9841 (0.8926 to 0.9977)	
4 Months	0.9853 (0.9002 to 0.9979)	0.9543 (0.8827 to 0.9826)	0.9250 (0.8405 to 0.9656)	0.9683 (0.8790 to 0.9920)	
6 Months	0.9853 (0.9002 to 0.9979)	0.9295 (0.8496 to 0.9677)	0.9250 (0.8405 to 0.9656)	0.9683 (0.8790 to 0.9920)	
8 Months	0.9853 (0.9002 to 0.9979)	0.9295 (0.8496 to 0.9677)	0.9081 (0.8158 to 0.9554)	0.9683 (0.8790 to 0.9920)	
10 Months	0.9853 (0.9002 to 0.9979)	0.9154 (0.8302 to 0.9589)	0.9081 (0.8158 to 0.9554)	0.9683 (0.8790 to 0.9920)	
12 Months	0.9853 (0.9002 to 0.9979)	0.9009 (0.8107 to 0.9494)	0.9081 (0.8158 to 0.9554)	0.9683 (0.8790 to 0.9920)	
14 Months	0.9853 (0.9002 to 0.9979)	0.9009 (0.8107 to 0.9494)	0.9081 (0.8158 to 0.9554)	0.9683 (0.8790 to 0.9920)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.11 Treatment emergent severe adverse event including death per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.9853 (0.9002 to 0.9979)	0.8853 (0.7899 to 0.9390)	0.9081 (0.8158 to 0.9554)	0.9452 (0.8364 to 0.9824)	
18 Months	0.9853 (0.9002 to 0.9979)	0.8853 (0.7899 to 0.9390)	0.9081 (0.8158 to 0.9554)	0.9452 (0.8364 to 0.9824)	
20 Months	0.9853 (0.9002 to 0.9979)	0.8853 (0.7899 to 0.9390)	0.9081 (0.8158 to 0.9554)	0.9452 (0.8364 to 0.9824)	
22 Months	0.9853 (0.9002 to 0.9979)	0.8853 (0.7899 to 0.9390)	0.9081 (0.8158 to 0.9554)	0.9452 (0.8364 to 0.9824)	
24 Months	0.9853 (0.9002 to 0.9979)	0.8657 (0.7615 to 0.9265)	0.9081 (0.8158 to 0.9554)	0.9452 (0.8364 to 0.9824)	
26 Months	0.9853 (0.9002 to 0.9979)	0.8429 (0.7283 to 0.9120)	0.9081 (0.8158 to 0.9554)	0.9452 (0.8364 to 0.9824)	
Number of patients at risk[c]					
2 Months	64	83	73	62	
4 Months	61	78	68	58	
6 Months	54	70	59	53	

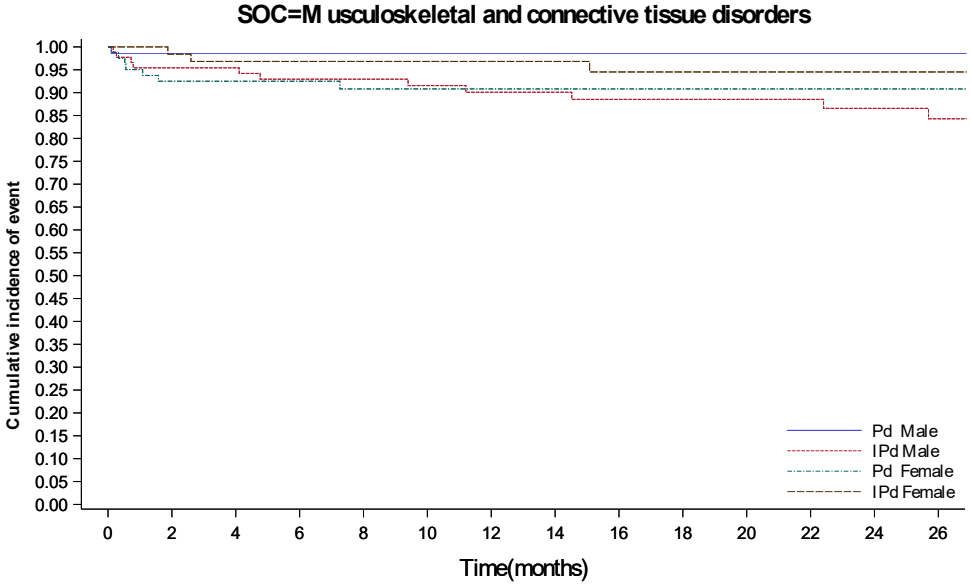
SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae345soc_sex_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.11 Treatment emergent severe adverse event including death per SOC by treatment group according to gender - Safety population

	Male		Female		
	Pd (N=68)	**IPd (N=88)**	**Pd (N=81)**	**IPd (N=64)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	52	70	49	52	
10 Months	49	64	48	50	
12 Months	44	60	46	46	
14 Months	41	59	44	46	
16 Months	38	54	41	40	
18 Months	34	50	38	38	
20 Months	33	49	35	35	
22 Months	31	45	35	31	
24 Months	30	41	35	31	
26 Months	28	36	34	29	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae345soc_sex_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.43 Subgroup analysis by gender
16.2.7.1.43.12 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death per SOC by treatment group according to gender - Safety population



Number at Risk

Pd Male	68	64	61	54	52	49	44	41	38	34	33	31	30	28
IPd Male	88	83	78	70	70	64	60	59	54	50	49	45	41	36
Pd Female	81	73	68	59	49	48	46	44	41	38	35	35	35	34
IPd Female	64	62	58	53	52	50	46	46	40	38	35	31	31	29

16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.1 Treatment emergent adverse event per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
Musculoskeletal chest pain (days)					
Number (%) of events	3 (2.5)	11 (9.5)	4 (21.1)	1 (4.2)	0.0226
Number (%) of patients censored	119 (97.5)	105 (90.5)	15 (78.9)	23 (95.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.5113 to NC)	NC (2.2341 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0497		0.2412	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	3.3511 (0.9309 to 12.0634)		0.2900 (0.0321 to 2.6201)	
P-value	-	0.0643		0.2703	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_race_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.1 Treatment emergent adverse event per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9655 (0.9107 to 0.9869)	0.9474 (0.6812 to 0.9924)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9911 (0.9383 to 0.9987)	0.9385 (0.8753 to 0.9702)	0.8421 (0.5865 to 0.9462)	0.9565 (0.7293 to 0.9938)	
6 Months	0.9911 (0.9383 to 0.9987)	0.9292 (0.8634 to 0.9640)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
8 Months	0.9803 (0.9230 to 0.9951)	0.9292 (0.8634 to 0.9640)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
10 Months	0.9803 (0.9230 to 0.9951)	0.9079 (0.8350 to 0.9495)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
12 Months	0.9674 (0.9010 to 0.9895)	0.9079 (0.8350 to 0.9495)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
14 Months	0.9674 (0.9010 to 0.9895)	0.9079 (0.8350 to 0.9495)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.1 Treatment emergent adverse event per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.9674 (0.9010 to 0.9895)	0.9079 (0.8350 to 0.9495)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
18 Months	0.9674 (0.9010 to 0.9895)	0.9079 (0.8350 to 0.9495)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
20 Months	0.9674 (0.9010 to 0.9895)	0.8939 (0.8149 to 0.9404)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
22 Months	0.9674 (0.9010 to 0.9895)	0.8939 (0.8149 to 0.9404)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
24 Months	0.9674 (0.9010 to 0.9895)	0.8939 (0.8149 to 0.9404)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
26 Months	0.9674 (0.9010 to 0.9895)	0.8939 (0.8149 to 0.9404)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
Number of patients at risk[c]					
2 Months	116	112	18	23	
4 Months	108	104	16	21	
6 Months	93	94	15	21	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.1 Treatment emergent adverse event per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	82	91	14	20	
10 Months	80	83	14	19	
12 Months	73	76	13	19	
14 Months	69	75	11	19	
16 Months	62	69	11	18	
18 Months	56	66	11	16	
20 Months	52	64	11	13	
22 Months	50	56	11	12	
24 Months	50	53	10	12	
26 Months	48	49	10	10	
Neutropenia (days)					
Number (%) of events	46 (37.7)	53 (45.7)	6 (31.6)	20 (83.3)	0.0115
Number (%) of patients censored	76 (62.3)	63 (54.3)	13 (68.4)	4 (16.7)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.1 Treatment emergent adverse event per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
25% quantile (95% CI)	1.4456 (0.7885 to 3.3840)	0.8542 (0.7556 to 1.4456)	4.6653 (1.1499 to NC)	0.6571 (0.2300 to 0.8542)	
Median (95% CI)	NC (20.6653 to NC)	NC (7.4908 to NC)	NC (4.6653 to NC)	1.4456 (0.7228 to 9.3306)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	10.4476 (2.7926 to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2489		0.0012	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.2621 (0.8492 to 1.8757)		4.2718 (1.6490 to 11.0663)	
P-value	-	0.2496		0.0028	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.2341 (0.0904 to 0.6064)		
Events probability (95% CI)[c]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.1 Treatment emergent adverse event per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
2 Months	0.7329 (0.6440 to 0.8030)	0.6379 (0.5434 to 0.7179)	0.7895 (0.5319 to 0.9153)	0.4545 (0.2515 to 0.6374)	
4 Months	0.6710 (0.5783 to 0.7478)	0.6116 (0.5166 to 0.6935)	0.7895 (0.5319 to 0.9153)	0.3636 (0.1783 to 0.5524)	
6 Months	0.6315 (0.5364 to 0.7124)	0.6116 (0.5166 to 0.6935)	0.7368 (0.4789 to 0.8810)	0.3182 (0.1447 to 0.5075)	
8 Months	0.6315 (0.5364 to 0.7124)	0.5908 (0.4948 to 0.6747)	0.6802 (0.4214 to 0.8421)	0.3182 (0.1447 to 0.5075)	
10 Months	0.6315 (0.5364 to 0.7124)	0.5790 (0.4822 to 0.6641)	0.6802 (0.4214 to 0.8421)	0.2727 (0.1132 to 0.4608)	
12 Months	0.6315 (0.5364 to 0.7124)	0.5790 (0.4822 to 0.6641)	0.6802 (0.4214 to 0.8421)	0.2273 (0.0841 to 0.4121)	
14 Months	0.6315 (0.5364 to 0.7124)	0.5664 (0.4686 to 0.6530)	0.6802 (0.4214 to 0.8421)	0.2273 (0.0841 to 0.4121)	
16 Months	0.6315 (0.5364 to 0.7124)	0.5664 (0.4686 to 0.6530)	0.6802 (0.4214 to 0.8421)	0.2273 (0.0841 to 0.4121)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.1 Treatment emergent adverse event per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
18 Months	0.6158 (0.5177 to 0.6996)	0.5664 (0.4686 to 0.6530)	0.6802 (0.4214 to 0.8421)	0.1705 (0.0486 to 0.3552)	
20 Months	0.6158 (0.5177 to 0.6996)	0.5664 (0.4686 to 0.6530)	0.6802 (0.4214 to 0.8421)	0.1705 (0.0486 to 0.3552)	
22 Months	0.5976 (0.4958 to 0.6854)	0.5507 (0.4507 to 0.6398)	0.6802 (0.4214 to 0.8421)	0.1705 (0.0486 to 0.3552)	
24 Months	0.5976 (0.4958 to 0.6854)	0.5010 (0.3955 to 0.5975)	0.6802 (0.4214 to 0.8421)	0.1705 (0.0486 to 0.3552)	
26 Months	0.5976 (0.4958 to 0.6854)	0.5010 (0.3955 to 0.5975)	0.6802 (0.4214 to 0.8421)	0.1705 (0.0486 to 0.3552)	
Number of patients at risk[c]					
2 Months	87	74	15	10	
4 Months	73	67	15	8	
6 Months	61	60	14	7	
8 Months	54	55	12	7	
10 Months	52	48	12	6	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.1 Treatment emergent adverse event per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	50	46	11	5	
14 Months	46	45	9	5	
16 Months	41	43	9	5	
18 Months	38	41	9	3	
20 Months	35	41	9	3	
22 Months	33	35	9	2	
24 Months	33	29	8	2	
26 Months	31	26	7	2	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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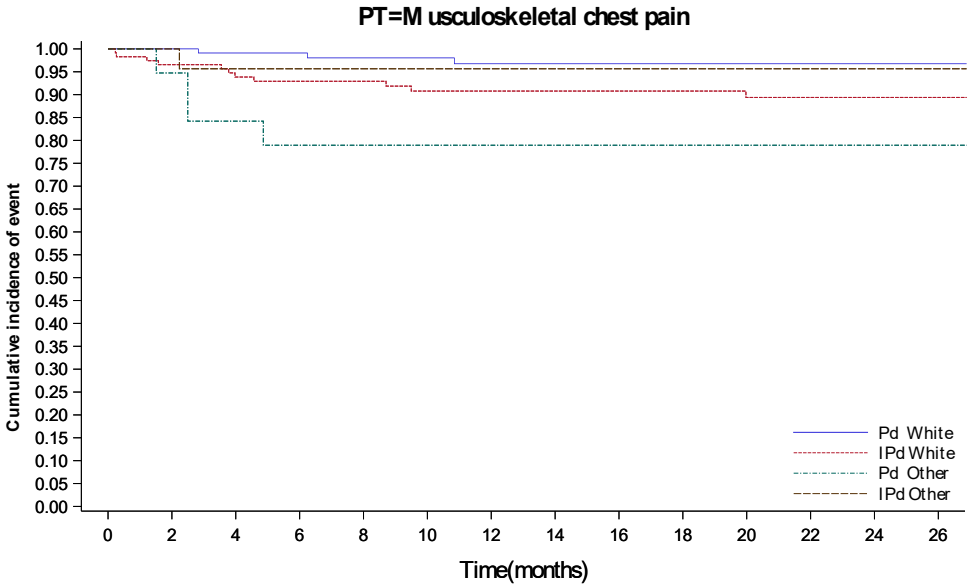
16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to race - Safety population

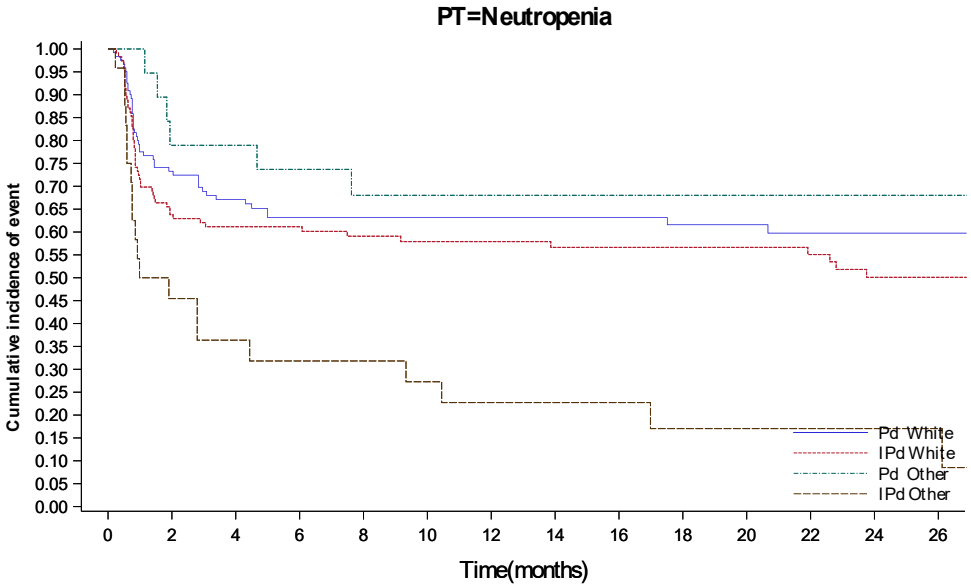


Number at Risk

Pd White	122	116	108	93	82	80	73	69	62	56	52	50	50	48
IPd White	116	112	104	94	91	83	76	75	69	66	64	56	53	49
Pd Other	19	18	16	15	14	14	13	11	11	11	11	11	10	10
IPd Other	24	23	21	21	20	19	19	19	18	16	13	12	12	10

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_teaept_race_s_f_x.rtf (17NOV2020 14:44)

16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to race - Safety population



Number at Risk

Pd White	122	87	73	61	54	52	50	46	41	38	35	33	33	31
IPd White	116	74	67	60	55	48	46	45	43	41	41	35	29	26
Pd Other	19	15	15	14	12	12	11	9	9	9	9	9	8	7
IPd Other	24	10	8	7	7	6	5	5	5	3	3	2	2	2

PT are presented if at least 10 events in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.3 Treatment emergent not severe adverse event per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
Musculoskeletal chest pain (days)					
Number (%) of events	3 (2.5)	11 (9.5)	4 (21.1)	1 (4.2)	0.0226
Number (%) of patients censored	119 (97.5)	105 (90.5)	15 (78.9)	23 (95.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.5113 to NC)	NC (2.2341 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0497		0.2412	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	3.3511 (0.9309 to 12.0634)		0.2900 (0.0321 to 2.6201)	
P-value	-	0.0643		0.2703	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.3 Treatment emergent not severe adverse event per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9655 (0.9107 to 0.9869)	0.9474 (0.6812 to 0.9924)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9911 (0.9383 to 0.9987)	0.9385 (0.8753 to 0.9702)	0.8421 (0.5865 to 0.9462)	0.9565 (0.7293 to 0.9938)	
6 Months	0.9911 (0.9383 to 0.9987)	0.9292 (0.8634 to 0.9640)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
8 Months	0.9803 (0.9230 to 0.9951)	0.9292 (0.8634 to 0.9640)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
10 Months	0.9803 (0.9230 to 0.9951)	0.9079 (0.8350 to 0.9495)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
12 Months	0.9674 (0.9010 to 0.9895)	0.9079 (0.8350 to 0.9495)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
14 Months	0.9674 (0.9010 to 0.9895)	0.9079 (0.8350 to 0.9495)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.3 Treatment emergent not severe adverse event per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.9674 (0.9010 to 0.9895)	0.9079 (0.8350 to 0.9495)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
18 Months	0.9674 (0.9010 to 0.9895)	0.9079 (0.8350 to 0.9495)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
20 Months	0.9674 (0.9010 to 0.9895)	0.8939 (0.8149 to 0.9404)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
22 Months	0.9674 (0.9010 to 0.9895)	0.8939 (0.8149 to 0.9404)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
24 Months	0.9674 (0.9010 to 0.9895)	0.8939 (0.8149 to 0.9404)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
26 Months	0.9674 (0.9010 to 0.9895)	0.8939 (0.8149 to 0.9404)	0.7895 (0.5319 to 0.9153)	0.9565 (0.7293 to 0.9938)	
Number of patients at risk[c]					
2 Months	116	112	18	23	
4 Months	108	104	16	21	
6 Months	93	94	15	21	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_race_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.3 Treatment emergent not severe adverse event per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	82	91	14	20	
10 Months	80	83	14	19	
12 Months	73	76	13	19	
14 Months	69	75	11	19	
16 Months	62	69	11	18	
18 Months	56	66	11	16	
20 Months	52	64	11	13	
22 Months	50	56	11	12	
24 Months	50	53	10	12	
26 Months	48	49	10	10	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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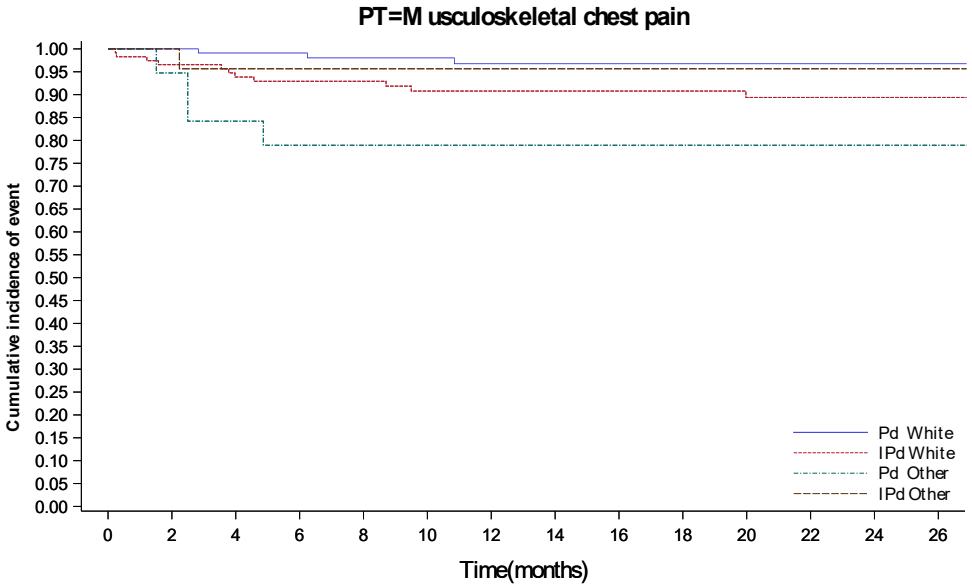
16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.4 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per PT by treatment group according to race - Safety population



Number at Risk

Pd White	122	116	108	93	82	80	73	69	62	56	52	50	50	48
IPd White	116	112	104	94	91	83	76	75	69	66	64	56	53	49
Pd Other	19	18	16	15	14	14	13	11	11	11	11	11	10	10
IPd Other	24	23	21	21	20	19	19	19	18	16	13	12	12	10

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_race_s_f_x.rtf (17NOV2020 14:44)

16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.5 Treatment emergent severe adverse event per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
Neutropenia (days)					
Number (%) of events	45 (36.9)	53 (45.7)	6 (31.6)	19 (79.2)	0.0196
Number (%) of patients censored	77 (63.1)	63 (54.3)	13 (68.4)	5 (20.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.4456 (0.7885 to 3.3840)	0.8542 (0.7556 to 1.4456)	4.6653 (1.1499 to NC)	0.6571 (0.2300 to 0.8542)	
Median (95% CI)	NC (31.4415 to NC)	NC (7.4908 to NC)	NC (4.6653 to NC)	1.4456 (0.7228 to 10.4476)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	16.9856 (2.7926 to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2047		0.0012	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae34pt_race_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.5 Treatment emergent severe adverse event per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.2935 (0.8683 to 1.9268)		4.2718 (1.6490 to 11.0663)	
P-value	-	0.2057		0.0028	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.2341 (0.0904 to 0.6064)		
Events probability (95% CI)[c]					
2 Months	0.7329 (0.6440 to 0.8030)	0.6379 (0.5434 to 0.7179)	0.7895 (0.5319 to 0.9153)	0.4545 (0.2515 to 0.6374)	
4 Months	0.6710 (0.5783 to 0.7478)	0.6116 (0.5166 to 0.6935)	0.7895 (0.5319 to 0.9153)	0.3636 (0.1783 to 0.5524)	
6 Months	0.6414 (0.5468 to 0.7213)	0.6116 (0.5166 to 0.6935)	0.7368 (0.4789 to 0.8810)	0.3636 (0.1783 to 0.5524)	
8 Months	0.6414 (0.5468 to 0.7213)	0.5908 (0.4948 to 0.6747)	0.6802 (0.4214 to 0.8421)	0.3636 (0.1783 to 0.5524)	
10 Months	0.6414 (0.5468 to 0.7213)	0.5790 (0.4822 to 0.6641)	0.6802 (0.4214 to 0.8421)	0.3117 (0.1379 to 0.5037)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.5 Treatment emergent severe adverse event per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	0.6414 (0.5468 to 0.7213)	0.5790 (0.4822 to 0.6641)	0.6802 (0.4214 to 0.8421)	0.2597 (0.1012 to 0.4523)	
14 Months	0.6414 (0.5468 to 0.7213)	0.5664 (0.4686 to 0.6530)	0.6802 (0.4214 to 0.8421)	0.2597 (0.1012 to 0.4523)	
16 Months	0.6414 (0.5468 to 0.7213)	0.5664 (0.4686 to 0.6530)	0.6802 (0.4214 to 0.8421)	0.2597 (0.1012 to 0.4523)	
18 Months	0.6258 (0.5282 to 0.7087)	0.5664 (0.4686 to 0.6530)	0.6802 (0.4214 to 0.8421)	0.1948 (0.0575 to 0.3918)	
20 Months	0.6258 (0.5282 to 0.7087)	0.5664 (0.4686 to 0.6530)	0.6802 (0.4214 to 0.8421)	0.1948 (0.0575 to 0.3918)	
22 Months	0.6079 (0.5065 to 0.6947)	0.5507 (0.4507 to 0.6398)	0.6802 (0.4214 to 0.8421)	0.1948 (0.0575 to 0.3918)	
24 Months	0.6079 (0.5065 to 0.6947)	0.5010 (0.3955 to 0.5975)	0.6802 (0.4214 to 0.8421)	0.1948 (0.0575 to 0.3918)	
26 Months	0.6079 (0.5065 to 0.6947)	0.5010 (0.3955 to 0.5975)	0.6802 (0.4214 to 0.8421)	0.1948 (0.0575 to 0.3918)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.5 Treatment emergent severe adverse event per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
Number of patients at risk[c]					
2 Months	87	74	15	10	
4 Months	73	67	15	8	
6 Months	62	60	14	8	
8 Months	55	55	12	8	
10 Months	53	48	12	6	
12 Months	51	46	11	5	
14 Months	47	45	9	5	
16 Months	42	43	9	5	
18 Months	39	41	9	3	
20 Months	36	41	9	3	
22 Months	34	35	9	2	
24 Months	34	29	8	2	
26 Months	32	26	7	2	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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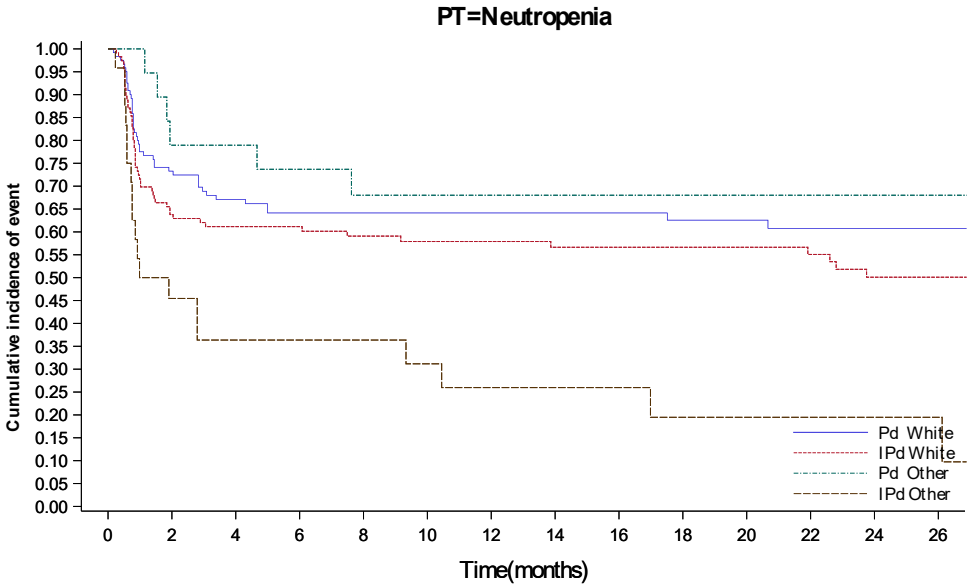
16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.6 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event per PT by treatment group according to race - Safety population



Number at Risk

Pd White	122	87	73	62	55	53	51	47	42	39	36	34	34	32
IPd White	116	74	67	60	55	48	46	45	43	41	41	35	29	26
Pd Other	19	15	15	14	12	12	11	9	9	9	9	9	8	7
IPd Other	24	10	8	8	8	6	5	5	5	3	3	2	2	2

PT are presented if at least 5% of patients in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.7 Treatment emergent severe adverse event including death per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
Neutropenia (days)					
Number (%) of events	45 (36.9)	53 (45.7)	6 (31.6)	19 (79.2)	0.0196
Number (%) of patients censored	77 (63.1)	63 (54.3)	13 (68.4)	5 (20.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.4456 (0.7885 to 3.3840)	0.8542 (0.7556 to 1.4456)	4.6653 (1.1499 to NC)	0.6571 (0.2300 to 0.8542)	
Median (95% CI)	NC (31.4415 to NC)	NC (7.4908 to NC)	NC (4.6653 to NC)	1.4456 (0.7228 to 10.4476)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	16.9856 (2.7926 to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2047		0.0012	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.7 Treatment emergent severe adverse event including death per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.2935 (0.8683 to 1.9268)		4.2718 (1.6490 to 11.0663)	
P-value	-	0.2057		0.0028	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.2341 (0.0904 to 0.6064)		
Events probability (95% CI)[c]					
2 Months	0.7329 (0.6440 to 0.8030)	0.6379 (0.5434 to 0.7179)	0.7895 (0.5319 to 0.9153)	0.4545 (0.2515 to 0.6374)	
4 Months	0.6710 (0.5783 to 0.7478)	0.6116 (0.5166 to 0.6935)	0.7895 (0.5319 to 0.9153)	0.3636 (0.1783 to 0.5524)	
6 Months	0.6414 (0.5468 to 0.7213)	0.6116 (0.5166 to 0.6935)	0.7368 (0.4789 to 0.8810)	0.3636 (0.1783 to 0.5524)	
8 Months	0.6414 (0.5468 to 0.7213)	0.5908 (0.4948 to 0.6747)	0.6802 (0.4214 to 0.8421)	0.3636 (0.1783 to 0.5524)	
10 Months	0.6414 (0.5468 to 0.7213)	0.5790 (0.4822 to 0.6641)	0.6802 (0.4214 to 0.8421)	0.3117 (0.1379 to 0.5037)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.7 Treatment emergent severe adverse event including death per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	0.6414 (0.5468 to 0.7213)	0.5790 (0.4822 to 0.6641)	0.6802 (0.4214 to 0.8421)	0.2597 (0.1012 to 0.4523)	
14 Months	0.6414 (0.5468 to 0.7213)	0.5664 (0.4686 to 0.6530)	0.6802 (0.4214 to 0.8421)	0.2597 (0.1012 to 0.4523)	
16 Months	0.6414 (0.5468 to 0.7213)	0.5664 (0.4686 to 0.6530)	0.6802 (0.4214 to 0.8421)	0.2597 (0.1012 to 0.4523)	
18 Months	0.6258 (0.5282 to 0.7087)	0.5664 (0.4686 to 0.6530)	0.6802 (0.4214 to 0.8421)	0.1948 (0.0575 to 0.3918)	
20 Months	0.6258 (0.5282 to 0.7087)	0.5664 (0.4686 to 0.6530)	0.6802 (0.4214 to 0.8421)	0.1948 (0.0575 to 0.3918)	
22 Months	0.6079 (0.5065 to 0.6947)	0.5507 (0.4507 to 0.6398)	0.6802 (0.4214 to 0.8421)	0.1948 (0.0575 to 0.3918)	
24 Months	0.6079 (0.5065 to 0.6947)	0.5010 (0.3955 to 0.5975)	0.6802 (0.4214 to 0.8421)	0.1948 (0.0575 to 0.3918)	
26 Months	0.6079 (0.5065 to 0.6947)	0.5010 (0.3955 to 0.5975)	0.6802 (0.4214 to 0.8421)	0.1948 (0.0575 to 0.3918)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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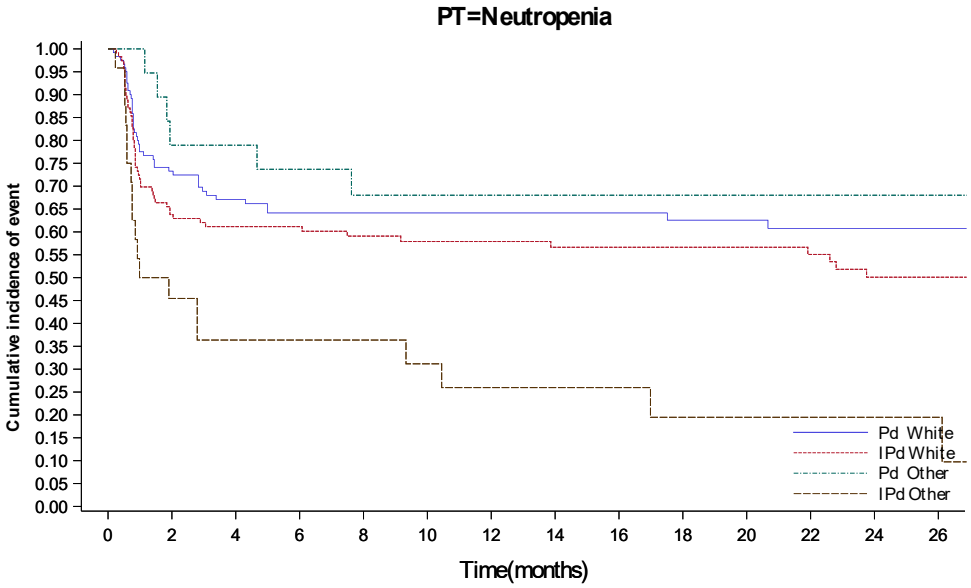
16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.7 Treatment emergent severe adverse event including death per PT by treatment group according to race - Safety population

	White		Other		
	Pd (N=122)	**IPd (N=116)**	**Pd (N=19)**	**IPd (N=24)**	**p-value of treatment-by-sub group interaction[d]**
Number of patients at risk[c]					
2 Months	87	74	15	10	
4 Months	73	67	15	8	
6 Months	62	60	14	8	
8 Months	55	55	12	8	
10 Months	53	48	12	6	
12 Months	51	46	11	5	
14 Months	47	45	9	5	
16 Months	42	43	9	5	
18 Months	39	41	9	3	
20 Months	36	41	9	3	
22 Months	34	35	9	2	
24 Months	34	29	8	2	
26 Months	32	26	7	2	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae345pt_race_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.44 Subgroup analysis by race
16.2.7.1.44.8 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death per PT by treatment group according to race - Safety population



Number at Risk

Pd White	122	87	73	62	55	53	51	47	42	39	36	34	34	32
IPd White	116	74	67	60	55	48	46	45	43	41	41	35	29	26
Pd Other	19	15	15	14	12	12	11	9	9	9	9	9	8	7
IPd Other	24	10	8	8	8	6	5	5	5	3	3	2	2	2

PT are presented if at least 5% of patients in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae345pt_race_s_f_x.rtf (17NOV2020 14:44)

16.2.7.1 Safety endpoints
16.2.7.1.45 Subgroup analysis by ethnicity
16.2.7.1.45.1 Treatment emergent adverse event per SOC by treatment group according to ethnicity - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[d]**
General disorders and administration site conditions (days)					
Number (%) of events	3 (100.0)	2 (50.0)	79 (60.8)	74 (57.8)	0.0379
Number (%) of patients censored	0 (0.0)	2 (50.0)	51 (39.2)	54 (42.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.3285 (0.3285 to 1.1170)	5.2074 (0.6899 to NC)	0.9528 (0.4928 to 1.5441)	1.8891 (0.8214 to 2.7598)	
Median (95% CI)	0.3614 (0.3285 to 1.1170)	NC (0.6899 to NC)	4.2710 (2.9897 to 8.3450)	9.3306 (4.4025 to 22.8008)	
75% quantile (95% CI)	1.1170 (0.3285 to 1.1170)	NC (0.6899 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3508		0.2026	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_ethnic_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.45 Subgroup analysis by ethnicity
16.2.7.1.45.1 Treatment emergent adverse event per SOC by treatment group according to ethnicity - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.2887 (0.0179 to 4.6484)		0.8116 (0.5883 to 1.1196)	
P-value	-	0.3809		0.2034	
Events probability (95% CI)[c]					
2 Months	0.3333 (0.0090 to 0.7741)	0.7500 (0.1279 to 0.9605)	0.6324 (0.5425 to 0.7094)	0.7344 (0.6488 to 0.8023)	
4 Months	0.3333 (0.0090 to 0.7741)	0.7500 (0.1279 to 0.9605)	0.5109 (0.4205 to 0.5941)	0.6169 (0.5268 to 0.6948)	
6 Months	0.3333 (0.0090 to 0.7741)	0.7500 (0.1279 to 0.9605)	0.4594 (0.3699 to 0.5441)	0.5528 (0.4623 to 0.6343)	
8 Months	0.3333 (0.0090 to 0.7741)	0.7500 (0.1279 to 0.9605)	0.4147 (0.3267 to 0.5003)	0.5187 (0.4281 to 0.6017)	
10 Months	0.3333 (0.0090 to 0.7741)	0.5000 (0.0578 to 0.8449)	0.3948 (0.3074 to 0.4810)	0.4813 (0.3906 to 0.5661)	
12 Months	0.3333 (0.0090 to 0.7741)	0.5000 (0.0578 to 0.8449)	0.3735 (0.2865 to 0.4603)	0.4708 (0.3799 to 0.5563)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.45 Subgroup analysis by ethnicity
16.2.7.1.45.1 Treatment emergent adverse event per SOC by treatment group according to ethnicity - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.3333 (0.0090 to 0.7741)	0.5000 (0.0578 to 0.8449)	0.3735 (0.2865 to 0.4603)	0.4603 (0.3694 to 0.5464)	
16 Months	0.3333 (0.0090 to 0.7741)	0.5000 (0.0578 to 0.8449)	0.3735 (0.2865 to 0.4603)	0.4361 (0.3444 to 0.5241)	
18 Months	0.3333 (0.0090 to 0.7741)	0.5000 (0.0578 to 0.8449)	0.3735 (0.2865 to 0.4603)	0.4236 (0.3317 to 0.5125)	
20 Months	0.3333 (0.0090 to 0.7741)	0.5000 (0.0578 to 0.8449)	0.3735 (0.2865 to 0.4603)	0.4236 (0.3317 to 0.5125)	
22 Months	0.3333 (0.0090 to 0.7741)	0.5000 (0.0578 to 0.8449)	0.3735 (0.2865 to 0.4603)	0.4236 (0.3317 to 0.5125)	
24 Months	0.3333 (0.0090 to 0.7741)	0.5000 (0.0578 to 0.8449)	0.3735 (0.2865 to 0.4603)	0.3963 (0.3035 to 0.4875)	
26 Months	0.3333 (0.0090 to 0.7741)	0.5000 (0.0578 to 0.8449)	0.3735 (0.2865 to 0.4603)	0.3816 (0.2884 to 0.4741)	
Number of patients at risk[c]					
2 Months	0	3	80	94	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.45 Subgroup analysis by ethnicity
16.2.7.1.45.1 Treatment emergent adverse event per SOC by treatment group according to ethnicity - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	0	3	62	78	
6 Months	0	3	52	66	
8 Months	0	3	44	60	
10 Months	0	2	38	50	
12 Months	0	2	35	45	
14 Months	0	2	33	44	
16 Months	0	2	31	37	
18 Months	0	2	30	33	
20 Months	0	2	28	33	
22 Months	0	2	28	31	
24 Months	0	1	28	28	
26 Months	0	1	27	24	
Nervous system disorders (days)					
Number (%) of events	2 (66.7)	1 (25.0)	41 (31.5)	56 (43.8)	0.0375
Number (%) of patients censored	1 (33.3)	3 (75.0)	89 (68.5)	72 (56.3)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.45 Subgroup analysis by ethnicity
16.2.7.1.45.1 Treatment emergent adverse event per SOC by treatment group according to ethnicity - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[d]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.3285 (0.3285 to 5.3552)	NC (5.8480 to NC)	5.7823 (3.3511 to 21.0267)	3.3183 (1.6756 to 5.9138)	
Median (95% CI)	5.3552 (0.3285 to 5.3552)	NC (5.8480 to NC)	NC (NC to NC)	NC (9.3963 to NC)	
75% quantile (95% CI)	5.3552 (0.3285 to 5.3552)	NC (5.8480 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0455		0.0750	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	NC		1.4509 (0.9610 to 2.1904)	
P-value	-	0.9986		0.0766	
Events probability (95% CI)[c]					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.45 Subgroup analysis by ethnicity
16.2.7.1.45.1 Treatment emergent adverse event per SOC by treatment group according to ethnicity - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[d]**
2 Months	0.6667 (0.0541 to 0.9452)	1.0000 (1.0000 to 1.0000)	0.8411 (0.7646 to 0.8945)	0.8045 (0.7245 to 0.8634)	
4 Months	0.6667 (0.0541 to 0.9452)	1.0000 (1.0000 to 1.0000)	0.7984 (0.7162 to 0.8591)	0.7330 (0.6470 to 0.8012)	
6 Months	0.6667 (0.0541 to 0.9452)	0.7500 (0.1279 to 0.9605)	0.7426 (0.6539 to 0.8119)	0.6724 (0.5822 to 0.7473)	
8 Months	0.6667 (0.0541 to 0.9452)	0.7500 (0.1279 to 0.9605)	0.7224 (0.6314 to 0.7946)	0.6168 (0.5237 to 0.6971)	
10 Months	0.6667 (0.0541 to 0.9452)	0.7500 (0.1279 to 0.9605)	0.7116 (0.6194 to 0.7854)	0.5867 (0.4921 to 0.6696)	
12 Months	0.6667 (0.0541 to 0.9452)	0.7500 (0.1279 to 0.9605)	0.6998 (0.6059 to 0.7754)	0.5657 (0.4702 to 0.6504)	
14 Months	0.6667 (0.0541 to 0.9452)	0.7500 (0.1279 to 0.9605)	0.6998 (0.6059 to 0.7754)	0.5546 (0.4586 to 0.6403)	
16 Months	0.6667 (0.0541 to 0.9452)	0.7500 (0.1279 to 0.9605)	0.6998 (0.6059 to 0.7754)	0.5546 (0.4586 to 0.6403)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.45 Subgroup analysis by ethnicity
16.2.7.1.45.1 Treatment emergent adverse event per SOC by treatment group according to ethnicity - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[d]**
18 Months	0.6667 (0.0541 to 0.9452)	0.7500 (0.1279 to 0.9605)	0.6998 (0.6059 to 0.7754)	0.5546 (0.4586 to 0.6403)	
20 Months	0.6667 (0.0541 to 0.9452)	0.7500 (0.1279 to 0.9605)	0.6693 (0.5694 to 0.7511)	0.5414 (0.4443 to 0.6287)	
22 Months	0.6667 (0.0541 to 0.9452)	0.7500 (0.1279 to 0.9605)	0.6534 (0.5506 to 0.7382)	0.5275 (0.4292 to 0.6166)	
24 Months	0.6667 (0.0541 to 0.9452)	0.7500 (0.1279 to 0.9605)	0.6534 (0.5506 to 0.7382)	0.5275 (0.4292 to 0.6166)	
26 Months	0.6667 (0.0541 to 0.9452)	0.7500 (0.1279 to 0.9605)	0.6366 (0.5310 to 0.7246)	0.5275 (0.4292 to 0.6166)	
Number of patients at risk[c]					
2 Months	1	4	103	102	
4 Months	1	4	93	90	
6 Months	0	3	77	75	
8 Months	0	3	68	65	
10 Months	0	3	63	57	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.45 Subgroup analysis by ethnicity
16.2.7.1.45.1 Treatment emergent adverse event per SOC by treatment group according to ethnicity - Safety population

	Hispanic or Latino		Not Hispanic or Latino		
	Pd (N=3)	**IPd (N=4)**	**Pd (N=130)**	**IPd (N=128)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	0	3	59	51	
14 Months	0	3	57	50	
16 Months	0	3	54	45	
18 Months	0	3	49	42	
20 Months	0	3	43	41	
22 Months	0	2	41	37	
24 Months	0	1	40	36	
26 Months	0	1	36	31	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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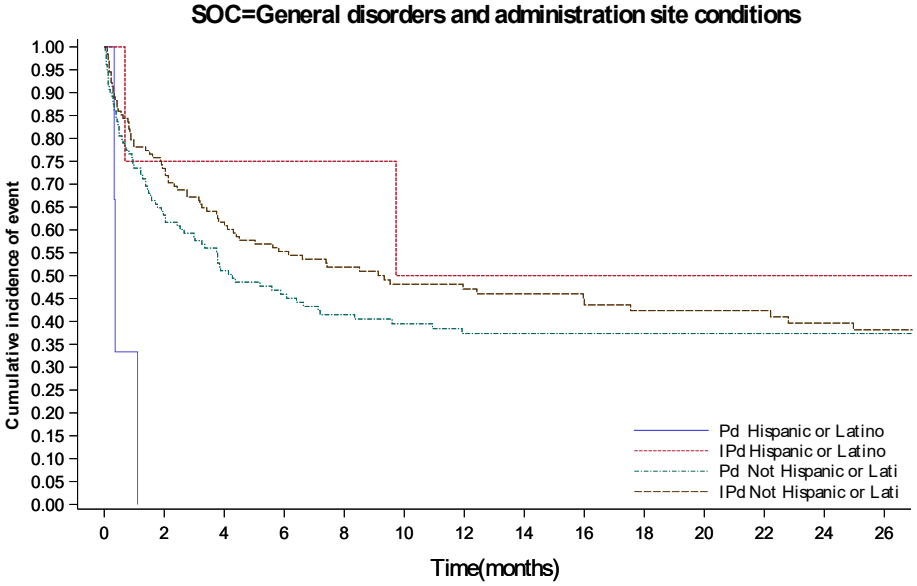
16.2.7.1 Safety endpoints
16.2.7.1.45 Subgroup analysis by ethnicity
16.2.7.1.45.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per SOC by treatment group according to ethnicity - Safety population

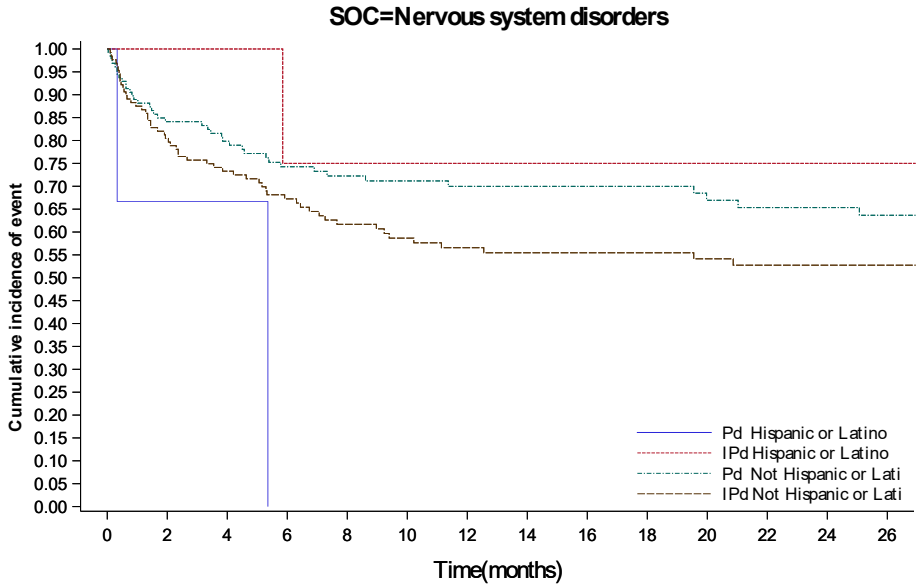


Number at Risk

Pd Hispanic or Latino	3	0												
IPd Hispanic or Latino	4	3	3	3	3	2	2	2	2	2	2	2	1	1
Pd Not Hispanic or Lati	129	80	62	52	44	38	35	33	31	30	28	28	28	27
IPd Not Hispanic or Lati	128	94	78	66	60	50	45	44	37	33	33	31	28	24

SOC are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_ethnic_s_f_x.rtf (17NOV2020 14:46)

16.2.7.1 Safety endpoints
16.2.7.1.45 Subgroup analysis by ethnicity
16.2.7.1.45.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per SOC by treatment group according to ethnicity - Safety population



Number at Risk

Pd Hispanic or Latino	3	1	1	0										
IPd Hispanic or Latino	4	4	4	3	3	3	3	3	3	3	3	2	1	1
Pd Not Hispanic or Lati	128	103	93	77	68	63	59	57	54	49	43	41	40	36
IPd Not Hispanic or Lati	128	102	90	75	65	57	51	50	45	42	41	37	36	31

SOC are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_ethnic_s_f_x.rtf (17NOV2020 14:46)

16.2.7.1 Safety endpoints
16.2.7.1.46 Subgroup analysis by baseline ECOG PS
16.2.7.1.46.1 Treatment emergent serious adverse event per SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[d]**
Infections and infestations (days)					
Number (%) of events	49 (36.3)	63 (46.3)	5 (35.7)	13 (81.3)	0.0171
Number (%) of patients censored	86 (63.7)	73 (53.7)	9 (64.3)	3 (18.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	4.9610 (2.2669 to 13.7988)	5.8809 (3.9097 to 9.8563)	2.3326 (0.4271 to NC)	0.8214 (0.1643 to 1.9384)	
Median (95% CI)	NC (24.2136 to NC)	24.8706 (16.3285 to NC)	NC (1.7741 to NC)	3.0226 (0.7228 to 7.7536)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	7.7536 (1.9384 to 14.4887)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3812		0.0140	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_seraesoc_ecog_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.46 Subgroup analysis by baseline ECOG PS
16.2.7.1.46.1 Treatment emergent serious adverse event per SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.1824 (0.8123 to 1.7213)		4.5670 (1.2358 to 16.8778)	
P-value	-	0.3818		0.0228	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.2190 (0.0592 to 0.8092)		
Events probability (95% CI)[c]					
2 Months	0.8565 (0.7843 to 0.9060)	0.8675 (0.7980 to 0.9144)	0.7857 (0.4725 to 0.9254)	0.5026 (0.2305 to 0.7243)	
4 Months	0.7620 (0.6789 to 0.8263)	0.8151 (0.7387 to 0.8711)	0.6429 (0.3433 to 0.8331)	0.4308 (0.1786 to 0.6625)	
6 Months	0.7285 (0.6424 to 0.7970)	0.7371 (0.6532 to 0.8037)	0.6429 (0.3433 to 0.8331)	0.3446 (0.1172 to 0.5890)	
8 Months	0.7107 (0.6231 to 0.7815)	0.7043 (0.6180 to 0.7747)	0.6429 (0.3433 to 0.8331)	0.2297 (0.0454 to 0.4969)	
10 Months	0.7009 (0.6124 to 0.7730)	0.6624 (0.5736 to 0.7369)	0.6429 (0.3433 to 0.8331)	0.1149 (0.0075 to 0.3840)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.46 Subgroup analysis by baseline ECOG PS
16.2.7.1.46.1 Treatment emergent serious adverse event per SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	0.6806 (0.5899 to 0.7554)	0.6188 (0.5280 to 0.6972)	0.6429 (0.3433 to 0.8331)	0.1149 (0.0075 to 0.3840)	
14 Months	0.6696 (0.5777 to 0.7459)	0.6188 (0.5280 to 0.6972)	0.6429 (0.3433 to 0.8331)	0.1149 (0.0075 to 0.3840)	
16 Months	0.6465 (0.5521 to 0.7260)	0.5999 (0.5081 to 0.6799)	0.6429 (0.3433 to 0.8331)	0.1149 (0.0075 to 0.3840)	
18 Months	0.6343 (0.5386 to 0.7155)	0.5897 (0.4974 to 0.6707)	0.6429 (0.3433 to 0.8331)	0.1149 (0.0075 to 0.3840)	
20 Months	0.6214 (0.5241 to 0.7044)	0.5454 (0.4504 to 0.6307)	0.6429 (0.3433 to 0.8331)	0.1149 (0.0075 to 0.3840)	
22 Months	0.6214 (0.5241 to 0.7044)	0.5343 (0.4389 to 0.6206)	0.6429 (0.3433 to 0.8331)	0.1149 (0.0075 to 0.3840)	
24 Months	0.6073 (0.5081 to 0.6925)	0.5215 (0.4253 to 0.6092)	0.6429 (0.3433 to 0.8331)	0.1149 (0.0075 to 0.3840)	
26 Months	0.5928 (0.4919 to 0.6802)	0.4816 (0.3831 to 0.5733)	0.6429 (0.3433 to 0.8331)	0.1149 (0.0075 to 0.3840)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.46 Subgroup analysis by baseline ECOG PS
16.2.7.1.46.1 Treatment emergent serious adverse event per SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		2		
	Pd (N=135)	**IPd (N=136)**	**Pd (N=14)**	**IPd (N=16)**	**p-value of treatment-by-sub group interaction[d]**
Number of patients at risk[c]					
2 Months	111	117	11	7	
4 Months	95	107	9	5	
6 Months	84	91	8	3	
8 Months	74	86	7	2	
10 Months	72	78	7	1	
12 Months	65	69	7	1	
14 Months	60	68	6	1	
16 Months	55	60	4	0	
18 Months	49	54	4	0	
20 Months	46	49	4	0	
22 Months	44	44	4	0	
24 Months	42	41	4	0	
26 Months	39	34	4	0	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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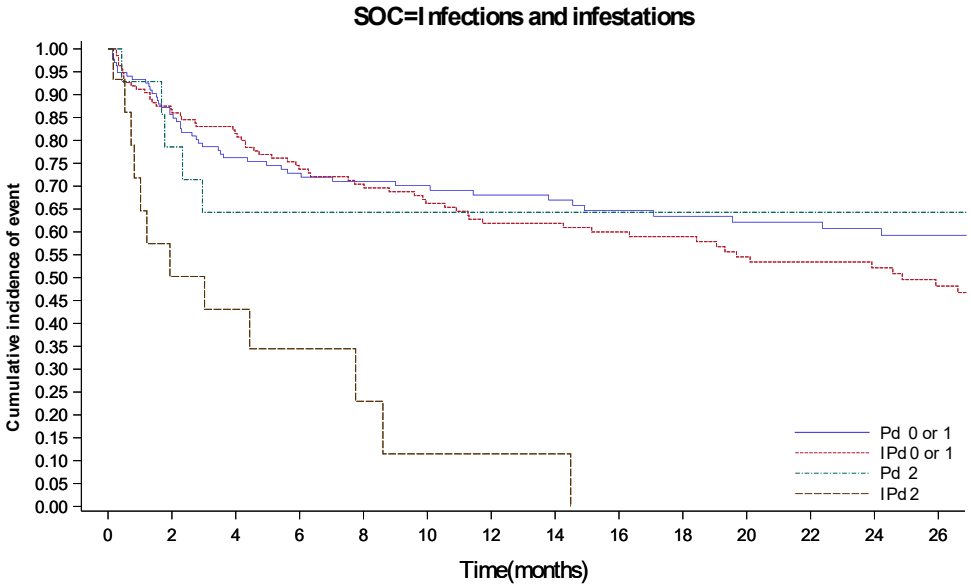
16.2.7.1 Safety endpoints
16.2.7.1.46 Subgroup analysis by baseline ECOG PS
16.2.7.1.46.2 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event per SOC by treatment group according to baseline ECOG PS - Safety population



Number at Risk

Pd 0 or 1	135	111	95	84	74	72	65	60	55	49	46	44	42	39
IPd 0 or 1	136	117	107	91	86	78	69	68	60	54	49	44	41	34
Pd 2	14	11	9	8	7	7	7	6	4	4	4	4	4	4
IPd 2	15	7	5	3	2	1	1	1	0					

SOC are presented if at least 5% of patients in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.47 Subgroup analysis by R-ISS staging
16.2.7.1.47.1 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I		II		III		
	Pd (N=38)	**IPd (N=43)**	**Pd (N=83)**	**IPd (N=86)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[d]**
Fatigue (days)							
Number (%) of events	6 (15.8)	11 (25.6)	24 (28.9)	13 (15.1)	1 (4.8)	3 (20.0)	0.0316
Number (%) of patients censored	32 (84.2)	32 (74.4)	59 (71.1)	73 (84.9)	20 (95.2)	12 (80.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (6.6366 to NC)	34.3655 (0.9856 to NC)	2.5298 (1.2156 to NC)	NC (9.3306 to NC)	NC (0.4928 to NC)	NC (0.2628 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.1766 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3331		0.0264		0.3807	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.47 Subgroup analysis by R-ISS staging
16.2.7.1.47.1 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I		II		III		
	Pd (N=38)	**IPd (N=43)**	**Pd (N=83)**	**IPd (N=86)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.6420 (0.5954 to 4.5283)		0.4720 (0.2396 to 0.9299)		2.6515 (0.2748 to 25.5805)	
P-value	-	0.3380		0.0300		0.3991	
Events probability (95% CI)[c]							
2 Months	0.9211 (0.7749 to 0.9738)	0.8605 (0.7155 to 0.9348)	0.7787 (0.6719 to 0.8545)	0.9302 (0.8513 to 0.9680)	0.9474 (0.6812 to 0.9924)	0.8615 (0.5497 to 0.9636)	
4 Months	0.9211 (0.7749 to 0.9738)	0.8133 (0.6611 to 0.9019)	0.7155 (0.6034 to 0.8010)	0.9177 (0.8349 to 0.9599)	0.9474 (0.6812 to 0.9924)	0.8615 (0.5497 to 0.9636)	
6 Months	0.9211 (0.7749 to 0.9738)	0.7879 (0.6316 to 0.8836)	0.7155 (0.6034 to 0.8010)	0.9051 (0.8190 to 0.9514)	0.9474 (0.6812 to 0.9924)	0.8615 (0.5497 to 0.9636)	
8 Months	0.8669 (0.7092 to 0.9423)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8764 (0.7816 to 0.9318)	0.9474 (0.6812 to 0.9924)	0.7538 (0.3980 to 0.9170)	
10 Months	0.8389 (0.6758 to 0.9243)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8453 (0.7421 to 0.9096)	0.9474 (0.6812 to 0.9924)	0.7538 (0.3980 to 0.9170)	
12 Months	0.8389 (0.6758 to 0.9243)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8453 (0.7421 to 0.9096)	0.9474 (0.6812 to 0.9924)	0.7538 (0.3980 to 0.9170)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.47 Subgroup analysis by R-ISS staging
16.2.7.1.47.1 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I		II		III		
	Pd (N=38)	**IPd (N=43)**	**Pd (N=83)**	**IPd (N=86)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.8389 (0.6758 to 0.9243)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8453 (0.7421 to 0.9096)	0.9474 (0.6812 to 0.9924)	0.7538 (0.3980 to 0.9170)	
16 Months	0.8389 (0.6758 to 0.9243)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8453 (0.7421 to 0.9096)	0.9474 (0.6812 to 0.9924)	0.7538 (0.3980 to 0.9170)	
18 Months	0.8389 (0.6758 to 0.9243)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8453 (0.7421 to 0.9096)	0.9474 (0.6812 to 0.9924)	0.7538 (0.3980 to 0.9170)	
20 Months	0.8389 (0.6758 to 0.9243)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8453 (0.7421 to 0.9096)	0.9474 (0.6812 to 0.9924)	0.7538 (0.3980 to 0.9170)	
22 Months	0.8389 (0.6758 to 0.9243)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8453 (0.7421 to 0.9096)	0.9474 (0.6812 to 0.9924)	0.7538 (0.3980 to 0.9170)	
24 Months	0.8389 (0.6758 to 0.9243)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8197 (0.7031 to 0.8938)	0.9474 (0.6812 to 0.9924)	0.7538 (0.3980 to 0.9170)	
26 Months	0.8389 (0.6758 to 0.9243)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8197 (0.7031 to 0.8938)	0.9474 (0.6812 to 0.9924)	0.7538 (0.3980 to 0.9170)	
Number of patients at risk[c]							
2 Months	35	37	62	78	16	12	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.47 Subgroup analysis by R-ISS staging
16.2.7.1.47.1 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I		II		III		
	Pd (N=38)	**IPd (N=43)**	**Pd (N=83)**	**IPd (N=86)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	34	34	56	73	12	9	
6 Months	34	31	49	64	7	8	
8 Months	31	30	43	60	6	6	
10 Months	30	29	39	53	6	5	
12 Months	30	28	35	50	5	5	
14 Months	30	28	33	49	5	5	
16 Months	29	27	30	42	4	4	
18 Months	27	26	27	38	3	3	
20 Months	26	26	25	36	3	3	
22 Months	26	24	24	33	3	2	
24 Months	26	22	23	32	3	2	
26 Months	25	20	23	28	2	2	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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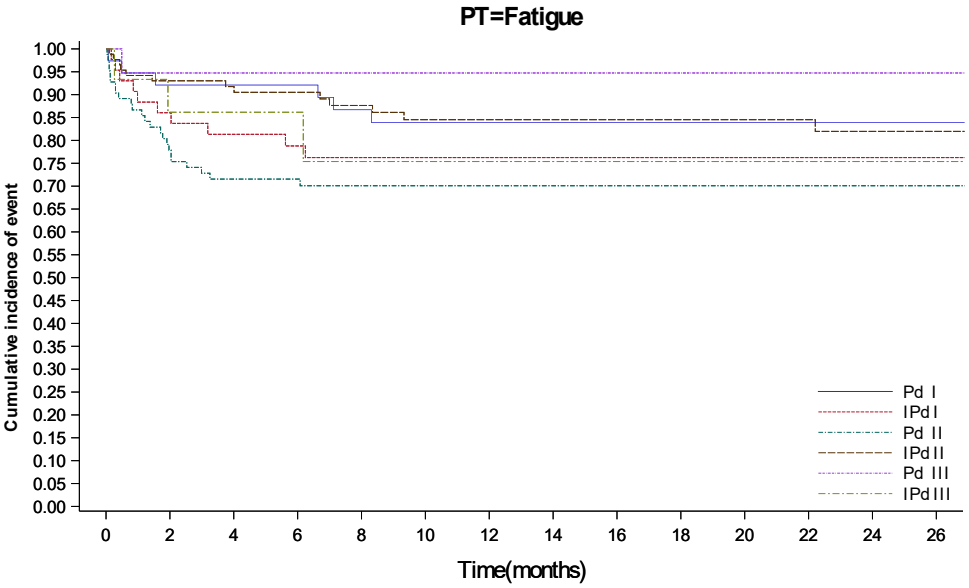
16.2.7.1 Safety endpoints
16.2.7.1.47 Subgroup analysis by R-ISS staging
16.2.7.1.47.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population



Number at Risk

Pd I	38	35	34	34	31	30	30	30	29	27	26	26	26	25
IPd I	43	37	34	31	30	29	28	28	27	26	26	24	22	20
Pd II	83	62	56	49	43	39	35	33	30	27	25	24	23	23
IPd II	86	78	73	64	60	53	50	49	42	38	36	33	32	28
Pd III	21	16	12	7	6	6	5	5	4	3	3	3	3	2
IPd III	15	12	9	8	6	5	5	5	4	3	3	2	2	2

PT are presented if at least 10 events in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.48 Subgroup analysis by ISS staging at study entry
16.2.7.1.48.1 Treatment emergent not severe adverse event per SOC by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=61)**	**Pd (N=55)**	**IPd (N=55)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[d]**
Psychiatric disorders (days)							
Number (%) of events	16 (31.4)	9 (14.8)	8 (14.5)	13 (23.6)	4 (10.0)	7 (21.2)	0.0449
Number (%) of patients censored	35 (68.6)	52 (85.2)	47 (85.5)	42 (76.4)	36 (90.0)	26 (78.8)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	6.2423 (2.1355 to NC)	NC (15.0144 to NC)	NC (4.6653 to NC)	35.0226 (3.8439 to NC)	NC (10.7433 to NC)	NC (0.2957 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (35.0226 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0139		0.3868		0.4229	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.48 Subgroup analysis by ISS staging at study entry
16.2.7.1.48.1 Treatment emergent not severe adverse event per SOC by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=61)**	**Pd (N=55)**	**IPd (N=55)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.3427 (0.1403 to 0.8371)		1.4795 (0.6061 to 3.6112)		1.6867 (0.4646 to 6.1227)	
P-value	-	0.0188		0.3896		0.4268	
Events probability (95% CI)[c]							
2 Months	0.8824 (0.7567 to 0.9453)	0.9180 (0.8142 to 0.9650)	0.9077 (0.7922 to 0.9605)	0.9091 (0.7953 to 0.9611)	0.9500 (0.8145 to 0.9873)	0.8777 (0.7062 to 0.9523)	
4 Months	0.8235 (0.6883 to 0.9040)	0.9180 (0.8142 to 0.9650)	0.8888 (0.7689 to 0.9484)	0.8699 (0.7461 to 0.9359)	0.9161 (0.7585 to 0.9726)	0.8127 (0.6294 to 0.9113)	
6 Months	0.7633 (0.6208 to 0.8581)	0.9000 (0.7907 to 0.9539)	0.8686 (0.7436 to 0.9351)	0.7875 (0.6483 to 0.8766)	0.9161 (0.7585 to 0.9726)	0.7774 (0.5879 to 0.8875)	
8 Months	0.7220 (0.5758 to 0.8251)	0.9000 (0.7907 to 0.9539)	0.8686 (0.7436 to 0.9351)	0.7875 (0.6483 to 0.8766)	0.9161 (0.7585 to 0.9726)	0.7774 (0.5879 to 0.8875)	
10 Months	0.7220 (0.5758 to 0.8251)	0.8805 (0.7649 to 0.9413)	0.8686 (0.7436 to 0.9351)	0.7875 (0.6483 to 0.8766)	0.9161 (0.7585 to 0.9726)	0.7774 (0.5879 to 0.8875)	
12 Months	0.7220 (0.5758 to 0.8251)	0.8805 (0.7649 to 0.9413)	0.8686 (0.7436 to 0.9351)	0.7875 (0.6483 to 0.8766)	0.8456 (0.6006 to 0.9463)	0.7774 (0.5879 to 0.8875)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12soc_iss_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.48 Subgroup analysis by ISS staging at study entry
16.2.7.1.48.1 Treatment emergent not severe adverse event per SOC by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=61)**	**Pd (N=55)**	**IPd (N=55)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.7001 (0.5521 to 0.8073)	0.8805 (0.7649 to 0.9413)	0.8686 (0.7436 to 0.9351)	0.7875 (0.6483 to 0.8766)	0.8456 (0.6006 to 0.9463)	0.7774 (0.5879 to 0.8875)	
16 Months	0.6767 (0.5266 to 0.7884)	0.8605 (0.7392 to 0.9280)	0.8686 (0.7436 to 0.9351)	0.7875 (0.6483 to 0.8766)	0.8456 (0.6006 to 0.9463)	0.7774 (0.5879 to 0.8875)	
18 Months	0.6767 (0.5266 to 0.7884)	0.8605 (0.7392 to 0.9280)	0.8686 (0.7436 to 0.9351)	0.7572 (0.6081 to 0.8560)	0.8456 (0.6006 to 0.9463)	0.7774 (0.5879 to 0.8875)	
20 Months	0.6767 (0.5266 to 0.7884)	0.8605 (0.7392 to 0.9280)	0.8686 (0.7436 to 0.9351)	0.7572 (0.6081 to 0.8560)	0.8456 (0.6006 to 0.9463)	0.7774 (0.5879 to 0.8875)	
22 Months	0.6767 (0.5266 to 0.7884)	0.8605 (0.7392 to 0.9280)	0.8686 (0.7436 to 0.9351)	0.7572 (0.6081 to 0.8560)	0.8456 (0.6006 to 0.9463)	0.7774 (0.5879 to 0.8875)	
24 Months	0.6767 (0.5266 to 0.7884)	0.8605 (0.7392 to 0.9280)	0.8175 (0.6426 to 0.9122)	0.7572 (0.6081 to 0.8560)	0.8456 (0.6006 to 0.9463)	0.7774 (0.5879 to 0.8875)	
26 Months	0.6767 (0.5266 to 0.7884)	0.8327 (0.6987 to 0.9108)	0.8175 (0.6426 to 0.9122)	0.7572 (0.6081 to 0.8560)	0.8456 (0.6006 to 0.9463)	0.7774 (0.5879 to 0.8875)	
Number of patients at risk[c]							
2 Months	45	56	48	48	33	28	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.48 Subgroup analysis by ISS staging at study entry
16.2.7.1.48.1 Treatment emergent not severe adverse event per SOC by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Pd (N=51)	**IPd (N=61)**	**Pd (N=55)**	**IPd (N=55)**	**Pd (N=40)**	**IPd (N=33)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	41	55	47	43	26	24	
6 Months	38	49	39	36	18	21	
8 Months	34	48	35	35	16	18	
10 Months	34	45	33	31	15	17	
12 Months	33	44	28	29	12	15	
14 Months	31	44	27	29	11	14	
16 Months	28	41	23	26	10	10	
18 Months	25	39	21	25	8	8	
20 Months	24	37	18	23	8	8	
22 Months	24	34	17	21	7	7	
24 Months	24	31	15	21	7	7	
26 Months	22	27	15	19	6	7	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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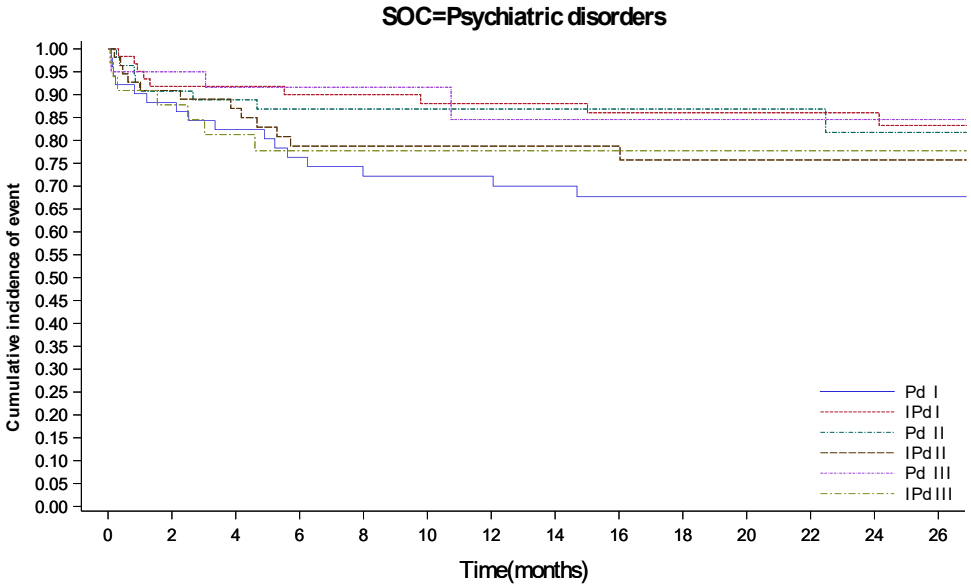
16.2.7.1 Safety endpoints
16.2.7.1.48 Subgroup analysis by ISS staging at study entry
16.2.7.1.48.2 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per SOC by treatment group according to ISS staging at study entry - Safety population



Number at Risk

Pd I	51	45	41	38	34	34	33	31	28	25	24	24	24	22
IPd I	61	56	55	49	48	45	44	44	41	39	37	34	31	27
Pd II	55	48	47	39	35	33	28	27	23	21	18	17	15	15
IPd II	55	48	43	36	35	31	29	29	26	25	23	21	21	19
Pd III	40	33	26	18	16	15	12	11	10	8	8	7	7	6
IPd III	33	28	24	21	18	17	15	14	10	8	8	7	7	7

SOC are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12soc_iss_s_f_x.rtf (17NOV2020 14:45)

16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by R-ISS staging
16.2.7.1.49.1 Treatment emergent not severe adverse event per PT by treatment group according to R-ISS staging - Safety population

	I		II		III		
	Pd (N=38)	**IPd (N=43)**	**Pd (N=83)**	**IPd (N=86)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[d]**
Fatigue (days)							
Number (%) of events	6 (15.8)	11 (25.6)	24 (28.9)	11 (12.8)	1 (4.8)	3 (20.0)	0.0164
Number (%) of patients censored	32 (84.2)	32 (74.4)	59 (71.1)	75 (87.2)	20 (95.2)	12 (80.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (6.6366 to NC)	34.3655 (0.9856 to NC)	2.5298 (1.2156 to NC)	NC (22.2094 to NC)	NC (0.4928 to NC)	15.8686 (0.2628 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.8686 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd							
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3331		0.0080		0.4295	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by R-ISS staging
16.2.7.1.49.1 Treatment emergent not severe adverse event per PT by treatment group according to R-ISS staging - Safety population

	I		II		III		
	Pd (N=38)	**IPd (N=43)**	**Pd (N=83)**	**IPd (N=86)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.6420 (0.5954 to 4.5283)		0.3921 (0.1914 to 0.8030)		2.4347 (0.2495 to 23.7553)	
P-value	-	0.3380		0.0105		0.4439	
Events probability (95% CI)[c]							
2 Months	0.9211 (0.7749 to 0.9738)	0.8605 (0.7155 to 0.9348)	0.7787 (0.6719 to 0.8545)	0.9419 (0.8660 to 0.9754)	0.9474 (0.6812 to 0.9924)	0.9333 (0.6126 to 0.9903)	
4 Months	0.9211 (0.7749 to 0.9738)	0.8133 (0.6611 to 0.9019)	0.7155 (0.6034 to 0.8010)	0.9293 (0.8493 to 0.9676)	0.9474 (0.6812 to 0.9924)	0.8556 (0.5327 to 0.9621)	
6 Months	0.9211 (0.7749 to 0.9738)	0.7879 (0.6316 to 0.8836)	0.7155 (0.6034 to 0.8010)	0.9167 (0.8331 to 0.9595)	0.9474 (0.6812 to 0.9924)	0.8556 (0.5327 to 0.9621)	
8 Months	0.8669 (0.7092 to 0.9423)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8881 (0.7952 to 0.9404)	0.9474 (0.6812 to 0.9924)	0.8556 (0.5327 to 0.9621)	
10 Months	0.8389 (0.6758 to 0.9243)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8722 (0.7742 to 0.9296)	0.9474 (0.6812 to 0.9924)	0.8556 (0.5327 to 0.9621)	
12 Months	0.8389 (0.6758 to 0.9243)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8722 (0.7742 to 0.9296)	0.9474 (0.6812 to 0.9924)	0.8556 (0.5327 to 0.9621)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by R-ISS staging
16.2.7.1.49.1 Treatment emergent not severe adverse event per PT by treatment group according to R-ISS staging - Safety population

	I		II		III		
	Pd (N=38)	**IPd (N=43)**	**Pd (N=83)**	**IPd (N=86)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.8389 (0.6758 to 0.9243)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8722 (0.7742 to 0.9296)	0.9474 (0.6812 to 0.9924)	0.8556 (0.5327 to 0.9621)	
16 Months	0.8389 (0.6758 to 0.9243)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8722 (0.7742 to 0.9296)	0.9474 (0.6812 to 0.9924)	0.6844 (0.2520 to 0.9010)	
18 Months	0.8389 (0.6758 to 0.9243)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8722 (0.7742 to 0.9296)	0.9474 (0.6812 to 0.9924)	0.6844 (0.2520 to 0.9010)	
20 Months	0.8389 (0.6758 to 0.9243)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8722 (0.7742 to 0.9296)	0.9474 (0.6812 to 0.9924)	0.6844 (0.2520 to 0.9010)	
22 Months	0.8389 (0.6758 to 0.9243)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8722 (0.7742 to 0.9296)	0.9474 (0.6812 to 0.9924)	0.6844 (0.2520 to 0.9010)	
24 Months	0.8389 (0.6758 to 0.9243)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8473 (0.7348 to 0.9148)	0.9474 (0.6812 to 0.9924)	0.6844 (0.2520 to 0.9010)	
26 Months	0.8389 (0.6758 to 0.9243)	0.7625 (0.6029 to 0.8647)	0.7009 (0.5873 to 0.7887)	0.8473 (0.7348 to 0.9148)	0.9474 (0.6812 to 0.9924)	0.6844 (0.2520 to 0.9010)	
Number of patients at risk[c]							
2 Months	35	37	62	79	16	13	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by R-ISS staging
16.2.7.1.49.1 Treatment emergent not severe adverse event per PT by treatment group according to R-ISS staging - Safety population

	I		II		III		
	Pd (N=38)	**IPd (N=43)**	**Pd (N=83)**	**IPd (N=86)**	**Pd (N=21)**	**IPd (N=15)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	34	34	56	74	12	9	
6 Months	34	31	49	65	7	8	
8 Months	31	30	43	61	6	7	
10 Months	30	29	39	55	6	6	
12 Months	30	28	35	52	5	6	
14 Months	30	28	33	51	5	6	
16 Months	29	27	30	44	4	4	
18 Months	27	26	27	40	3	3	
20 Months	26	26	25	38	3	3	
22 Months	26	24	24	35	3	2	
24 Months	26	22	23	34	3	2	
26 Months	25	20	23	30	2	2	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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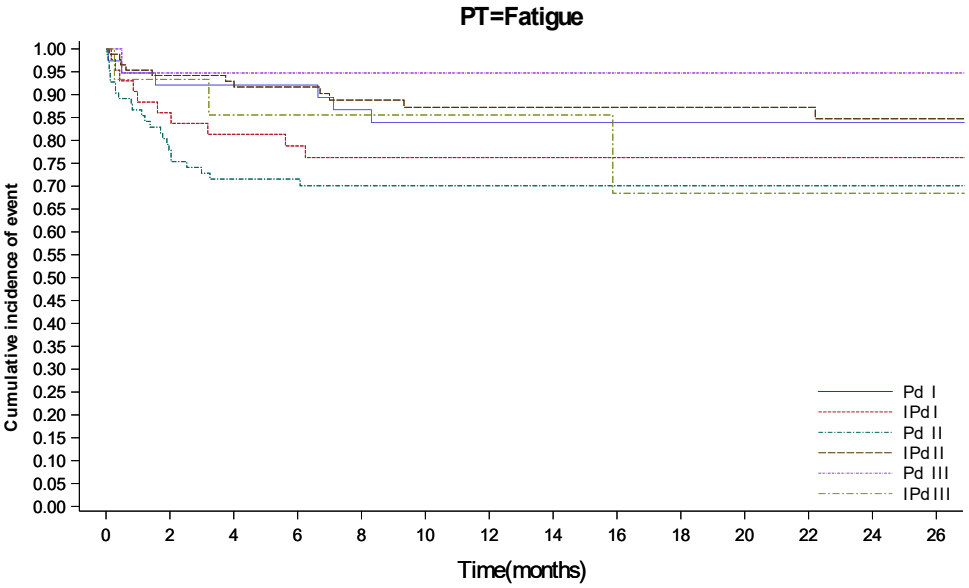
16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by R-ISS staging
16.2.7.1.49.2 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per PT by treatment group according to R-ISS staging - Safety population



Number at Risk

Pd I	38	35	34	34	31	30	30	30	29	27	26	26	26	25
IPd I	43	37	34	31	30	29	28	28	27	26	26	24	22	20
Pd II	83	62	56	49	43	39	35	33	30	27	25	24	23	23
IPd II	86	79	74	65	61	55	52	51	44	40	38	35	34	30
Pd III	21	16	12	7	6	6	5	5	4	3	3	3	3	2
IPd III	15	13	9	8	7	6	6	6	4	3	3	2	2	2

PT are presented if at least 10 events in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.1 Treatment emergent adverse event per SOC by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
Respiratory, thoracic and mediastinal disorders (days)					
Number (%) of events	7 (20.6)	12 (52.2)	32 (42.1)	42 (40.8)	0.0193
Number (%) of patients censored	27 (79.4)	11 (47.8)	44 (57.9)	61 (59.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	12.4517 (0.8542 to NC)	2.7269 (0.1314 to 6.4394)	1.7084 (0.7228 to 4.3368)	3.8768 (1.6756 to 7.6879)	
Median (95% CI)	NC (NC to NC)	7.3922 (2.7269 to NC)	NC (7.2279 to NC)	NC (13.2074 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (7.3922 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0143		0.4683	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	3.1258 (1.2025 to 8.1254)		0.8417 (0.5280 to 1.3417)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.1 Treatment emergent adverse event per SOC by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
P-value	-	0.0194		0.4688	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.3199 (0.1231 to 0.8316)				
Events probability (95% CI)[c]					
2 Months	0.8785 (0.7078 to 0.9526)	0.7716 (0.5348 to 0.8982)	0.7207 (0.6044 to 0.8081)	0.7961 (0.7047 to 0.8620)	
4 Months	0.8448 (0.6657 to 0.9325)	0.6678 (0.4237 to 0.8271)	0.6673 (0.5486 to 0.7614)	0.7458 (0.6495 to 0.8193)	
6 Months	0.8448 (0.6657 to 0.9325)	0.6121 (0.3680 to 0.7859)	0.6242 (0.5037 to 0.7233)	0.6931 (0.5927 to 0.7734)	
8 Months	0.7951 (0.5912 to 0.9048)	0.4664 (0.2228 to 0.6787)	0.6086 (0.4874 to 0.7096)	0.6474 (0.5440 to 0.7331)	
10 Months	0.7951 (0.5912 to 0.9048)	0.3887 (0.1592 to 0.6150)	0.5926 (0.4707 to 0.6954)	0.6230 (0.5180 to 0.7114)	
12 Months	0.7951 (0.5912 to 0.9048)	0.2915 (0.0865 to 0.5375)	0.5926 (0.4707 to 0.6954)	0.6097 (0.5038 to 0.6998)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_care_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.1 Treatment emergent adverse event per SOC by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.7421 (0.5208 to 0.8725)	0.2915 (0.0865 to 0.5375)	0.5556 (0.4311 to 0.6632)	0.5681 (0.4596 to 0.6629)	
16 Months	0.7421 (0.5208 to 0.8725)	0.2915 (0.0865 to 0.5375)	0.5556 (0.4311 to 0.6632)	0.5681 (0.4596 to 0.6629)	
18 Months	0.7421 (0.5208 to 0.8725)	0.2915 (0.0865 to 0.5375)	0.5556 (0.4311 to 0.6632)	0.5681 (0.4596 to 0.6629)	
20 Months	0.7421 (0.5208 to 0.8725)	0.2915 (0.0865 to 0.5375)	0.5556 (0.4311 to 0.6632)	0.5681 (0.4596 to 0.6629)	
22 Months	0.7421 (0.5208 to 0.8725)	0.2915 (0.0865 to 0.5375)	0.5556 (0.4311 to 0.6632)	0.5681 (0.4596 to 0.6629)	
24 Months	0.7421 (0.5208 to 0.8725)	0.2915 (0.0865 to 0.5375)	0.5556 (0.4311 to 0.6632)	0.5681 (0.4596 to 0.6629)	
26 Months	0.7421 (0.5208 to 0.8725)	0.2915 (0.0865 to 0.5375)	0.5556 (0.4311 to 0.6632)	0.5681 (0.4596 to 0.6629)	
Number of patients at risk[c]					
2 Months	27	16	54	82	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.1 Treatment emergent adverse event per SOC by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	22	12	50	73	
6 Months	17	10	41	61	
8 Months	16	6	39	56	
10 Months	16	4	36	49	
12 Months	15	3	32	45	
14 Months	14	3	28	41	
16 Months	12	2	26	38	
18 Months	11	1	24	34	
20 Months	10	1	24	33	
22 Months	9	1	23	28	
24 Months	9	1	23	26	
26 Months	8	1	22	24	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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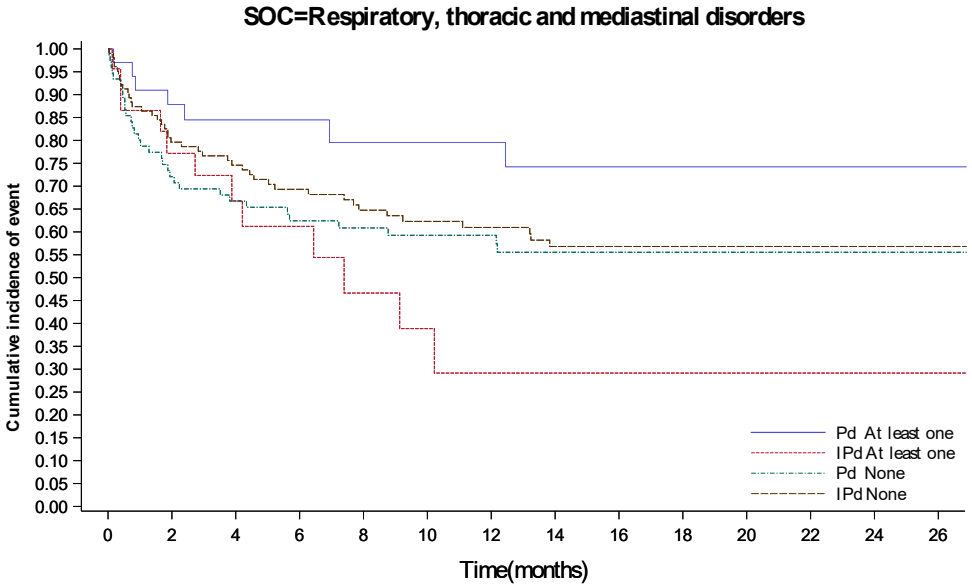
16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per SOC by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population



Number at Risk

Pd At least one	34	27	22	17	16	16	15	14	12	11	10	9	9	8
IPd At least one	23	16	12	10	6	4	3	3	2	1	1	1	1	1
Pd None	76	54	50	41	39	36	32	28	26	24	24	23	23	22
IPd None	103	82	73	61	56	49	45	41	38	34	33	28	26	24

16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.3 Treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
Cough (days)					
Number (%) of events	2 (5.9)	6 (26.1)	8 (10.5)	7 (6.8)	0.0303
Number (%) of patients censored	32 (94.1)	17 (73.9)	68 (89.5)	96 (93.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (12.4517 to NC)	7.3922 (0.3943 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (7.3922 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0370		0.1994	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	4.9044 (0.9573 to 25.1266)		0.5100 (0.1792 to 1.4512)	
P-value	-	0.0564		0.2070	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.3 Treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9068 (0.6758 to 0.9759)	0.9333 (0.8472 to 0.9717)	0.9806 (0.9246 to 0.9951)	
4 Months	0.9643 (0.7724 to 0.9949)	0.8501 (0.6010 to 0.9495)	0.9198 (0.8301 to 0.9631)	0.9606 (0.8983 to 0.9850)	
6 Months	0.9643 (0.7724 to 0.9949)	0.7935 (0.5357 to 0.9178)	0.8916 (0.7948 to 0.9443)	0.9606 (0.8983 to 0.9850)	
8 Months	0.9643 (0.7724 to 0.9949)	0.7213 (0.4455 to 0.8764)	0.8916 (0.7948 to 0.9443)	0.9269 (0.8525 to 0.9646)	
10 Months	0.9643 (0.7724 to 0.9949)	0.6492 (0.3692 to 0.8292)	0.8916 (0.7948 to 0.9443)	0.9269 (0.8525 to 0.9646)	
12 Months	0.9643 (0.7724 to 0.9949)	0.6492 (0.3692 to 0.8292)	0.8916 (0.7948 to 0.9443)	0.9269 (0.8525 to 0.9646)	
14 Months	0.9076 (0.6671 to 0.9770)	0.6492 (0.3692 to 0.8292)	0.8916 (0.7948 to 0.9443)	0.9269 (0.8525 to 0.9646)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.3 Treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.9076 (0.6671 to 0.9770)	0.6492 (0.3692 to 0.8292)	0.8916 (0.7948 to 0.9443)	0.9269 (0.8525 to 0.9646)	
18 Months	0.9076 (0.6671 to 0.9770)	0.6492 (0.3692 to 0.8292)	0.8916 (0.7948 to 0.9443)	0.9269 (0.8525 to 0.9646)	
20 Months	0.9076 (0.6671 to 0.9770)	0.6492 (0.3692 to 0.8292)	0.8916 (0.7948 to 0.9443)	0.9269 (0.8525 to 0.9646)	
22 Months	0.9076 (0.6671 to 0.9770)	0.6492 (0.3692 to 0.8292)	0.8916 (0.7948 to 0.9443)	0.9269 (0.8525 to 0.9646)	
24 Months	0.9076 (0.6671 to 0.9770)	0.6492 (0.3692 to 0.8292)	0.8916 (0.7948 to 0.9443)	0.9269 (0.8525 to 0.9646)	
26 Months	0.9076 (0.6671 to 0.9770)	0.6492 (0.3692 to 0.8292)	0.8916 (0.7948 to 0.9443)	0.9269 (0.8525 to 0.9646)	
Number of patients at risk[c]					
2 Months	31	19	69	101	
4 Months	26	15	68	94	
6 Months	19	13	58	86	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.3 Treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	19	10	53	82	
10 Months	19	8	50	76	
12 Months	17	8	45	71	
14 Months	15	8	42	70	
16 Months	13	6	39	66	
18 Months	12	5	36	60	
20 Months	11	5	35	58	
22 Months	10	5	34	51	
24 Months	10	5	34	48	
26 Months	9	4	32	44	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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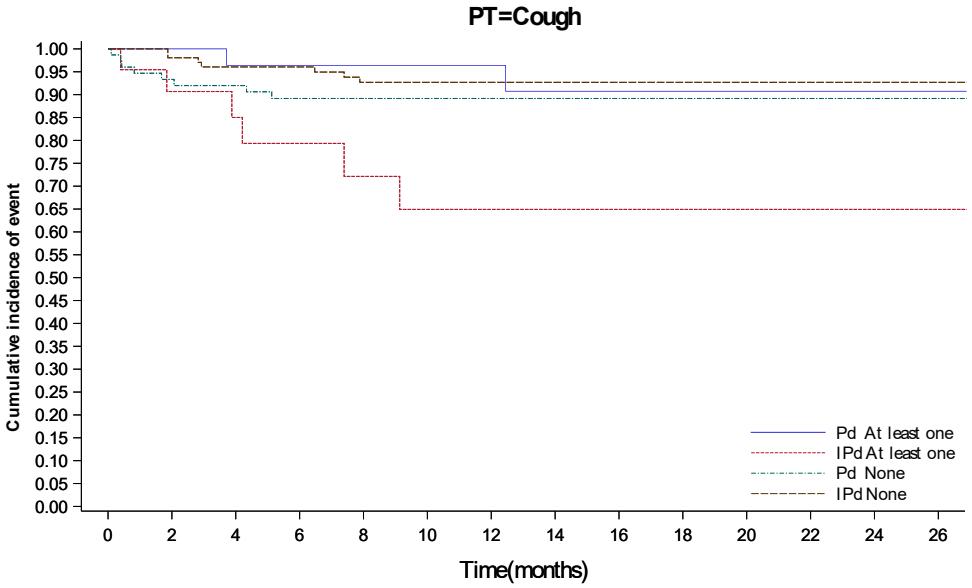
16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population



Number at Risk

Pd At least one	34	31	26	19	19	19	17	15	13	12	11	10	10	9
IPd At least one	23	19	15	13	10	8	8	8	6	5	5	5	5	4
Pd None	76	69	68	58	53	50	45	42	39	36	35	34	34	32
IPd None	103	101	94	86	82	76	71	70	66	60	58	51	48	44

PT are presented if at least 10 events in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.5 Treatment emergent not severe adverse event per SOC by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
Respiratory, thoracic and mediastinal disorders (days)					
Number (%) of events	6 (17.6)	12 (52.2)	25 (32.9)	41 (39.8)	0.0392
Number (%) of patients censored	28 (82.4)	11 (47.8)	51 (67.1)	62 (60.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (1.8727 to NC)	2.7269 (0.3943 to 6.4394)	1.9384 (0.8214 to NC)	3.8768 (1.7741 to 9.2320)	
Median (95% CI)	NC (NC to NC)	7.3922 (2.7269 to NC)	NC (NC to NC)	NC (13.8316 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (7.3922 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0036		0.7678	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	3.9983 (1.4697 to 10.8778)		1.0787 (0.6524 to 1.7837)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.5 Treatment emergent not severe adverse event per SOC by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
P-value	-	0.0066		0.7678	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.2501 (0.0919 to 0.6804)				
Events probability (95% CI)[c]					
2 Months	0.9081 (0.7414 to 0.9694)	0.7701 (0.5325 to 0.8973)	0.7459 (0.6310 to 0.8298)	0.8058 (0.7154 to 0.8701)	
4 Months	0.8744 (0.6987 to 0.9510)	0.6664 (0.4222 to 0.8261)	0.6917 (0.5733 to 0.7832)	0.7455 (0.6490 to 0.8190)	
6 Months	0.8744 (0.6987 to 0.9510)	0.6109 (0.3667 to 0.7849)	0.6616 (0.5412 to 0.7573)	0.6927 (0.5923 to 0.7731)	
8 Months	0.8259 (0.6233 to 0.9255)	0.4654 (0.2222 to 0.6778)	0.6616 (0.5412 to 0.7573)	0.6700 (0.5679 to 0.7532)	
10 Months	0.8259 (0.6233 to 0.9255)	0.3878 (0.1588 to 0.6141)	0.6616 (0.5412 to 0.7573)	0.6576 (0.5545 to 0.7424)	
12 Months	0.8259 (0.6233 to 0.9255)	0.2909 (0.0863 to 0.5366)	0.6616 (0.5412 to 0.7573)	0.6445 (0.5401 to 0.7310)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.5 Treatment emergent not severe adverse event per SOC by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.7743 (0.5535 to 0.8952)	0.2909 (0.0863 to 0.5366)	0.6616 (0.5412 to 0.7573)	0.6033 (0.4955 to 0.6951)	
16 Months	0.7743 (0.5535 to 0.8952)	0.2909 (0.0863 to 0.5366)	0.6616 (0.5412 to 0.7573)	0.5749 (0.4652 to 0.6700)	
18 Months	0.7743 (0.5535 to 0.8952)	0.2909 (0.0863 to 0.5366)	0.6616 (0.5412 to 0.7573)	0.5749 (0.4652 to 0.6700)	
20 Months	0.7743 (0.5535 to 0.8952)	0.2909 (0.0863 to 0.5366)	0.6616 (0.5412 to 0.7573)	0.5749 (0.4652 to 0.6700)	
22 Months	0.7743 (0.5535 to 0.8952)	0.2909 (0.0863 to 0.5366)	0.6616 (0.5412 to 0.7573)	0.5749 (0.4652 to 0.6700)	
24 Months	0.7743 (0.5535 to 0.8952)	0.2909 (0.0863 to 0.5366)	0.6616 (0.5412 to 0.7573)	0.5749 (0.4652 to 0.6700)	
26 Months	0.7743 (0.5535 to 0.8952)	0.2909 (0.0863 to 0.5366)	0.6616 (0.5412 to 0.7573)	0.5749 (0.4652 to 0.6700)	
Number of patients at risk[c]					
2 Months	28	16	55	83	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12soc_care_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.5 Treatment emergent not severe adverse event per SOC by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	23	12	51	73	
6 Months	18	10	43	61	
8 Months	17	6	41	58	
10 Months	17	4	39	52	
12 Months	16	3	35	48	
14 Months	14	3	33	44	
16 Months	12	2	30	39	
18 Months	11	1	27	35	
20 Months	10	1	27	34	
22 Months	9	1	26	29	
24 Months	9	1	26	27	
26 Months	8	1	24	25	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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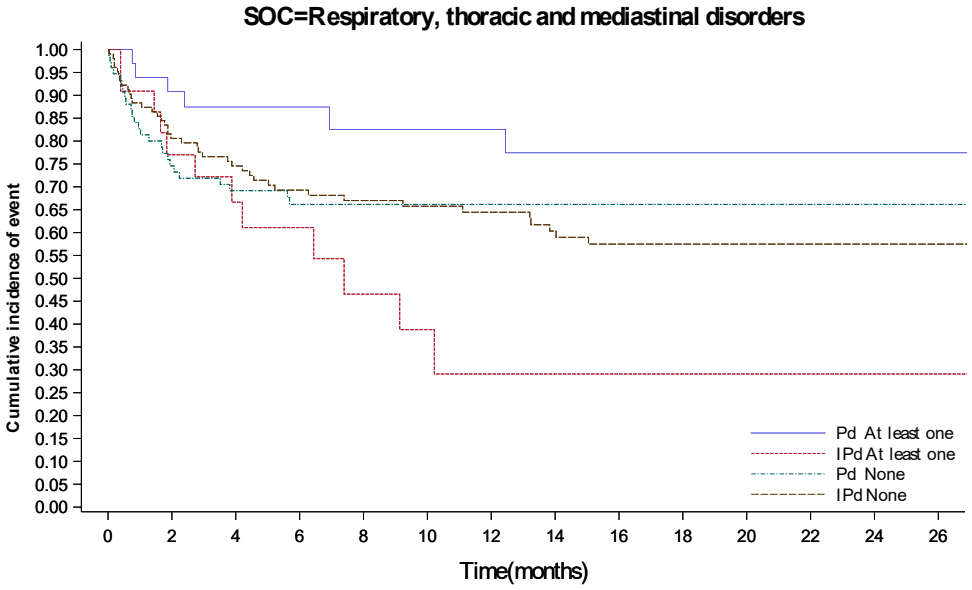
16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.6 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per SOC by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population



Number at Risk

Pd At least one	34	28	23	18	17	17	16	14	12	11	10	9	9	8
IPd At least one	23	16	12	10	6	4	3	3	2	1	1	1	1	1
Pd None	76	55	51	43	41	39	35	33	30	27	27	26	26	24
IPd None	103	83	73	61	58	52	48	44	39	35	34	29	27	25

SOC are presented if at least 10 events in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.7 Treatment emergent not severe adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
Cough (days)					
Number (%) of events	2 (5.9)	6 (26.1)	7 (9.2)	7 (6.8)	0.0449
Number (%) of patients censored	32 (94.1)	17 (73.9)	69 (90.8)	96 (93.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (12.4517 to NC)	7.3922 (0.3943 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (7.3922 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0370		0.3108	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	4.9044 (0.9573 to 25.1266)		0.5756 (0.1954 to 1.6952)	
P-value	-	0.0564		0.3162	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.7 Treatment emergent not severe adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]					
2 Months	1.0000 (1.0000 to 1.0000)	0.9068 (0.6758 to 0.9759)	0.9333 (0.8472 to 0.9717)	0.9806 (0.9246 to 0.9951)	
4 Months	0.9643 (0.7724 to 0.9949)	0.8501 (0.6010 to 0.9495)	0.9198 (0.8301 to 0.9631)	0.9606 (0.8983 to 0.9850)	
6 Months	0.9643 (0.7724 to 0.9949)	0.7935 (0.5357 to 0.9178)	0.9052 (0.8112 to 0.9537)	0.9606 (0.8983 to 0.9850)	
8 Months	0.9643 (0.7724 to 0.9949)	0.7213 (0.4455 to 0.8764)	0.9052 (0.8112 to 0.9537)	0.9269 (0.8525 to 0.9646)	
10 Months	0.9643 (0.7724 to 0.9949)	0.6492 (0.3692 to 0.8292)	0.9052 (0.8112 to 0.9537)	0.9269 (0.8525 to 0.9646)	
12 Months	0.9643 (0.7724 to 0.9949)	0.6492 (0.3692 to 0.8292)	0.9052 (0.8112 to 0.9537)	0.9269 (0.8525 to 0.9646)	
14 Months	0.9076 (0.6671 to 0.9770)	0.6492 (0.3692 to 0.8292)	0.9052 (0.8112 to 0.9537)	0.9269 (0.8525 to 0.9646)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.7 Treatment emergent not severe adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.9076 (0.6671 to 0.9770)	0.6492 (0.3692 to 0.8292)	0.9052 (0.8112 to 0.9537)	0.9269 (0.8525 to 0.9646)	
18 Months	0.9076 (0.6671 to 0.9770)	0.6492 (0.3692 to 0.8292)	0.9052 (0.8112 to 0.9537)	0.9269 (0.8525 to 0.9646)	
20 Months	0.9076 (0.6671 to 0.9770)	0.6492 (0.3692 to 0.8292)	0.9052 (0.8112 to 0.9537)	0.9269 (0.8525 to 0.9646)	
22 Months	0.9076 (0.6671 to 0.9770)	0.6492 (0.3692 to 0.8292)	0.9052 (0.8112 to 0.9537)	0.9269 (0.8525 to 0.9646)	
24 Months	0.9076 (0.6671 to 0.9770)	0.6492 (0.3692 to 0.8292)	0.9052 (0.8112 to 0.9537)	0.9269 (0.8525 to 0.9646)	
26 Months	0.9076 (0.6671 to 0.9770)	0.6492 (0.3692 to 0.8292)	0.9052 (0.8112 to 0.9537)	0.9269 (0.8525 to 0.9646)	
Number of patients at risk[c]					
2 Months	31	19	69	101	
4 Months	26	15	68	94	
6 Months	19	13	59	86	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.7 Treatment emergent not severe adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Pd (N=34)	**IPd (N=23)**	**Pd (N=76)**	**IPd (N=103)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	19	10	54	82	
10 Months	19	8	51	76	
12 Months	17	8	46	71	
14 Months	15	8	43	70	
16 Months	13	6	39	66	
18 Months	12	5	36	60	
20 Months	11	5	35	58	
22 Months	10	5	34	51	
24 Months	10	5	34	48	
26 Months	9	4	32	44	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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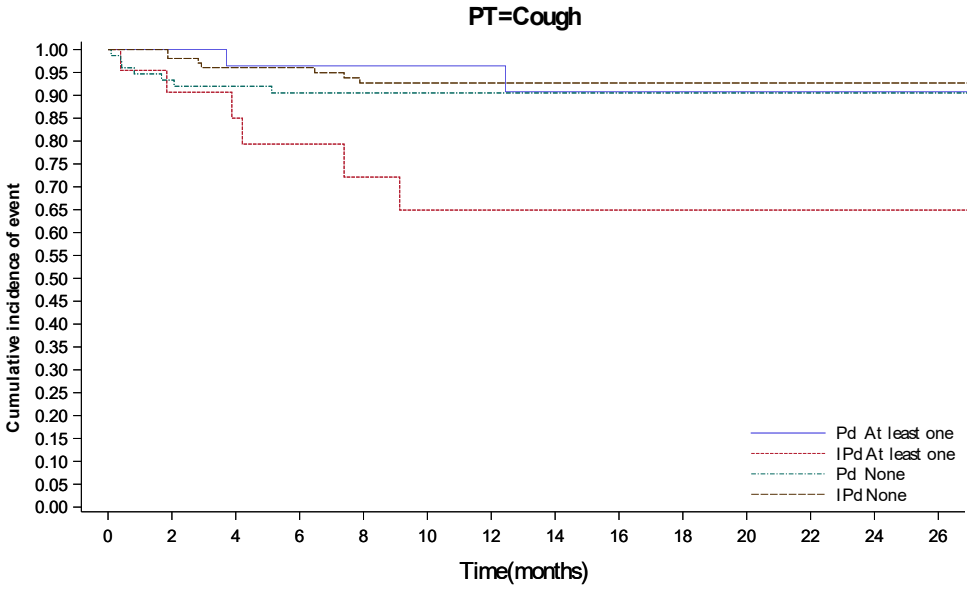
16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.50.8 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population



Number at Risk

Pd At least one	34	31	26	19	19	19	17	15	13	12	11	10	10	9
IPd At least one	23	19	15	13	10	8	8	8	6	5	5	5	5	4
Pd None	76	69	68	59	54	51	46	43	39	36	35	34	34	32
IPd None	103	101	94	86	82	76	71	70	66	60	58	51	48	44

PT are presented if at least 10 events in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.1 Treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[d]**
Psychiatric disorders (days)					
Number (%) of events	25 (28.4)	15 (18.5)	7 (11.5)	16 (22.5)	0.0445
Number (%) of patients censored	63 (71.6)	66 (81.5)	54 (88.5)	55 (77.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	10.7433 (3.3511 to NC)	35.0226 (12.2875 to NC)	NC (NC to NC)	NC (3.8439 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0565		0.2005	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.5333 (0.2766 to 1.0283)		1.7777 (0.7278 to 4.3420)	
P-value	-	0.0606		0.2067	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.1 Treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]					
2 Months	0.8862 (0.7988 to 0.9371)	0.9128 (0.8257 to 0.9574)	0.8965 (0.7839 to 0.9522)	0.8873 (0.7873 to 0.9420)	
4 Months	0.8383 (0.7421 to 0.9009)	0.9001 (0.8101 to 0.9487)	0.8778 (0.7604 to 0.9399)	0.8432 (0.7346 to 0.9100)	
6 Months	0.7828 (0.6766 to 0.8578)	0.8591 (0.7597 to 0.9195)	0.8778 (0.7604 to 0.9399)	0.7960 (0.6794 to 0.8740)	
8 Months	0.7535 (0.6429 to 0.8342)	0.8591 (0.7597 to 0.9195)	0.8778 (0.7604 to 0.9399)	0.7960 (0.6794 to 0.8740)	
10 Months	0.7535 (0.6429 to 0.8342)	0.8591 (0.7597 to 0.9195)	0.8778 (0.7604 to 0.9399)	0.7783 (0.6585 to 0.8604)	
12 Months	0.7368 (0.6232 to 0.8210)	0.8591 (0.7597 to 0.9195)	0.8778 (0.7604 to 0.9399)	0.7783 (0.6585 to 0.8604)	
14 Months	0.7193 (0.6026 to 0.8070)	0.8412 (0.7359 to 0.9071)	0.8778 (0.7604 to 0.9399)	0.7783 (0.6585 to 0.8604)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.1 Treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.7003 (0.5803 to 0.7920)	0.8412 (0.7359 to 0.9071)	0.8778 (0.7604 to 0.9399)	0.7578 (0.6334 to 0.8450)	
18 Months	0.7003 (0.5803 to 0.7920)	0.8217 (0.7099 to 0.8935)	0.8778 (0.7604 to 0.9399)	0.7578 (0.6334 to 0.8450)	
20 Months	0.7003 (0.5803 to 0.7920)	0.8217 (0.7099 to 0.8935)	0.8778 (0.7604 to 0.9399)	0.7578 (0.6334 to 0.8450)	
22 Months	0.7003 (0.5803 to 0.7920)	0.8217 (0.7099 to 0.8935)	0.8778 (0.7604 to 0.9399)	0.7578 (0.6334 to 0.8450)	
24 Months	0.6762 (0.5500 to 0.7741)	0.8217 (0.7099 to 0.8935)	0.8778 (0.7604 to 0.9399)	0.7578 (0.6334 to 0.8450)	
26 Months	0.6762 (0.5500 to 0.7741)	0.7943 (0.6694 to 0.8762)	0.8778 (0.7604 to 0.9399)	0.7578 (0.6334 to 0.8450)	
Number of patients at risk[c]					
2 Months	76	72	50	62	
4 Months	67	68	47	56	
6 Months	55	60	40	48	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.1 Treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	50	55	35	48	
10 Months	48	51	34	44	
12 Months	42	48	31	42	
14 Months	40	46	28	42	
16 Months	35	43	26	35	
18 Months	31	40	23	33	
20 Months	30	40	20	29	
22 Months	29	33	19	29	
24 Months	27	30	19	29	
26 Months	25	26	18	27	
Skin and subcutaneous tissue disorders (days)					
Number (%) of events	27 (30.7)	22 (27.2)	10 (16.4)	25 (35.2)	0.0400
Number (%) of patients censored	61 (69.3)	59 (72.8)	51 (83.6)	46 (64.8)	
Kaplan-Meier estimates of event in months					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_auto_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.1 Treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[d]**
25% quantile (95% CI)	3.6140 (0.4600 to NC)	10.2177 (4.5996 to NC)	NC (5.1910 to NC)	6.3409 (0.9528 to 22.5380)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.5380 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5979		0.0310	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.8576 (0.4837 to 1.5205)		2.2060 (1.0554 to 4.6111)	
P-value	-	0.5991		0.0354	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.4533 (0.2169 to 0.9475)		
Events probability (95% CI)[c]					
2 Months	0.7839 (0.6824 to 0.8563)	0.8633 (0.7668 to 0.9219)	0.9503 (0.8537 to 0.9837)	0.8310 (0.7216 to 0.9003)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.1 Treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	0.7477 (0.6425 to 0.8261)	0.8505 (0.7516 to 0.9122)	0.9130 (0.8030 to 0.9629)	0.7588 (0.6409 to 0.8426)	
6 Months	0.7189 (0.6097 to 0.8025)	0.8367 (0.7353 to 0.9018)	0.8699 (0.7446 to 0.9363)	0.7588 (0.6409 to 0.8426)	
8 Months	0.7040 (0.5928 to 0.7901)	0.8057 (0.6976 to 0.8785)	0.8241 (0.6866 to 0.9053)	0.7416 (0.6211 to 0.8289)	
10 Months	0.7040 (0.5928 to 0.7901)	0.7542 (0.6360 to 0.8388)	0.7975 (0.6525 to 0.8871)	0.7062 (0.5811 to 0.8002)	
12 Months	0.7040 (0.5928 to 0.7901)	0.7363 (0.6151 to 0.8246)	0.7975 (0.6525 to 0.8871)	0.6876 (0.5602 to 0.7850)	
14 Months	0.6859 (0.5715 to 0.7757)	0.7174 (0.5932 to 0.8096)	0.7975 (0.6525 to 0.8871)	0.6876 (0.5602 to 0.7850)	
16 Months	0.6859 (0.5715 to 0.7757)	0.7174 (0.5932 to 0.8096)	0.7975 (0.6525 to 0.8871)	0.6483 (0.5165 to 0.7525)	
18 Months	0.6859 (0.5715 to 0.7757)	0.6957 (0.5672 to 0.7928)	0.7975 (0.6525 to 0.8871)	0.6483 (0.5165 to 0.7525)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.1 Treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[d]**
20 Months	0.6859 (0.5715 to 0.7757)	0.6957 (0.5672 to 0.7928)	0.7975 (0.6525 to 0.8871)	0.6483 (0.5165 to 0.7525)	
22 Months	0.6859 (0.5715 to 0.7757)	0.6957 (0.5672 to 0.7928)	0.7975 (0.6525 to 0.8871)	0.6483 (0.5165 to 0.7525)	
24 Months	0.6859 (0.5715 to 0.7757)	0.6957 (0.5672 to 0.7928)	0.7975 (0.6525 to 0.8871)	0.6223 (0.4857 to 0.7324)	
26 Months	0.6859 (0.5715 to 0.7757)	0.6957 (0.5672 to 0.7928)	0.7975 (0.6525 to 0.8871)	0.6223 (0.4857 to 0.7324)	
Number of patients at risk[c]					
2 Months	67	68	53	58	
4 Months	60	64	48	50	
6 Months	48	57	39	44	
8 Months	44	50	32	43	
10 Months	42	43	30	38	
12 Months	39	39	27	37	
14 Months	37	37	25	37	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.1 Treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	33	35	23	31	
18 Months	30	32	20	27	
20 Months	29	32	17	25	
22 Months	28	27	16	25	
24 Months	27	24	16	24	
26 Months	25	20	15	23	
Vascular disorders (days)					
Number (%) of events	14 (15.9)	8 (9.9)	6 (9.8)	21 (29.6)	0.0108
Number (%) of patients censored	74 (84.1)	73 (90.1)	55 (90.2)	50 (70.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (6.7023 to NC)	NC (NC to NC)	NC (16.7885 to NC)	11.1376 (3.7454 to 29.4374)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (29.4374 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.1 Treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[d]**
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2880		0.0194	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.6251 (0.2607 to 1.4987)		2.8321 (1.1378 to 7.0493)	
P-value	-	0.2923		0.0253	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.3531 (0.1419 to 0.8789)		
Events probability (95% CI)[c]					
2 Months	0.9430 (0.8686 to 0.9759)	1.0000 (1.0000 to 1.0000)	0.9825 (0.8819 to 0.9975)	0.8871 (0.7869 to 0.9419)	
4 Months	0.9198 (0.8390 to 0.9609)	0.9489 (0.8694 to 0.9805)	0.9447 (0.8380 to 0.9818)	0.8276 (0.7162 to 0.8983)	
6 Months	0.8936 (0.8051 to 0.9433)	0.9355 (0.8519 to 0.9726)	0.9057 (0.7879 to 0.9597)	0.8123 (0.6984 to 0.8865)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.1 Treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	0.8496 (0.7490 to 0.9122)	0.9355 (0.8519 to 0.9726)	0.9057 (0.7879 to 0.9597)	0.7950 (0.6778 to 0.8734)	
10 Months	0.8496 (0.7490 to 0.9122)	0.9196 (0.8292 to 0.9632)	0.9057 (0.7879 to 0.9597)	0.7950 (0.6778 to 0.8734)	
12 Months	0.8326 (0.7272 to 0.9001)	0.9196 (0.8292 to 0.9632)	0.9057 (0.7879 to 0.9597)	0.7382 (0.6107 to 0.8296)	
14 Months	0.8326 (0.7272 to 0.9001)	0.8825 (0.7760 to 0.9402)	0.9057 (0.7879 to 0.9597)	0.7382 (0.6107 to 0.8296)	
16 Months	0.8326 (0.7272 to 0.9001)	0.8825 (0.7760 to 0.9402)	0.9057 (0.7879 to 0.9597)	0.7165 (0.5849 to 0.8128)	
18 Months	0.8133 (0.7017 to 0.8864)	0.8825 (0.7760 to 0.9402)	0.8680 (0.7177 to 0.9413)	0.7165 (0.5849 to 0.8128)	
20 Months	0.8133 (0.7017 to 0.8864)	0.8825 (0.7760 to 0.9402)	0.8680 (0.7177 to 0.9413)	0.6900 (0.5518 to 0.7932)	
22 Months	0.8133 (0.7017 to 0.8864)	0.8825 (0.7760 to 0.9402)	0.8680 (0.7177 to 0.9413)	0.6900 (0.5518 to 0.7932)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.1 Treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[d]**
24 Months	0.8133 (0.7017 to 0.8864)	0.8825 (0.7760 to 0.9402)	0.8680 (0.7177 to 0.9413)	0.6900 (0.5518 to 0.7932)	
26 Months	0.8133 (0.7017 to 0.8864)	0.8825 (0.7760 to 0.9402)	0.8680 (0.7177 to 0.9413)	0.6571 (0.5091 to 0.7701)	
Number of patients at risk[c]					
2 Months	81	79	55	62	
4 Months	76	71	50	54	
6 Months	64	64	42	47	
8 Months	56	59	36	46	
10 Months	54	54	34	43	
12 Months	49	50	31	39	
14 Months	47	47	28	39	
16 Months	44	46	26	32	
18 Months	39	44	22	28	
20 Months	38	44	19	23	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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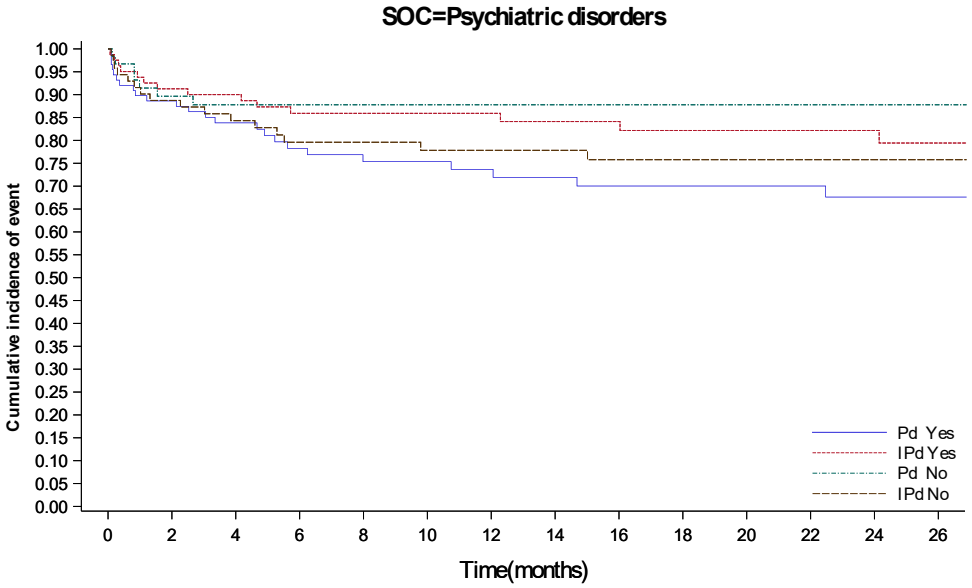
16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.1 Treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[d]**
22 Months	37	37	18	23	
24 Months	36	34	18	23	
26 Months	34	30	17	20	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_auto_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

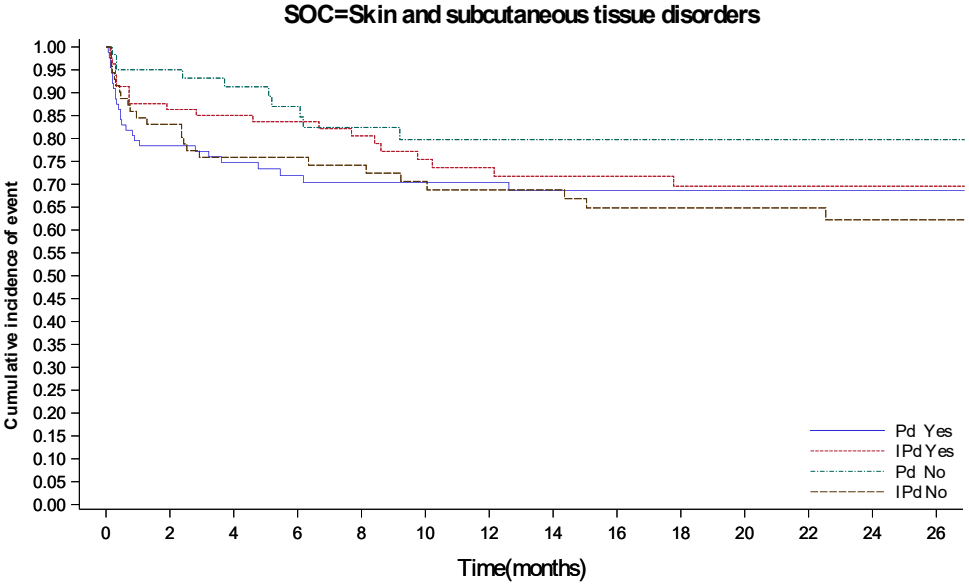


Number at Risk

Pd Yes	88	76	67	55	50	48	42	40	35	31	30	29	27	25
IPd Yes	81	72	68	60	55	51	48	46	43	40	40	33	30	26
Pd No	61	50	47	40	35	34	31	28	26	23	20	19	19	18
IPd No	71	62	56	48	48	44	42	42	35	33	29	29	29	27

SOC are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_auto_s_f_x.rtf (17NOV2020 14:45)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

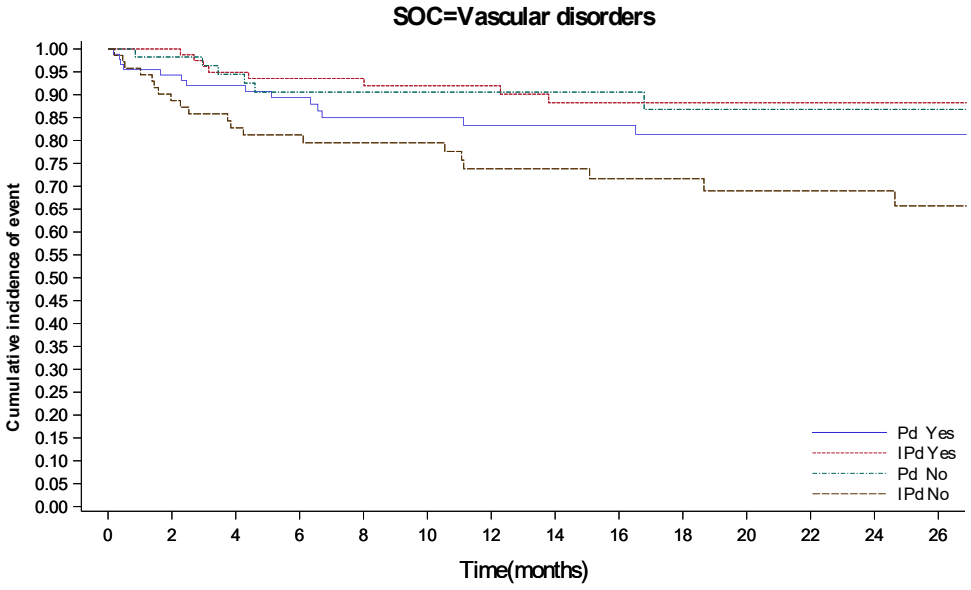


Number at Risk

Pd Yes	88	67	60	48	44	42	39	37	33	30	29	28	27	25
IPd Yes	81	68	64	57	50	43	39	37	35	32	32	27	24	20
Pd No	61	53	48	39	32	30	27	25	23	20	17	16	16	15
IPd No	71	58	50	44	43	38	37	37	31	27	25	25	24	23

SOC are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_auto_s_f_x.rtf (17NOV2020 14:45)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population



Number at Risk

Pd Yes	88	81	76	64	56	54	49	47	44	39	38	37	36	34
IPd Yes	81	79	71	64	59	54	50	47	46	44	44	37	34	30
Pd No	61	55	50	42	36	34	31	28	26	22	19	18	18	17
IPd No	71	62	54	47	46	43	39	39	32	28	23	23	23	20

SOC are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_auto_s_f_x.rtf (17NOV2020 14:45)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.3 Treatment emergent not severe adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[d]**
Musculoskeletal and connective tissue disorders (days)					
Number (%) of events	50 (56.8)	45 (55.6)	23 (37.7)	43 (60.6)	0.0490
Number (%) of patients censored	38 (43.2)	36 (44.4)	38 (62.3)	28 (39.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.9713 (0.6899 to 3.0554)	2.1684 (1.1170 to 3.8439)	4.0739 (1.0513 to 6.5051)	1.8070 (1.0185 to 3.7125)	
Median (95% CI)	6.2094 (3.9097 to 21.7823)	10.1848 (7.0308 to 26.6448)	NC (6.5051 to NC)	6.8008 (4.2382 to 18.8583)	
75% quantile (95% CI)	NC (27.5647 to NC)	NC (26.6448 to NC)	NC (NC to NC)	NC (18.8583 to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5881		0.0813	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12soc_auto_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.3 Treatment emergent not severe adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.8917 (0.5891 to 1.3499)		1.5774 (0.9408 to 2.6448)	
P-value	-	0.5881		0.0839	
Events probability (95% CI)[c]					
2 Months	0.7487 (0.6439 to 0.8268)	0.8008 (0.6955 to 0.8729)	0.8235 (0.6965 to 0.9010)	0.7462 (0.6279 to 0.8318)	
4 Months	0.6035 (0.4913 to 0.6984)	0.6468 (0.5307 to 0.7410)	0.7655 (0.6300 to 0.8569)	0.6291 (0.5047 to 0.7304)	
6 Months	0.5193 (0.4052 to 0.6217)	0.6327 (0.5160 to 0.7286)	0.6570 (0.5094 to 0.7699)	0.5830 (0.4578 to 0.6889)	
8 Months	0.4725 (0.3579 to 0.5786)	0.5591 (0.4401 to 0.6625)	0.6327 (0.4830 to 0.7498)	0.4664 (0.3424 to 0.5811)	
10 Months	0.4375 (0.3227 to 0.5465)	0.5150 (0.3962 to 0.6215)	0.6327 (0.4830 to 0.7498)	0.4317 (0.3093 to 0.5481)	
12 Months	0.4185 (0.3035 to 0.5291)	0.4696 (0.3518 to 0.5787)	0.5661 (0.4056 to 0.6985)	0.4137 (0.2923 to 0.5309)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.3 Treatment emergent not severe adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.3985 (0.2835 to 0.5109)	0.4387 (0.3223 to 0.5492)	0.5661 (0.4056 to 0.6985)	0.4137 (0.2923 to 0.5309)	
16 Months	0.3985 (0.2835 to 0.5109)	0.4219 (0.3060 to 0.5331)	0.5284 (0.3630 to 0.6692)	0.3920 (0.2709 to 0.5109)	
18 Months	0.3985 (0.2835 to 0.5109)	0.4219 (0.3060 to 0.5331)	0.5284 (0.3630 to 0.6692)	0.3920 (0.2709 to 0.5109)	
20 Months	0.3985 (0.2835 to 0.5109)	0.4219 (0.3060 to 0.5331)	0.5284 (0.3630 to 0.6692)	0.3675 (0.2464 to 0.4889)	
22 Months	0.3751 (0.2594 to 0.4904)	0.4219 (0.3060 to 0.5331)	0.5284 (0.3630 to 0.6692)	0.3675 (0.2464 to 0.4889)	
24 Months	0.3751 (0.2594 to 0.4904)	0.4219 (0.3060 to 0.5331)	0.5284 (0.3630 to 0.6692)	0.3675 (0.2464 to 0.4889)	
26 Months	0.3751 (0.2594 to 0.4904)	0.4219 (0.3060 to 0.5331)	0.5284 (0.3630 to 0.6692)	0.3675 (0.2464 to 0.4889)	
Number of patients at risk[c]					
2 Months	64	63	45	52	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.3 Treatment emergent not severe adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Pd (N=88)	**IPd (N=81)**	**Pd (N=61)**	**IPd (N=71)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	48	49	39	42	
6 Months	34	44	28	35	
8 Months	28	38	22	28	
10 Months	25	35	21	24	
12 Months	21	31	17	22	
14 Months	18	28	15	22	
16 Months	18	25	14	18	
18 Months	17	23	14	16	
20 Months	17	23	11	15	
22 Months	16	19	11	15	
24 Months	15	19	11	15	
26 Months	14	16	11	15	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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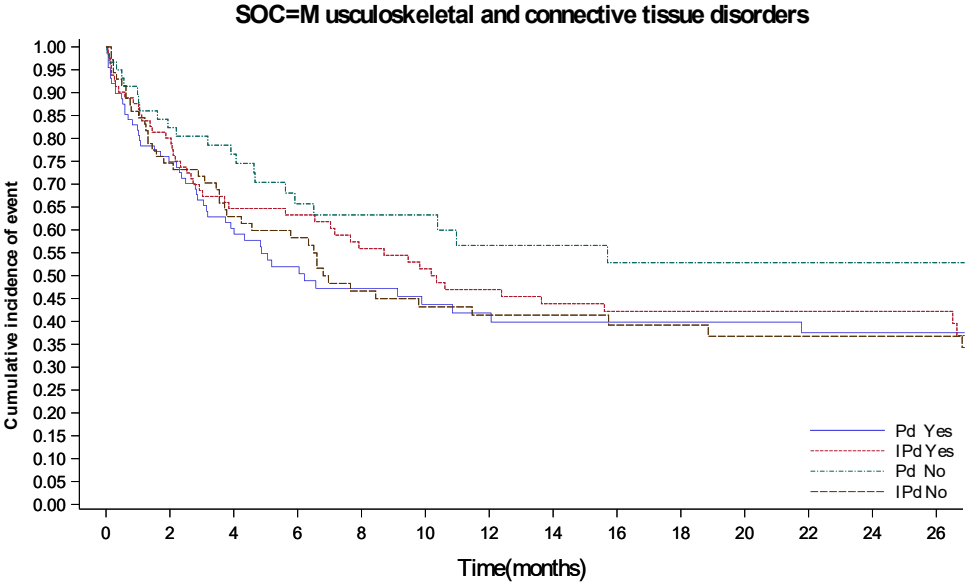
16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by previous autologous stem-cell
16.2.7.1.51.4 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population



Number at Risk

Pd Yes	88	64	48	34	28	25	21	18	18	17	17	16	15	14
IPd Yes	81	63	49	44	38	35	31	28	25	23	23	19	19	16
Pd No	60	45	39	28	22	21	17	15	14	14	11	11	11	11
IPd No	71	52	42	35	28	24	22	22	18	16	15	15	15	15

SOC are presented if at least 10 events in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by previous allogenic transplantation
16.2.7.1.52.1 Treatment emergent adverse event per PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[d]**
Upper respiratory tract infection (days)					
Number (%) of events	1 (50.0)	2 (100.0)	28 (19.0)	50 (33.3)	0.0071
Number (%) of patients censored	1 (50.0)	0 (0.0)	119 (81.0)	100 (66.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.3285 (0.3285 to NC)	0.1643 (0.1643 to 0.3943)	NC (8.9363 to NC)	7.9179 (5.3881 to 13.3060)	
Median (95% CI)	NC (0.3285 to NC)	0.2793 (0.1643 to 0.3943)	NC (NC to NC)	NC (19.0554 to NC)	
75% quantile (95% CI)	NC (0.3285 to NC)	0.3943 (0.1643 to 0.3943)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4328		0.0163	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by previous allogenic transplantation
16.2.7.1.52.1 Treatment emergent adverse event per PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.5614 (0.2253 to 29.1195)		1.7517 (1.1020 to 2.7846)	
P-value	-	0.4482		0.0178	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.5709 (0.3591 to 0.9075)		
Events probability (95% CI)[c]					
2 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.9088 (0.8481 to 0.9460)	0.9260 (0.8703 to 0.9583)	
4 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.8796 (0.8134 to 0.9234)	0.8559 (0.7875 to 0.9036)	
6 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.8629 (0.7932 to 0.9104)	0.7862 (0.7082 to 0.8456)	
8 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.8347 (0.7588 to 0.8884)	0.7438 (0.6608 to 0.8094)	
10 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.8147 (0.7348 to 0.8726)	0.7260 (0.6412 to 0.7940)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by previous allogenic transplantation
16.2.7.1.52.1 Treatment emergent adverse event per PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.8147 (0.7348 to 0.8726)	0.7064 (0.6192 to 0.7772)	
14 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.7922 (0.7075 to 0.8548)	0.6671 (0.5763 to 0.7429)	
16 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.7922 (0.7075 to 0.8548)	0.6456 (0.5527 to 0.7241)	
18 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.7922 (0.7075 to 0.8548)	0.6004 (0.5038 to 0.6842)	
20 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.7778 (0.6890 to 0.8441)	0.5879 (0.4901 to 0.6732)	
22 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.7778 (0.6890 to 0.8441)	0.5879 (0.4901 to 0.6732)	
24 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.7616 (0.6679 to 0.8321)	0.5879 (0.4901 to 0.6732)	
26 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.7616 (0.6679 to 0.8321)	0.5879 (0.4901 to 0.6732)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by previous allogenic transplantation
16.2.7.1.52.1 Treatment emergent adverse event per PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[d]**
Number of patients at risk[c]					
2 Months	1	0	127	136	
4 Months	1	0	115	119	
6 Months	1	0	97	97	
8 Months	1	0	86	87	
10 Months	1	0	81	79	
12 Months	1	0	75	72	
14 Months	1	0	69	68	
16 Months	1	0	63	60	
18 Months	1	0	55	49	
20 Months	1	0	50	46	
22 Months	1	0	48	40	
24 Months	1	0	46	40	
26 Months	1	0	44	36	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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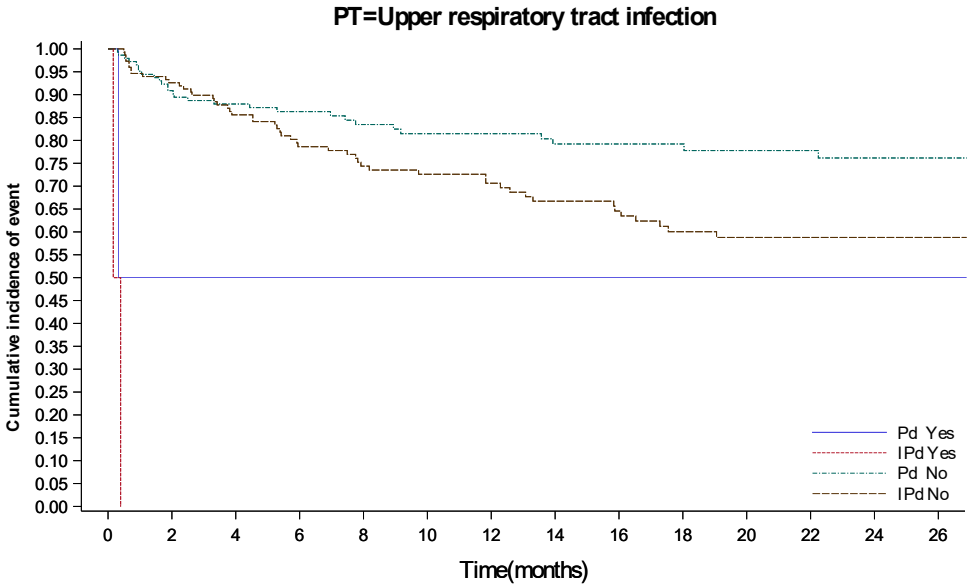
16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by previous allogenic transplantation
16.2.7.1.52.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to previous allogenic transplantation - Safety population



Number at Risk

Pd Yes	2	1	1	1	1	1	1	1	1	1	1	1	1	1
IPd Yes	2	0												
Pd No	147	127	115	97	86	81	75	69	63	55	50	48	46	44
IPd No	150	136	119	97	87	79	72	68	60	49	46	40	40	36

PT are presented if at least 10 events in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by previous allogenic transplantation
16.2.7.1.52.3 Treatment emergent not severe adverse event per PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[d]**
Upper respiratory tract infection (days)					
Number (%) of events	1 (50.0)	2 (100.0)	27 (18.4)	48 (32.0)	0.0050
Number (%) of patients censored	1 (50.0)	0 (0.0)	120 (81.6)	102 (68.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.3285 (0.3285 to NC)	0.1643 (0.1643 to 0.3943)	NC (9.1663 to NC)	8.1807 (5.4209 to 15.8357)	
Median (95% CI)	NC (0.3285 to NC)	0.2793 (0.1643 to 0.3943)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (0.3285 to NC)	0.3943 (0.1643 to 0.3943)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4328		0.0176	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by previous allogenic transplantation
16.2.7.1.52.3 Treatment emergent not severe adverse event per PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.5614 (0.2253 to 29.1195)		1.7595 (1.0969 to 2.8224)	
P-value	-	0.4482		0.0191	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.5684 (0.3543 to 0.9117)		
Events probability (95% CI)[c]					
2 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.9156 (0.8562 to 0.9512)	0.9260 (0.8703 to 0.9583)	
4 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.8864 (0.8213 to 0.9289)	0.8696 (0.8030 to 0.9148)	
6 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.8698 (0.8010 to 0.9160)	0.7994 (0.7223 to 0.8572)	
8 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.8416 (0.7665 to 0.8942)	0.7567 (0.6743 to 0.8210)	
10 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.8217 (0.7425 to 0.8785)	0.7389 (0.6544 to 0.8057)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_alltpfl_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by previous allogenic transplantation
16.2.7.1.52.3 Treatment emergent not severe adverse event per PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.8217 (0.7425 to 0.8785)	0.7192 (0.6323 to 0.7889)	
14 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.7994 (0.7153 to 0.8610)	0.6798 (0.5890 to 0.7547)	
16 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.7994 (0.7153 to 0.8610)	0.6578 (0.5647 to 0.7357)	
18 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.7994 (0.7153 to 0.8610)	0.6117 (0.5145 to 0.6953)	
20 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.7851 (0.6969 to 0.8503)	0.5990 (0.5005 to 0.6842)	
22 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.7851 (0.6969 to 0.8503)	0.5990 (0.5005 to 0.6842)	
24 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.7691 (0.6759 to 0.8386)	0.5990 (0.5005 to 0.6842)	
26 Months	0.5000 (0.0060 to 0.9104)	0.5000 (0.0060 to 0.9104)	0.7691 (0.6759 to 0.8386)	0.5990 (0.5005 to 0.6842)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_alltpfl_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by previous allogenic transplantation
16.2.7.1.52.3 Treatment emergent not severe adverse event per PT by treatment group according to previous allogenic transplantation - Safety population

	Yes		No		
	Pd (N=2)	**IPd (N=2)**	**Pd (N=147)**	**IPd (N=150)**	**p-value of treatment-by-sub group interaction[d]**
Number of patients at risk[c]					
2 Months	1	0	128	136	
4 Months	1	0	116	120	
6 Months	1	0	98	98	
8 Months	1	0	87	88	
10 Months	1	0	82	80	
12 Months	1	0	76	73	
14 Months	1	0	70	69	
16 Months	1	0	64	60	
18 Months	1	0	56	49	
20 Months	1	0	51	46	
22 Months	1	0	49	40	
24 Months	1	0	47	40	
26 Months	1	0	45	36	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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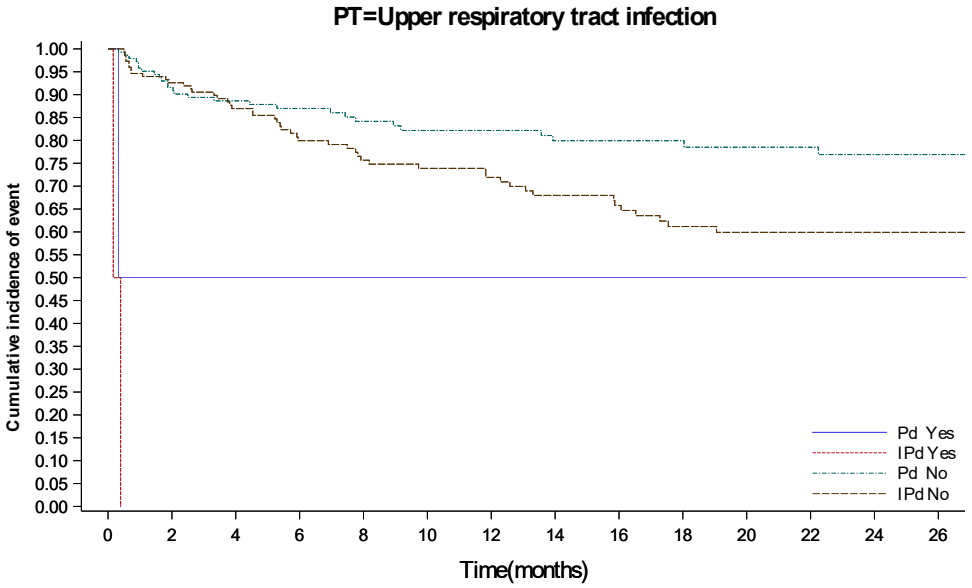
16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by previous allogenic transplantation
16.2.7.1.52.4 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per PT by treatment group according to previous allogenic transplantation - Safety population



Number at Risk

Pd Yes	2	1	1	1	1	1	1	1	1	1	1	1	1	1
IPd Yes	2	0												
Pd No	147	128	116	98	87	82	76	70	64	56	51	49	47	45
IPd No	150	136	120	98	88	80	73	69	60	49	46	40	40	36

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_alltpfl_s_f_x.rtf (17NOV2020 14:46)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.1 Treatment emergent adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Infections and infestations (days)					
Number (%) of events	75 (77.3)	82 (81.2)	25 (49.0)	43 (86.0)	0.0053
Number (%) of patients censored	22 (22.7)	19 (18.8)	26 (51.0)	7 (14.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	0.9528 (0.5914 to 1.4456)	0.6571 (0.4600 to 0.8214)	1.8070 (0.9528 to 2.2669)	0.7228 (0.4928 to 1.2813)	
Median (95% CI)	1.9713 (1.5770 to 3.3183)	2.6283 (1.3142 to 3.3183)	7.3265 (2.0698 to NC)	2.0041 (1.1499 to 3.2526)	
75% quantile (95% CI)	9.3306 (5.3224 to NC)	6.3409 (4.5339 to 14.3901)	NC (NC to NC)	3.9097 (2.6283 to 11.8275)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6332		0.0008	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_type_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.1 Treatment emergent adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0801 (0.7869 to 1.4825)		2.3602 (1.4123 to 3.9442)	
P-value	-	0.6334		0.0010	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.4237 (0.2535 to 0.7081)		
Events probability (95% CI)[c]					
2 Months	0.4973 (0.3934 to 0.5926)	0.5461 (0.4431 to 0.6379)	0.6758 (0.5262 to 0.7873)	0.5185 (0.3725 to 0.6461)	
4 Months	0.3676 (0.2713 to 0.4640)	0.3838 (0.2885 to 0.4782)	0.5442 (0.3932 to 0.6726)	0.2416 (0.1318 to 0.3694)	
6 Months	0.3327 (0.2393 to 0.4287)	0.2797 (0.1948 to 0.3707)	0.5442 (0.3932 to 0.6726)	0.1922 (0.0934 to 0.3174)	
8 Months	0.2834 (0.1947 to 0.3784)	0.2259 (0.1485 to 0.3133)	0.4883 (0.3360 to 0.6243)	0.1647 (0.0731 to 0.2884)	
10 Months	0.2447 (0.1607 to 0.3383)	0.2021 (0.1282 to 0.2880)	0.4883 (0.3360 to 0.6243)	0.1647 (0.0731 to 0.2884)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.1 Treatment emergent adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	0.2311 (0.1489 to 0.3242)	0.2021 (0.1282 to 0.2880)	0.4883 (0.3360 to 0.6243)	0.1098 (0.0374 to 0.2265)	
14 Months	0.2175 (0.1372 to 0.3099)	0.1769 (0.1070 to 0.2611)	0.4883 (0.3360 to 0.6243)	0.1098 (0.0374 to 0.2265)	
16 Months	0.2175 (0.1372 to 0.3099)	0.1642 (0.0967 to 0.2473)	0.4883 (0.3360 to 0.6243)	0.1098 (0.0374 to 0.2265)	
18 Months	0.2020 (0.1237 to 0.2941)	0.1642 (0.0967 to 0.2473)	0.4883 (0.3360 to 0.6243)	0.0824 (0.0225 to 0.1933)	
20 Months	0.2020 (0.1237 to 0.2941)	0.1642 (0.0967 to 0.2473)	0.4439 (0.2848 to 0.5915)	0.0824 (0.0225 to 0.1933)	
22 Months	0.2020 (0.1237 to 0.2941)	0.1642 (0.0967 to 0.2473)	0.4439 (0.2848 to 0.5915)	0.0824 (0.0225 to 0.1933)	
24 Months	0.2020 (0.1237 to 0.2941)	0.1642 (0.0967 to 0.2473)	0.4439 (0.2848 to 0.5915)	0.0824 (0.0225 to 0.1933)	
26 Months	0.2020 (0.1237 to 0.2941)	0.1642 (0.0967 to 0.2473)	0.4439 (0.2848 to 0.5915)	0.0824 (0.0225 to 0.1933)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.1 Treatment emergent adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Number of patients at risk[c]					
2 Months	47	54	32	25	
4 Months	34	37	23	11	
6 Months	28	26	21	7	
8 Months	22	21	17	6	
10 Months	19	17	16	6	
12 Months	17	16	15	4	
14 Months	14	14	15	4	
16 Months	14	12	12	4	
18 Months	13	11	11	2	
20 Months	12	11	9	1	
22 Months	12	10	7	1	
24 Months	12	10	6	1	
26 Months	12	8	4	1	
Injury, poisoning and procedural complications (days)					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.1 Treatment emergent adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	14 (14.4)	44 (43.6)	4 (7.8)	31 (62.0)	0.0325
Number (%) of patients censored	83 (85.6)	57 (56.4)	47 (92.2)	19 (38.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (9.1006 to NC)	0.1643 (0.0986 to 1.5113)	NC (NC to NC)	0.0657 (0.0657 to 0.1314)	
Median (95% CI)	NC (NC to NC)	32.8214 (11.4661 to NC)	NC (NC to NC)	0.1971 (0.1314 to 18.0370)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (18.0370 to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	<.0001		<.0001	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	3.8043 (2.0811 to 6.9543)		14.4444 (4.3733 to 47.7078)	
P-value	-	<.0001		<.0001	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.1 Treatment emergent adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.2629 (0.1438 to 0.4805)		0.0692 (0.0210 to 0.2287)		
Events probability (95% CI)[c]					
2 Months	0.9471 (0.8775 to 0.9776)	0.6629 (0.5617 to 0.7460)	0.9792 (0.8612 to 0.9970)	0.4800 (0.3371 to 0.6093)	
4 Months	0.9254 (0.8499 to 0.9638)	0.6526 (0.5510 to 0.7367)	0.9564 (0.8364 to 0.9889)	0.4600 (0.3188 to 0.5901)	
6 Months	0.9142 (0.8356 to 0.9561)	0.6413 (0.5391 to 0.7266)	0.9564 (0.8364 to 0.9889)	0.4391 (0.2997 to 0.5700)	
8 Months	0.8730 (0.7812 to 0.9280)	0.6065 (0.5026 to 0.6953)	0.9325 (0.8046 to 0.9778)	0.4147 (0.2766 to 0.5473)	
10 Months	0.8434 (0.7436 to 0.9067)	0.6065 (0.5026 to 0.6953)	0.9325 (0.8046 to 0.9778)	0.3903 (0.2540 to 0.5242)	
12 Months	0.8434 (0.7436 to 0.9067)	0.5918 (0.4863 to 0.6826)	0.9325 (0.8046 to 0.9778)	0.3903 (0.2540 to 0.5242)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.1 Treatment emergent adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.8434 (0.7436 to 0.9067)	0.5918 (0.4863 to 0.6826)	0.9325 (0.8046 to 0.9778)	0.3903 (0.2540 to 0.5242)	
16 Months	0.8434 (0.7436 to 0.9067)	0.5598 (0.4510 to 0.6552)	0.9325 (0.8046 to 0.9778)	0.3903 (0.2540 to 0.5242)	
18 Months	0.8434 (0.7436 to 0.9067)	0.5598 (0.4510 to 0.6552)	0.9325 (0.8046 to 0.9778)	0.3903 (0.2540 to 0.5242)	
20 Months	0.8434 (0.7436 to 0.9067)	0.5598 (0.4510 to 0.6552)	0.9325 (0.8046 to 0.9778)	0.3513 (0.2127 to 0.4930)	
22 Months	0.8434 (0.7436 to 0.9067)	0.5598 (0.4510 to 0.6552)	0.9325 (0.8046 to 0.9778)	0.3513 (0.2127 to 0.4930)	
24 Months	0.8434 (0.7436 to 0.9067)	0.5598 (0.4510 to 0.6552)	0.9325 (0.8046 to 0.9778)	0.3513 (0.2127 to 0.4930)	
26 Months	0.8434 (0.7436 to 0.9067)	0.5598 (0.4510 to 0.6552)	0.9325 (0.8046 to 0.9778)	0.3513 (0.2127 to 0.4930)	
Number of patients at risk[c]					
2 Months	88	66	46	24	

SOC are presented if at least 10 events in a arm
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[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.1 Treatment emergent adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	84	62	42	22	
6 Months	70	56	40	18	
8 Months	60	49	35	17	
10 Months	56	44	34	16	
12 Months	49	40	32	14	
14 Months	43	39	32	14	
16 Months	41	34	29	11	
18 Months	36	32	26	10	
20 Months	35	30	23	8	
22 Months	35	26	21	8	
24 Months	35	25	20	8	
26 Months	34	22	18	8	
Psychiatric disorders (days)					
Number (%) of events	27 (27.8)	20 (19.8)	5 (9.8)	11 (22.0)	0.0313
Number (%) of patients censored	70 (72.2)	81 (80.2)	46 (90.2)	39 (78.0)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.1 Treatment emergent adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	6.2423 (2.6612 to NC)	35.0226 (12.2875 to NC)	NC (14.6858 to NC)	NC (1.5441 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0724		0.2445	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.5907 (0.3304 to 1.0558)		1.9009 (0.6329 to 5.7093)	
P-value	-	0.0756		0.2523	
Events probability (95% CI)[c]					
2 Months	0.8641 (0.7774 to 0.9188)	0.9203 (0.8469 to 0.9593)	0.9403 (0.8262 to 0.9804)	0.8595 (0.7278 to 0.9304)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.1 Treatment emergent adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	0.8091 (0.7141 to 0.8753)	0.8899 (0.8100 to 0.9375)	0.9403 (0.8262 to 0.9804)	0.8375 (0.7009 to 0.9153)	
6 Months	0.7565 (0.6529 to 0.8331)	0.8460 (0.7573 to 0.9043)	0.9403 (0.8262 to 0.9804)	0.7922 (0.6473 to 0.8827)	
8 Months	0.7276 (0.6196 to 0.8096)	0.8460 (0.7573 to 0.9043)	0.9403 (0.8262 to 0.9804)	0.7922 (0.6473 to 0.8827)	
10 Months	0.7276 (0.6196 to 0.8096)	0.8460 (0.7573 to 0.9043)	0.9403 (0.8262 to 0.9804)	0.7674 (0.6180 to 0.8645)	
12 Months	0.7099 (0.5982 to 0.7957)	0.8460 (0.7573 to 0.9043)	0.9403 (0.8262 to 0.9804)	0.7674 (0.6180 to 0.8645)	
14 Months	0.7099 (0.5982 to 0.7957)	0.8321 (0.7397 to 0.8940)	0.9118 (0.7784 to 0.9666)	0.7674 (0.6180 to 0.8645)	
16 Months	0.7099 (0.5982 to 0.7957)	0.8172 (0.7209 to 0.8830)	0.8804 (0.7304 to 0.9497)	0.7674 (0.6180 to 0.8645)	
18 Months	0.7099 (0.5982 to 0.7957)	0.8018 (0.7016 to 0.8714)	0.8804 (0.7304 to 0.9497)	0.7674 (0.6180 to 0.8645)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.1 Treatment emergent adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
20 Months	0.7099 (0.5982 to 0.7957)	0.8018 (0.7016 to 0.8714)	0.8804 (0.7304 to 0.9497)	0.7674 (0.6180 to 0.8645)	
22 Months	0.7099 (0.5982 to 0.7957)	0.8018 (0.7016 to 0.8714)	0.8804 (0.7304 to 0.9497)	0.7674 (0.6180 to 0.8645)	
24 Months	0.6845 (0.5643 to 0.7779)	0.8018 (0.7016 to 0.8714)	0.8804 (0.7304 to 0.9497)	0.7674 (0.6180 to 0.8645)	
26 Months	0.6845 (0.5643 to 0.7779)	0.7818 (0.6745 to 0.8574)	0.8804 (0.7304 to 0.9497)	0.7674 (0.6180 to 0.8645)	
Number of patients at risk[c]					
2 Months	80	92	45	41	
4 Months	72	85	41	38	
6 Months	55	74	39	33	
8 Months	48	69	36	33	
10 Months	46	63	35	31	
12 Months	39	61	33	28	
14 Months	35	59	32	28	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.1 Treatment emergent adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	33	53	27	24	
18 Months	29	50	24	22	
20 Months	28	48	21	20	
22 Months	28	42	19	19	
24 Months	27	40	18	18	
26 Months	26	35	16	17	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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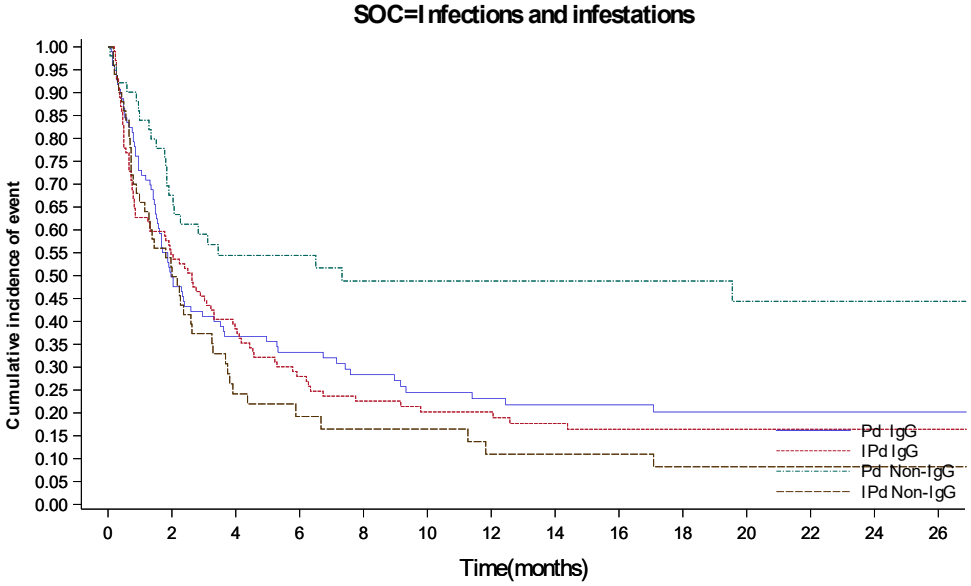
16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per SOC by treatment group according to MM type - Safety population



Number at Risk

Pd IgG	97	47	34	28	22	19	17	14	14	13	12	12	12	12
IPd IgG	100	54	37	26	21	17	16	14	12	11	11	10	10	8
Pd Non-IgG	51	32	23	21	17	16	15	15	12	11	9	7	6	4
IPd Non-IgG	50	25	11	7	6	6	4	4	4	2	1	1	1	1

SOC are presented if at least 10 events in a arm
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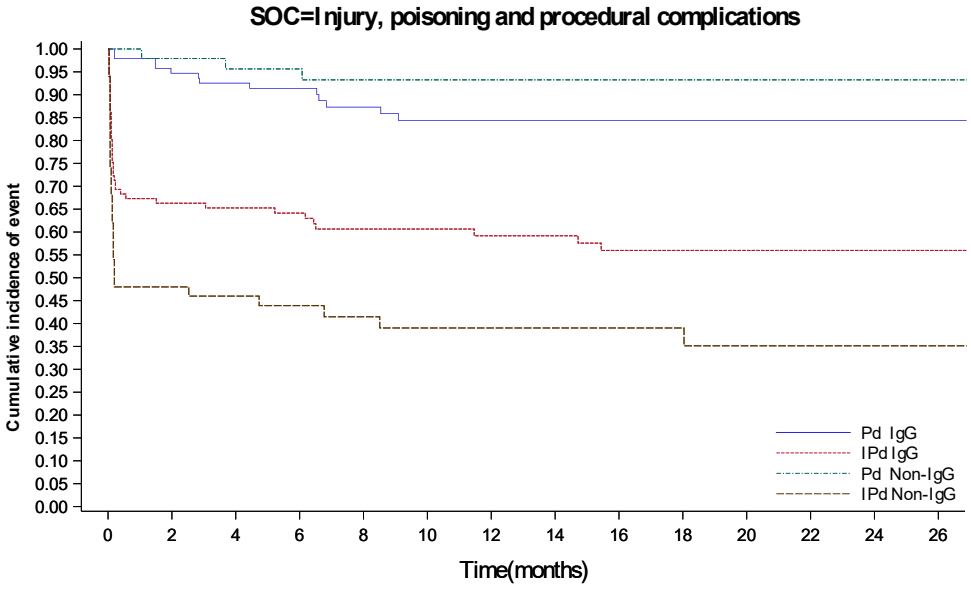
16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per SOC by treatment group according to MM type - Safety population



Number at Risk

Pd IgG	97	88	84	70	60	56	49	43	41	36	35	35	35	34
IPd IgG	101	66	62	56	49	44	40	39	34	32	30	26	25	22
Pd Non-IgG	50	46	42	40	35	34	32	32	29	26	23	21	20	18
IPd Non-IgG	50	24	22	18	17	16	14	14	11	10	8	8	8	8

SOC are presented if at least 10 events in a arm
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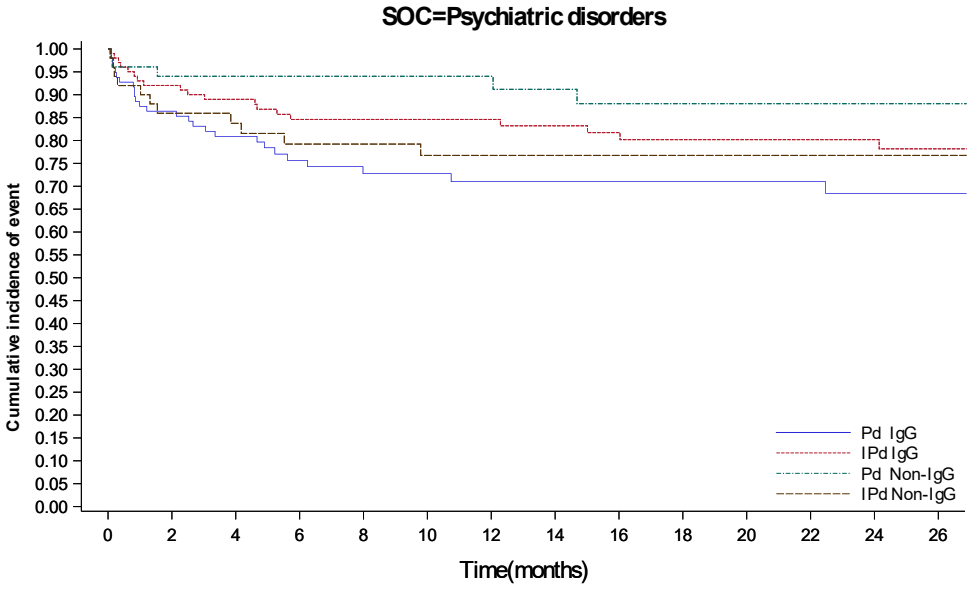
16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per SOC by treatment group according to MM type - Safety population



Number at Risk

Pd IgG	97	80	72	55	48	46	39	35	33	29	28	28	27	26
IPd IgG	101	92	85	74	69	63	61	59	53	50	48	42	40	35
Pd Non-IgG	51	45	41	39	36	35	33	32	27	24	21	19	18	16
IPd Non-IgG	50	41	38	33	33	31	28	28	24	22	20	19	18	17

SOC are presented if at least 10 events in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.3 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Insomnia (days)					
Number (%) of events	13 (13.4)	8 (7.9)	1 (2.0)	7 (14.0)	0.0243
Number (%) of patients censored	84 (86.6)	93 (92.1)	50 (98.0)	43 (86.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (28.6817 to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.8337 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1453		0.1117	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.5244 (0.2168 to 1.2687)		4.9174 (0.5699 to 42.4308)	
P-value	-	0.1522		0.1475	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.3 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]					
2 Months	0.9061 (0.8272 to 0.9500)	0.9601 (0.8972 to 0.9848)	1.0000 (1.0000 to 1.0000)	0.9600 (0.8494 to 0.9898)	
4 Months	0.8950 (0.8136 to 0.9421)	0.9601 (0.8972 to 0.9848)	1.0000 (1.0000 to 1.0000)	0.9377 (0.8187 to 0.9795)	
6 Months	0.8826 (0.7977 to 0.9333)	0.9267 (0.8522 to 0.9644)	1.0000 (1.0000 to 1.0000)	0.9136 (0.7851 to 0.9668)	
8 Months	0.8826 (0.7977 to 0.9333)	0.9267 (0.8522 to 0.9644)	1.0000 (1.0000 to 1.0000)	0.8629 (0.7183 to 0.9364)	
10 Months	0.8826 (0.7977 to 0.9333)	0.9267 (0.8522 to 0.9644)	1.0000 (1.0000 to 1.0000)	0.8367 (0.6859 to 0.9192)	
12 Months	0.8656 (0.7733 to 0.9222)	0.9267 (0.8522 to 0.9644)	1.0000 (1.0000 to 1.0000)	0.8367 (0.6859 to 0.9192)	
14 Months	0.8656 (0.7733 to 0.9222)	0.9127 (0.8319 to 0.9556)	1.0000 (1.0000 to 1.0000)	0.8367 (0.6859 to 0.9192)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.3 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.8656 (0.7733 to 0.9222)	0.9127 (0.8319 to 0.9556)	0.9667 (0.7861 to 0.9952)	0.8367 (0.6859 to 0.9192)	
18 Months	0.8656 (0.7733 to 0.9222)	0.9127 (0.8319 to 0.9556)	0.9667 (0.7861 to 0.9952)	0.8367 (0.6859 to 0.9192)	
20 Months	0.8656 (0.7733 to 0.9222)	0.9127 (0.8319 to 0.9556)	0.9667 (0.7861 to 0.9952)	0.8367 (0.6859 to 0.9192)	
22 Months	0.8656 (0.7733 to 0.9222)	0.9127 (0.8319 to 0.9556)	0.9667 (0.7861 to 0.9952)	0.8367 (0.6859 to 0.9192)	
24 Months	0.8656 (0.7733 to 0.9222)	0.9127 (0.8319 to 0.9556)	0.9667 (0.7861 to 0.9952)	0.8367 (0.6859 to 0.9192)	
26 Months	0.8656 (0.7733 to 0.9222)	0.9127 (0.8319 to 0.9556)	0.9667 (0.7861 to 0.9952)	0.8367 (0.6859 to 0.9192)	
Number of patients at risk[c]					
2 Months	84	96	48	46	
4 Months	80	91	43	42	
6 Months	65	80	41	36	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.3 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	59	75	37	34	
10 Months	57	69	35	32	
12 Months	49	66	33	29	
14 Months	43	64	33	29	
16 Months	40	59	28	25	
18 Months	36	55	25	23	
20 Months	35	53	22	21	
22 Months	35	47	20	20	
24 Months	35	45	19	19	
26 Months	34	40	17	18	
Muscle spasms (days)					
Number (%) of events	13 (13.4)	8 (7.9)	3 (5.9)	8 (16.0)	0.0426
Number (%) of patients censored	84 (86.6)	93 (92.1)	48 (94.1)	42 (84.0)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.3 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
25% quantile (95% CI)	NC (9.7248 to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.1294 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1332		0.1209	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.5144 (0.2127 to 1.2443)		2.7661 (0.7252 to 10.5508)	
P-value	-	0.1402		0.1363	
Events probability (95% CI)[c]					
2 Months	0.9363 (0.8636 to 0.9709)	0.9801 (0.9228 to 0.9950)	0.9796 (0.8638 to 0.9971)	0.9400 (0.8254 to 0.9802)	
4 Months	0.9035 (0.8226 to 0.9486)	0.9493 (0.8825 to 0.9786)	0.9587 (0.8449 to 0.9895)	0.9176 (0.7948 to 0.9683)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.3 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
6 Months	0.8782 (0.7902 to 0.9308)	0.9380 (0.8671 to 0.9717)	0.9587 (0.8449 to 0.9895)	0.9176 (0.7948 to 0.9683)	
8 Months	0.8782 (0.7902 to 0.9308)	0.9262 (0.8510 to 0.9642)	0.9587 (0.8449 to 0.9895)	0.8666 (0.7251 to 0.9383)	
10 Months	0.8462 (0.7475 to 0.9087)	0.9262 (0.8510 to 0.9642)	0.9587 (0.8449 to 0.9895)	0.8404 (0.6918 to 0.9212)	
12 Months	0.8462 (0.7475 to 0.9087)	0.9262 (0.8510 to 0.9642)	0.9587 (0.8449 to 0.9895)	0.8404 (0.6918 to 0.9212)	
14 Months	0.8462 (0.7475 to 0.9087)	0.9119 (0.8304 to 0.9553)	0.9587 (0.8449 to 0.9895)	0.8404 (0.6918 to 0.9212)	
16 Months	0.8462 (0.7475 to 0.9087)	0.9119 (0.8304 to 0.9553)	0.9232 (0.7711 to 0.9758)	0.8404 (0.6918 to 0.9212)	
18 Months	0.8462 (0.7475 to 0.9087)	0.9119 (0.8304 to 0.9553)	0.9232 (0.7711 to 0.9758)	0.8404 (0.6918 to 0.9212)	
20 Months	0.8462 (0.7475 to 0.9087)	0.9119 (0.8304 to 0.9553)	0.9232 (0.7711 to 0.9758)	0.8404 (0.6918 to 0.9212)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.3 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
22 Months	0.8462 (0.7475 to 0.9087)	0.9119 (0.8304 to 0.9553)	0.9232 (0.7711 to 0.9758)	0.8404 (0.6918 to 0.9212)	
24 Months	0.8462 (0.7475 to 0.9087)	0.9119 (0.8304 to 0.9553)	0.9232 (0.7711 to 0.9758)	0.7937 (0.6148 to 0.8961)	
26 Months	0.8462 (0.7475 to 0.9087)	0.9119 (0.8304 to 0.9553)	0.9232 (0.7711 to 0.9758)	0.7937 (0.6148 to 0.8961)	
Number of patients at risk[c]					
2 Months	87	98	47	45	
4 Months	81	90	41	41	
6 Months	64	81	39	36	
8 Months	57	75	35	34	
10 Months	53	69	33	32	
12 Months	47	66	31	29	
14 Months	41	64	31	29	
16 Months	38	59	26	24	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.3 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
18 Months	33	55	23	21	
20 Months	32	53	20	19	
22 Months	32	48	18	18	
24 Months	32	46	17	16	
26 Months	31	41	15	15	
Pathological fracture (days)					
Number (%) of events	7 (7.2)	5 (5.0)	1 (2.0)	7 (14.0)	0.0496
Number (%) of patients censored	90 (92.8)	96 (95.0)	50 (98.0)	43 (86.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.5216 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.3 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.4541		0.0847	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.6468 (0.2048 to 2.0426)		5.3705 (0.6369 to 45.2824)	
P-value	-	0.4577		0.1223	
Events probability (95% CI)[c]					
2 Months	0.9584 (0.8930 to 0.9842)	0.9700 (0.9099 to 0.9902)	1.0000 (1.0000 to 1.0000)	0.9600 (0.8494 to 0.9898)	
4 Months	0.9584 (0.8930 to 0.9842)	0.9600 (0.8969 to 0.9848)	1.0000 (1.0000 to 1.0000)	0.9600 (0.8494 to 0.9898)	
6 Months	0.9451 (0.8724 to 0.9769)	0.9600 (0.8969 to 0.9848)	0.9762 (0.8428 to 0.9966)	0.9600 (0.8494 to 0.9898)	
8 Months	0.9310 (0.8516 to 0.9687)	0.9600 (0.8969 to 0.9848)	0.9762 (0.8428 to 0.9966)	0.9360 (0.8135 to 0.9790)	
10 Months	0.9310 (0.8516 to 0.9687)	0.9472 (0.8771 to 0.9778)	0.9762 (0.8428 to 0.9966)	0.9360 (0.8135 to 0.9790)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.3 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	0.9150 (0.8276 to 0.9591)	0.9472 (0.8771 to 0.9778)	0.9762 (0.8428 to 0.9966)	0.9093 (0.7739 to 0.9653)	
14 Months	0.9150 (0.8276 to 0.9591)	0.9472 (0.8771 to 0.9778)	0.9762 (0.8428 to 0.9966)	0.9093 (0.7739 to 0.9653)	
16 Months	0.9150 (0.8276 to 0.9591)	0.9472 (0.8771 to 0.9778)	0.9762 (0.8428 to 0.9966)	0.8515 (0.6954 to 0.9313)	
18 Months	0.9150 (0.8276 to 0.9591)	0.9472 (0.8771 to 0.9778)	0.9762 (0.8428 to 0.9966)	0.8515 (0.6954 to 0.9313)	
20 Months	0.9150 (0.8276 to 0.9591)	0.9472 (0.8771 to 0.9778)	0.9762 (0.8428 to 0.9966)	0.8515 (0.6954 to 0.9313)	
22 Months	0.9150 (0.8276 to 0.9591)	0.9472 (0.8771 to 0.9778)	0.9762 (0.8428 to 0.9966)	0.8515 (0.6954 to 0.9313)	
24 Months	0.9150 (0.8276 to 0.9591)	0.9472 (0.8771 to 0.9778)	0.9762 (0.8428 to 0.9966)	0.8515 (0.6954 to 0.9313)	
26 Months	0.9150 (0.8276 to 0.9591)	0.9472 (0.8771 to 0.9778)	0.9762 (0.8428 to 0.9966)	0.8067 (0.6245 to 0.9066)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.3 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Number of patients at risk[c]					
2 Months	90	97	48	47	
4 Months	87	92	43	44	
6 Months	71	84	40	40	
8 Months	63	80	36	39	
10 Months	62	74	34	38	
12 Months	56	70	32	34	
14 Months	50	69	32	34	
16 Months	47	64	28	27	
18 Months	43	60	25	25	
20 Months	42	58	23	23	
22 Months	42	52	21	21	
24 Months	42	50	20	20	
26 Months	41	45	18	18	
Upper respiratory tract infection (days)					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.3 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	23 (23.7)	28 (27.7)	5 (9.8)	24 (48.0)	0.0023
Number (%) of patients censored	74 (76.3)	73 (72.3)	46 (90.2)	26 (52.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	13.9302 (4.4353 to NC)	11.8275 (5.4209 to NC)	NC (NC to NC)	3.8111 (2.5955 to 8.1807)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	13.3060 (7.9179 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (17.5441 to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9108		0.0001	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0320 (0.5939 to 1.7933)		5.5270 (2.0767 to 14.7097)	
P-value	-	0.9110		0.0006	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.3 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.1809 (0.0680 to 0.4815)		
Events probability (95% CI)[c]					
2 Months	0.8725 (0.7864 to 0.9255)	0.9200 (0.8464 to 0.9592)	0.9600 (0.8492 to 0.9898)	0.9000 (0.7763 to 0.9571)	
4 Months	0.8506 (0.7607 to 0.9087)	0.8893 (0.8090 to 0.9371)	0.9182 (0.7965 to 0.9685)	0.7472 (0.5971 to 0.8482)	
6 Months	0.8253 (0.7302 to 0.8894)	0.8103 (0.7153 to 0.8762)	0.9182 (0.7965 to 0.9685)	0.6996 (0.5446 to 0.8106)	
8 Months	0.7964 (0.6948 to 0.8673)	0.7732 (0.6727 to 0.8463)	0.9182 (0.7965 to 0.9685)	0.6458 (0.4853 to 0.7676)	
10 Months	0.7811 (0.6763 to 0.8555)	0.7597 (0.6570 to 0.8354)	0.8895 (0.7518 to 0.9531)	0.6189 (0.4569 to 0.7453)	
12 Months	0.7811 (0.6763 to 0.8555)	0.7453 (0.6403 to 0.8238)	0.8895 (0.7518 to 0.9531)	0.5879 (0.4233 to 0.7203)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.3 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.7451 (0.6319 to 0.8282)	0.7310 (0.6239 to 0.8121)	0.8895 (0.7518 to 0.9531)	0.4951 (0.3294 to 0.6408)	
16 Months	0.7451 (0.6319 to 0.8282)	0.6992 (0.5872 to 0.7863)	0.8895 (0.7518 to 0.9531)	0.4951 (0.3294 to 0.6408)	
18 Months	0.7451 (0.6319 to 0.8282)	0.6826 (0.5681 to 0.7726)	0.8895 (0.7518 to 0.9531)	0.3910 (0.2307 to 0.5482)	
20 Months	0.7226 (0.6027 to 0.8118)	0.6651 (0.5481 to 0.7583)	0.8895 (0.7518 to 0.9531)	0.3910 (0.2307 to 0.5482)	
22 Months	0.7226 (0.6027 to 0.8118)	0.6651 (0.5481 to 0.7583)	0.8895 (0.7518 to 0.9531)	0.3910 (0.2307 to 0.5482)	
24 Months	0.6993 (0.5734 to 0.7944)	0.6651 (0.5481 to 0.7583)	0.8895 (0.7518 to 0.9531)	0.3910 (0.2307 to 0.5482)	
26 Months	0.6993 (0.5734 to 0.7944)	0.6651 (0.5481 to 0.7583)	0.8895 (0.7518 to 0.9531)	0.3910 (0.2307 to 0.5482)	
Number of patients at risk[c]					
2 Months	81	92	46	43	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.3 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	76	85	39	33	
6 Months	60	70	37	26	
8 Months	53	62	34	24	
10 Months	51	56	31	22	
12 Months	46	52	30	19	
14 Months	40	51	30	16	
16 Months	38	44	26	15	
18 Months	33	39	23	9	
20 Months	31	37	20	8	
22 Months	31	32	18	7	
24 Months	30	32	17	7	
26 Months	30	29	15	6	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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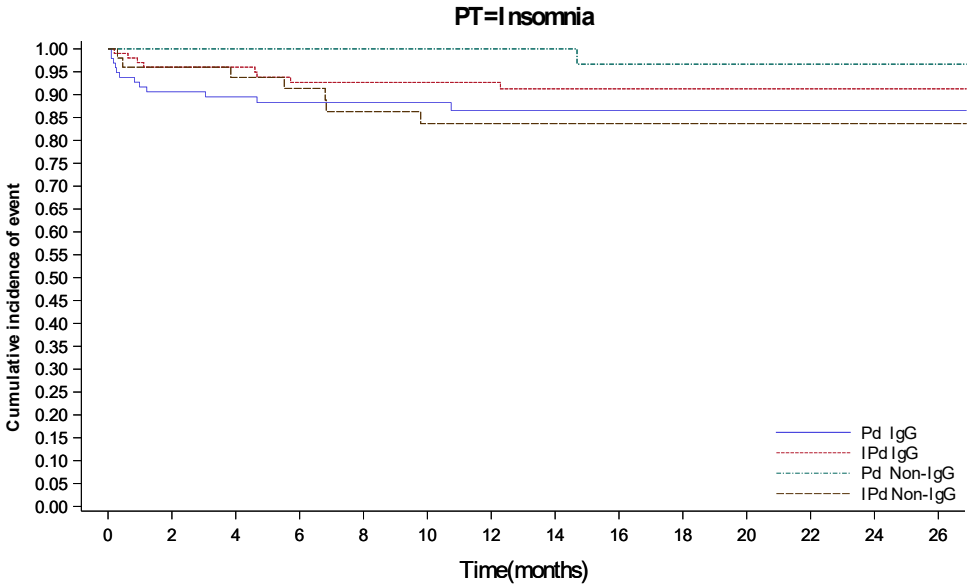
16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to MM type - Safety population



Number at Risk

Pd IgG	97	84	80	65	59	57	49	43	40	36	35	35	35	34
IPd IgG	101	96	91	80	75	69	66	64	59	55	53	47	45	40
Pd Non-IgG	51	48	43	41	37	35	33	33	28	25	22	20	19	17
IPd Non-IgG	50	46	42	36	34	32	29	29	25	23	21	20	19	18

PT are presented if at least 10 events in a arm
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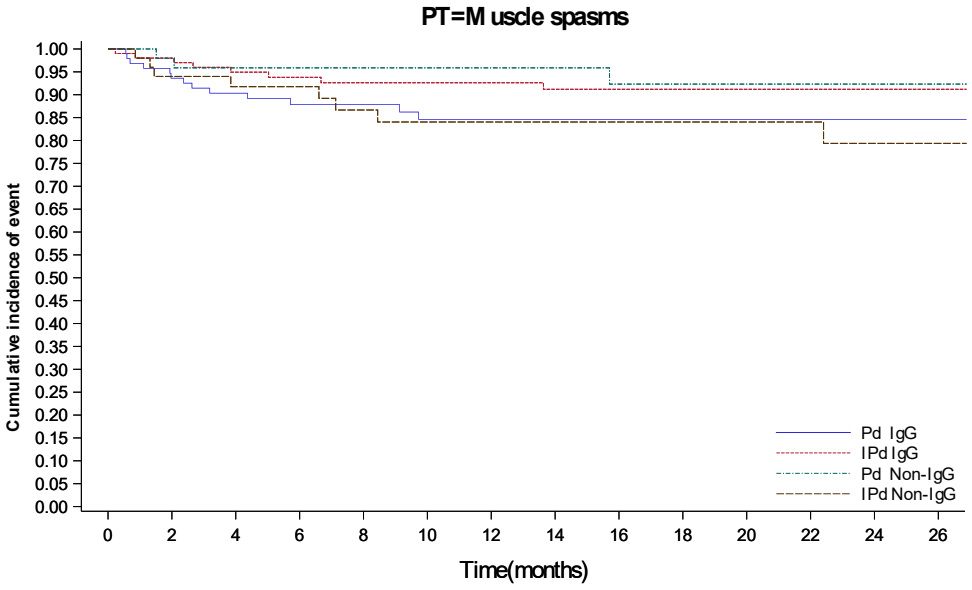
16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to MM type - Safety population



Number at Risk

Pd IgG	97	87	81	64	57	53	47	41	38	33	32	32	32	31
IPd IgG	101	98	90	81	75	69	66	64	59	55	53	48	46	41
Pd Non-IgG	51	47	41	39	35	33	31	31	26	23	20	18	17	15
IPd Non-IgG	50	45	41	36	34	32	29	29	24	21	19	18	16	15

PT are presented if at least 10 events in a arm
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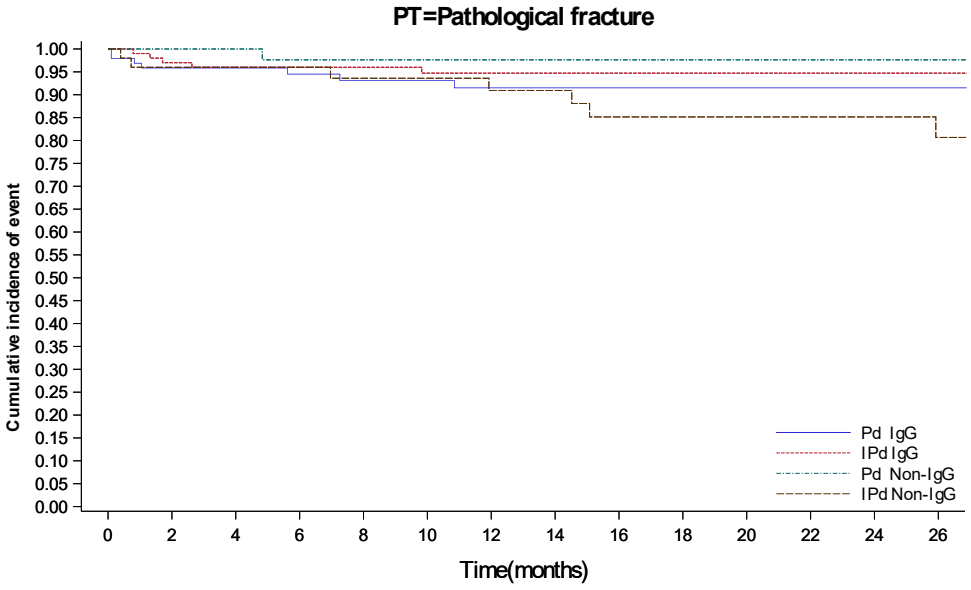
16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to MM type - Safety population



Number at Risk

Pd IgG	97	90	87	71	63	62	56	50	47	43	42	42	42	41
IPd IgG	101	97	92	84	80	74	70	69	64	60	58	52	50	45
Pd Non-IgG	51	48	43	40	36	34	32	32	28	25	23	21	20	18
IPd Non-IgG	50	47	44	40	39	38	34	34	27	25	23	21	20	18

PT are presented if at least 10 events in a arm
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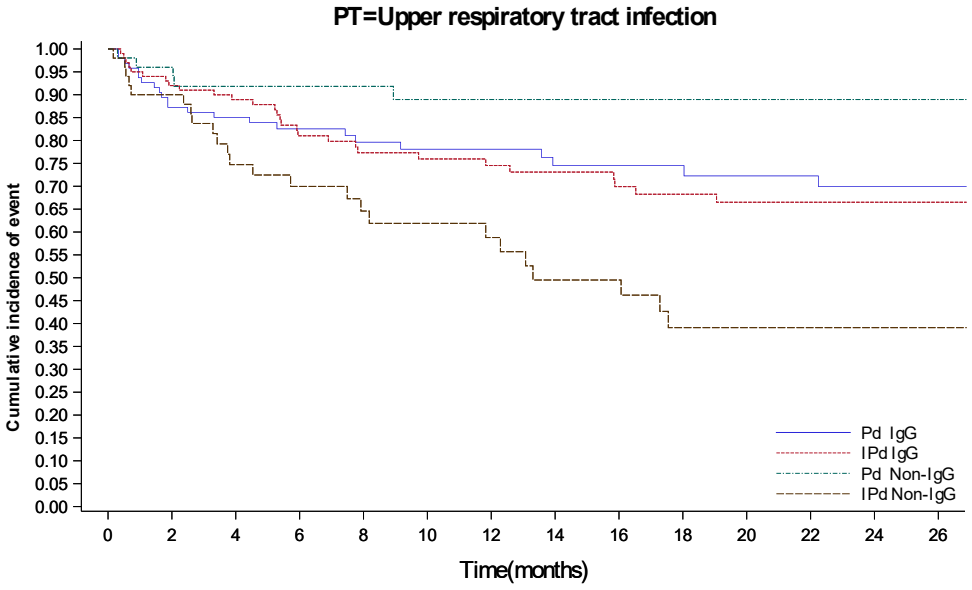
16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to MM type - Safety population



Number at Risk

Pd IgG	97	81	76	60	53	51	46	40	38	33	31	31	30	30
IPd IgG	101	92	85	70	62	56	52	51	44	39	37	32	32	29
Pd Non-IgG	51	46	39	37	34	31	30	30	26	23	20	18	17	15
IPd Non-IgG	50	43	33	26	24	22	19	16	15	9	8	7	7	6

PT are presented if at least 10 events in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.5 Treatment emergent serious adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Infections and infestations (days)					
Number (%) of events	42 (43.3)	50 (49.5)	11 (21.6)	26 (52.0)	0.0447
Number (%) of patients censored	55 (56.7)	51 (50.5)	40 (78.4)	24 (48.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	2.8255 (1.9384 to 6.0452)	4.3039 (2.2998 to 6.3409)	24.2136 (2.2669 to NC)	5.8809 (1.1499 to 10.5462)	
Median (95% CI)	34.9569 (13.7988 to NC)	20.1068 (9.9548 to NC)	NC (NC to NC)	14.4887 (9.5934 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (25.9220 to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.6789		0.0200	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0910 (0.7216 to 1.6494)		2.3171 (1.1202 to 4.7928)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.5 Treatment emergent serious adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
P-value	-	0.6796		0.0234	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.4316 (0.2086 to 0.8927)		
Events probability (95% CI)[c]					
2 Months	0.8224 (0.7299 to 0.8857)	0.8387 (0.7503 to 0.8979)	0.8987 (0.7735 to 0.9565)	0.8200 (0.6826 to 0.9020)	
4 Months	0.7049 (0.6019 to 0.7859)	0.7874 (0.6928 to 0.8559)	0.8343 (0.6955 to 0.9136)	0.7579 (0.6131 to 0.8547)	
6 Months	0.6714 (0.5665 to 0.7564)	0.6805 (0.5774 to 0.7636)	0.8112 (0.6678 to 0.8972)	0.7350 (0.5872 to 0.8369)	
8 Months	0.6597 (0.5540 to 0.7460)	0.6352 (0.5298 to 0.7231)	0.8112 (0.6678 to 0.8972)	0.7120 (0.5618 to 0.8187)	
10 Months	0.6467 (0.5401 to 0.7347)	0.5996 (0.4929 to 0.6909)	0.8112 (0.6678 to 0.8972)	0.6431 (0.4887 to 0.7617)	
12 Months	0.6200 (0.5114 to 0.7112)	0.5871 (0.4799 to 0.6796)	0.8112 (0.6678 to 0.8972)	0.5478 (0.3926 to 0.6789)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.5 Treatment emergent serious adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.6052 (0.4954 to 0.6984)	0.5871 (0.4799 to 0.6796)	0.8112 (0.6678 to 0.8972)	0.5478 (0.3926 to 0.6789)	
16 Months	0.5734 (0.4608 to 0.6708)	0.5738 (0.4659 to 0.6676)	0.8112 (0.6678 to 0.8972)	0.4957 (0.3413 to 0.6324)	
18 Months	0.5565 (0.4425 to 0.6562)	0.5598 (0.4512 to 0.6551)	0.8112 (0.6678 to 0.8972)	0.4957 (0.3413 to 0.6324)	
20 Months	0.5565 (0.4425 to 0.6562)	0.5144 (0.4036 to 0.6145)	0.7706 (0.6059 to 0.8733)	0.4626 (0.3072 to 0.6045)	
22 Months	0.5565 (0.4425 to 0.6562)	0.4993 (0.3881 to 0.6007)	0.7706 (0.6059 to 0.8733)	0.4626 (0.3072 to 0.6045)	
24 Months	0.5391 (0.4238 to 0.6411)	0.4814 (0.3692 to 0.5850)	0.7706 (0.6059 to 0.8733)	0.4626 (0.3072 to 0.6045)	
26 Months	0.5391 (0.4238 to 0.6411)	0.4636 (0.3506 to 0.5690)	0.7192 (0.5285 to 0.8434)	0.3855 (0.2293 to 0.5396)	
Number of patients at risk[c]					
2 Months	78	83	43	40	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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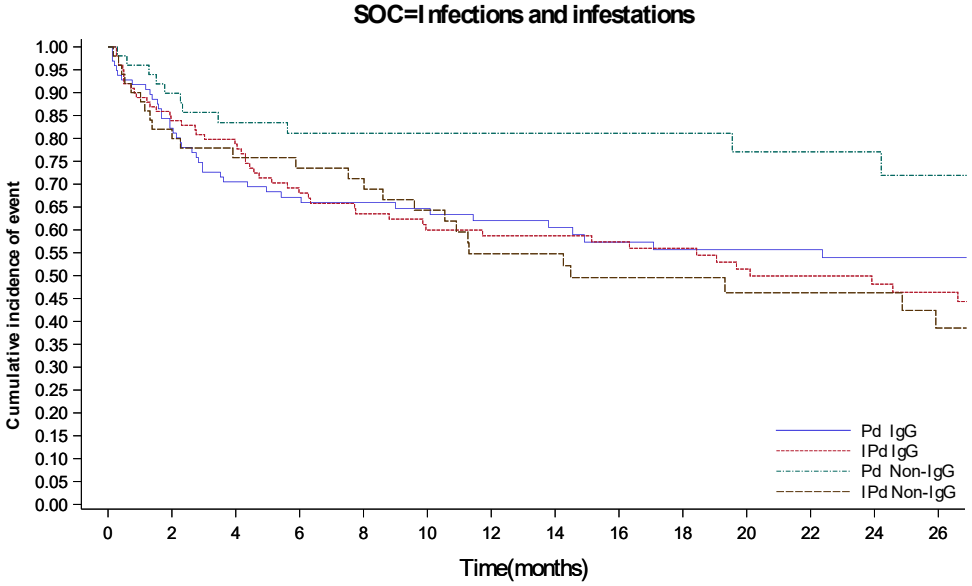
16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.5 Treatment emergent serious adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	66	75	37	36	
6 Months	57	61	34	32	
8 Months	51	56	30	31	
10 Months	50	50	29	28	
12 Months	45	47	27	22	
14 Months	39	46	27	22	
16 Months	36	42	23	17	
18 Months	33	37	20	16	
20 Months	32	34	18	14	
22 Months	32	30	16	13	
24 Months	31	27	15	13	
26 Months	31	23	12	10	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_seraesoc_type_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event per SOC by treatment group according to MM type - Safety population



Number at Risk

Pd IgG	97	78	66	57	51	50	45	39	36	33	32	32	31	31
IPd IgG	100	83	75	61	56	50	47	46	42	37	34	30	27	23
Pd Non-IgG	51	43	37	34	30	29	27	27	23	20	18	16	15	12
IPd Non-IgG	50	40	36	32	31	28	22	22	17	16	14	13	13	10

SOC are presented if at least 5% of patients in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.7 Treatment emergent not severe adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Infections and infestations (days)					
Number (%) of events	64 (66.0)	66 (65.3)	21 (41.2)	36 (72.0)	0.0040
Number (%) of patients censored	33 (34.0)	35 (34.7)	30 (58.8)	14 (28.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.4456 (0.8542 to 1.7084)	1.2156 (0.6571 to 2.2341)	2.0370 (1.5770 to 4.8624)	0.8871 (0.6571 to 2.1684)	
Median (95% CI)	3.3183 (1.9713 to 7.4251)	4.2382 (2.7926 to 6.2094)	NC (3.1211 to NC)	3.4168 (1.9713 to 4.3696)	
75% quantile (95% CI)	27.1704 (9.1663 to NC)	NC (12.0246 to NC)	NC (NC to NC)	11.2690 (3.9425 to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.7365		0.0062	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.7 Treatment emergent not severe adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.9423 (0.6666 to 1.3319)		2.1484 (1.2286 to 3.7568)	
P-value	-	0.7363		0.0073	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.4655 (0.2662 to 0.8139)		
Events probability (95% CI)[c]					
2 Months	0.5951 (0.4885 to 0.6866)	0.6805 (0.5795 to 0.7622)	0.7768 (0.6332 to 0.8697)	0.6375 (0.4877 to 0.7541)	
4 Months	0.4729 (0.3683 to 0.5704)	0.5269 (0.4242 to 0.6196)	0.6461 (0.4930 to 0.7636)	0.3630 (0.2262 to 0.5010)	
6 Months	0.4459 (0.3414 to 0.5449)	0.4072 (0.3087 to 0.5033)	0.6213 (0.4666 to 0.7429)	0.3105 (0.1807 to 0.4496)	
8 Months	0.3762 (0.2740 to 0.4780)	0.3840 (0.2867 to 0.4803)	0.5377 (0.3788 to 0.6726)	0.2795 (0.1537 to 0.4199)	
10 Months	0.3316 (0.2319 to 0.4344)	0.3579 (0.2618 to 0.4549)	0.5377 (0.3788 to 0.6726)	0.2795 (0.1537 to 0.4199)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.7 Treatment emergent not severe adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	0.3158 (0.2172 to 0.4189)	0.3579 (0.2618 to 0.4549)	0.5377 (0.3788 to 0.6726)	0.2096 (0.0960 to 0.3527)	
14 Months	0.3000 (0.2027 to 0.4032)	0.3150 (0.2210 to 0.4130)	0.5377 (0.3788 to 0.6726)	0.2096 (0.0960 to 0.3527)	
16 Months	0.3000 (0.2027 to 0.4032)	0.3006 (0.2078 to 0.3988)	0.5377 (0.3788 to 0.6726)	0.2096 (0.0960 to 0.3527)	
18 Months	0.3000 (0.2027 to 0.4032)	0.3006 (0.2078 to 0.3988)	0.5377 (0.3788 to 0.6726)	0.1677 (0.0640 to 0.3134)	
20 Months	0.2600 (0.1647 to 0.3656)	0.3006 (0.2078 to 0.3988)	0.5377 (0.3788 to 0.6726)	0.1677 (0.0640 to 0.3134)	
22 Months	0.2600 (0.1647 to 0.3656)	0.3006 (0.2078 to 0.3988)	0.5377 (0.3788 to 0.6726)	0.1677 (0.0640 to 0.3134)	
24 Months	0.2600 (0.1647 to 0.3656)	0.3006 (0.2078 to 0.3988)	0.5377 (0.3788 to 0.6726)	0.1677 (0.0640 to 0.3134)	
26 Months	0.2600 (0.1647 to 0.3656)	0.3006 (0.2078 to 0.3988)	0.5377 (0.3788 to 0.6726)	0.1677 (0.0640 to 0.3134)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.7 Treatment emergent not severe adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Number of patients at risk[c]					
2 Months	55	68	37	30	
4 Months	41	50	27	15	
6 Months	33	35	24	10	
8 Months	26	33	19	9	
10 Months	22	27	18	8	
12 Months	20	25	17	6	
14 Months	17	22	17	6	
16 Months	16	19	14	5	
18 Months	15	17	13	3	
20 Months	12	17	12	2	
22 Months	12	14	10	2	
24 Months	12	14	9	2	
26 Months	12	11	7	2	
Injury, poisoning and procedural complications (days)					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.7 Treatment emergent not severe adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Number (%) of events	12 (12.4)	38 (37.6)	4 (7.8)	30 (60.0)	0.0399
Number (%) of patients censored	85 (87.6)	63 (62.4)	47 (92.2)	20 (40.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (31.3101 to NC)	0.1971 (0.0986 to 11.4661)	NC (NC to NC)	0.0986 (0.0657 to 0.1643)	
Median (95% CI)	NC (NC to NC)	NC (30.4230 to NC)	NC (NC to NC)	1.3634 (0.1314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (18.0370 to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	<.0001		<.0001	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	3.7000 (1.9313 to 7.0885)		13.8241 (4.1771 to 45.7503)	
P-value	-	<.0001		<.0001	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12soc_type_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.7 Treatment emergent not severe adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.2703 (0.1411 to 0.5178)		0.0723 (0.0219 to 0.2394)		
Events probability (95% CI)[c]					
2 Months	0.9682 (0.9045 to 0.9896)	0.7127 (0.6137 to 0.7906)	0.9792 (0.8612 to 0.9970)	0.5000 (0.3556 to 0.6283)	
4 Months	0.9465 (0.8763 to 0.9774)	0.7024 (0.6028 to 0.7815)	0.9564 (0.8364 to 0.9889)	0.4792 (0.3361 to 0.6087)	
6 Months	0.9353 (0.8615 to 0.9704)	0.7024 (0.6028 to 0.7815)	0.9564 (0.8364 to 0.9889)	0.4574 (0.3157 to 0.5882)	
8 Months	0.8944 (0.8057 to 0.9440)	0.6669 (0.5642 to 0.7507)	0.9325 (0.8046 to 0.9778)	0.4320 (0.2911 to 0.5650)	
10 Months	0.8651 (0.7678 to 0.9235)	0.6669 (0.5642 to 0.7507)	0.9325 (0.8046 to 0.9778)	0.4066 (0.2672 to 0.5414)	
12 Months	0.8651 (0.7678 to 0.9235)	0.6517 (0.5468 to 0.7381)	0.9325 (0.8046 to 0.9778)	0.4066 (0.2672 to 0.5414)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.7 Treatment emergent not severe adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.8651 (0.7678 to 0.9235)	0.6517 (0.5468 to 0.7381)	0.9325 (0.8046 to 0.9778)	0.4066 (0.2672 to 0.5414)	
16 Months	0.8651 (0.7678 to 0.9235)	0.6191 (0.5096 to 0.7111)	0.9325 (0.8046 to 0.9778)	0.4066 (0.2672 to 0.5414)	
18 Months	0.8651 (0.7678 to 0.9235)	0.6191 (0.5096 to 0.7111)	0.9325 (0.8046 to 0.9778)	0.4066 (0.2672 to 0.5414)	
20 Months	0.8651 (0.7678 to 0.9235)	0.6191 (0.5096 to 0.7111)	0.9325 (0.8046 to 0.9778)	0.3659 (0.2233 to 0.5096)	
22 Months	0.8651 (0.7678 to 0.9235)	0.6191 (0.5096 to 0.7111)	0.9325 (0.8046 to 0.9778)	0.3659 (0.2233 to 0.5096)	
24 Months	0.8651 (0.7678 to 0.9235)	0.6191 (0.5096 to 0.7111)	0.9325 (0.8046 to 0.9778)	0.3659 (0.2233 to 0.5096)	
26 Months	0.8651 (0.7678 to 0.9235)	0.6191 (0.5096 to 0.7111)	0.9325 (0.8046 to 0.9778)	0.3659 (0.2233 to 0.5096)	
Number of patients at risk[c]					
2 Months	90	71	46	24	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.7 Treatment emergent not severe adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	86	66	42	22	
6 Months	72	60	40	18	
8 Months	62	53	35	17	
10 Months	58	47	34	16	
12 Months	51	43	32	14	
14 Months	45	42	32	14	
16 Months	42	37	29	11	
18 Months	37	35	26	10	
20 Months	36	33	23	8	
22 Months	36	28	21	8	
24 Months	36	27	20	8	
26 Months	35	24	18	8	
Psychiatric disorders (days)					
Number (%) of events	24 (24.7)	19 (18.8)	4 (7.8)	11 (22.0)	0.0250
Number (%) of patients censored	73 (75.3)	82 (81.2)	47 (92.2)	39 (78.0)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.7 Treatment emergent not severe adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	7.9836 (3.3511 to NC)	NC (15.0144 to NC)	NC (14.6858 to NC)	NC (1.5441 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1462		0.1456	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.6413 (0.3505 to 1.1733)		2.3485 (0.7185 to 7.6767)	
P-value	-	0.1494		0.1577	
Events probability (95% CI)[c]					
2 Months	0.8850 (0.8019 to 0.9346)	0.9302 (0.8591 to 0.9661)	0.9608 (0.8522 to 0.9900)	0.8595 (0.7278 to 0.9304)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.7 Treatment emergent not severe adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	0.8301 (0.7375 to 0.8923)	0.8998 (0.8218 to 0.9448)	0.9608 (0.8522 to 0.9900)	0.8375 (0.7009 to 0.9153)	
6 Months	0.7778 (0.6758 to 0.8512)	0.8559 (0.7686 to 0.9121)	0.9608 (0.8522 to 0.9900)	0.7922 (0.6473 to 0.8827)	
8 Months	0.7492 (0.6425 to 0.8282)	0.8559 (0.7686 to 0.9121)	0.9608 (0.8522 to 0.9900)	0.7922 (0.6473 to 0.8827)	
10 Months	0.7492 (0.6425 to 0.8282)	0.8559 (0.7686 to 0.9121)	0.9608 (0.8522 to 0.9900)	0.7674 (0.6180 to 0.8645)	
12 Months	0.7318 (0.6214 to 0.8147)	0.8559 (0.7686 to 0.9121)	0.9608 (0.8522 to 0.9900)	0.7674 (0.6180 to 0.8645)	
14 Months	0.7318 (0.6214 to 0.8147)	0.8421 (0.7510 to 0.9020)	0.9317 (0.7983 to 0.9780)	0.7674 (0.6180 to 0.8645)	
16 Months	0.7318 (0.6214 to 0.8147)	0.8274 (0.7321 to 0.8912)	0.8995 (0.7477 to 0.9622)	0.7674 (0.6180 to 0.8645)	
18 Months	0.7318 (0.6214 to 0.8147)	0.8120 (0.7128 to 0.8798)	0.8995 (0.7477 to 0.9622)	0.7674 (0.6180 to 0.8645)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.7 Treatment emergent not severe adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
20 Months	0.7318 (0.6214 to 0.8147)	0.8120 (0.7128 to 0.8798)	0.8995 (0.7477 to 0.9622)	0.7674 (0.6180 to 0.8645)	
22 Months	0.7318 (0.6214 to 0.8147)	0.8120 (0.7128 to 0.8798)	0.8995 (0.7477 to 0.9622)	0.7674 (0.6180 to 0.8645)	
24 Months	0.7065 (0.5871 to 0.7972)	0.8120 (0.7128 to 0.8798)	0.8995 (0.7477 to 0.9622)	0.7674 (0.6180 to 0.8645)	
26 Months	0.7065 (0.5871 to 0.7972)	0.7922 (0.6859 to 0.8660)	0.8995 (0.7477 to 0.9622)	0.7674 (0.6180 to 0.8645)	
Number of patients at risk[c]					
2 Months	82	93	46	41	
4 Months	74	86	41	38	
6 Months	57	75	39	33	
8 Months	50	70	36	33	
10 Months	48	64	35	31	
12 Months	41	62	33	28	
14 Months	37	60	32	28	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.7 Treatment emergent not severe adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	34	54	27	24	
18 Months	30	51	24	22	
20 Months	29	49	21	20	
22 Months	29	43	19	19	
24 Months	28	41	18	18	
26 Months	27	36	16	17	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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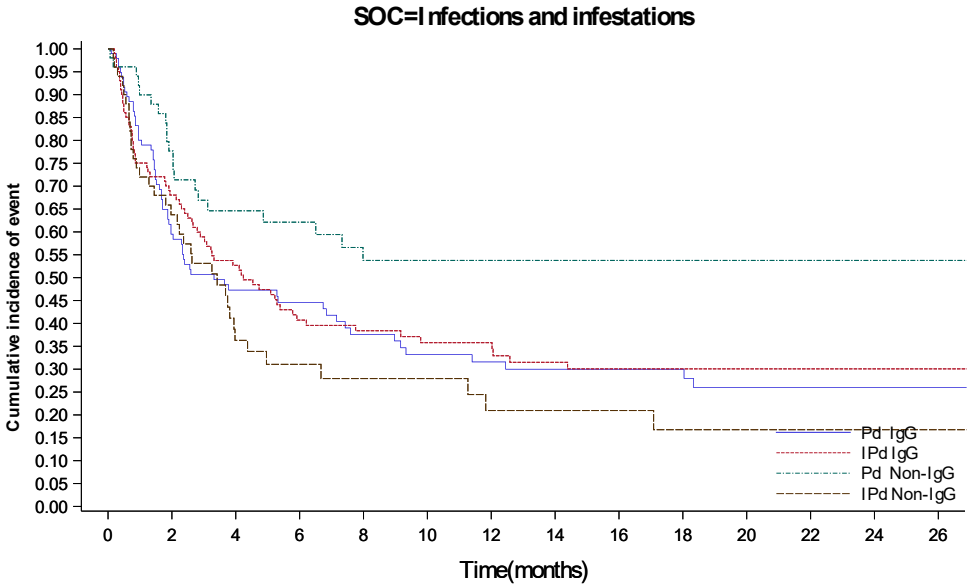
16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.8 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per SOC by treatment group according to MM type - Safety population



Number at Risk

Pd IgG	97	55	41	33	26	22	20	17	16	15	12	12	12	12
IPd IgG	101	68	50	35	33	27	25	22	19	17	17	14	14	11
Pd Non-IgG	51	37	27	24	19	18	17	17	14	13	12	10	9	7
IPd Non-IgG	50	30	15	10	9	8	6	6	5	3	2	2	2	2

SOC are presented if at least 10 events in a arm
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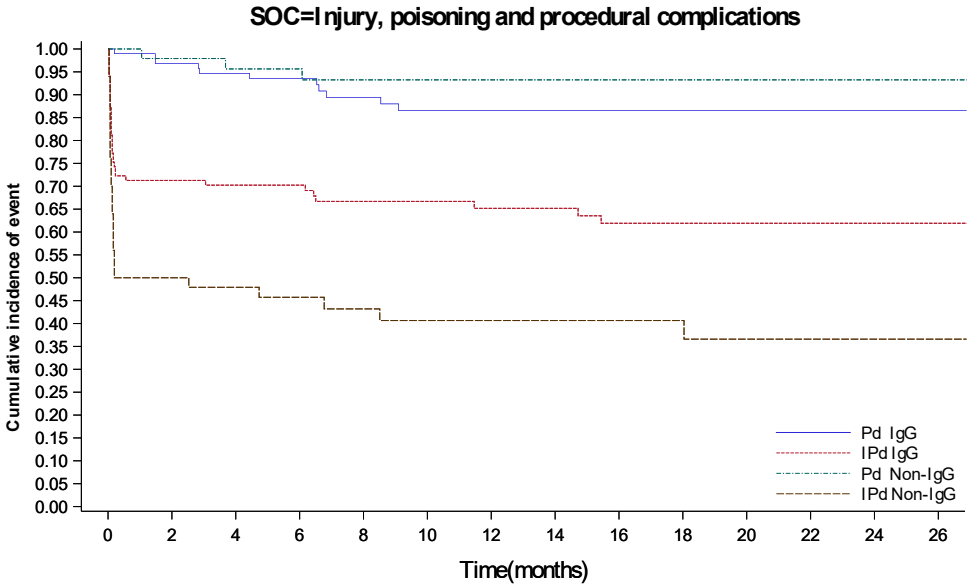
16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.8 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per SOC by treatment group according to MM type - Safety population

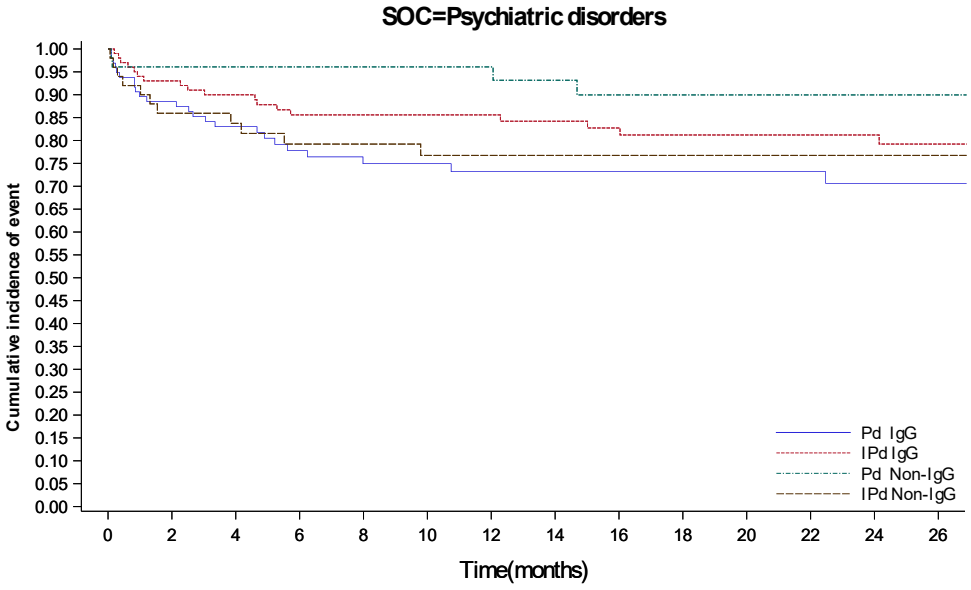


Number at Risk

Pd IgG	97	90	86	72	62	58	51	45	42	37	36	36	36	35
IPd IgG	101	71	66	60	53	47	43	42	37	35	33	28	27	24
Pd Non-IgG	50	46	42	40	35	34	32	32	29	26	23	21	20	18
IPd Non-IgG	50	24	22	18	17	16	14	14	11	10	8	8	8	8

SOC are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12soc_type_s_f_x.rtf (17NOV2020 14:45)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.8 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per SOC by treatment group according to MM type - Safety population



Number at Risk

Pd IgG	97	82	74	57	50	48	41	37	34	30	29	29	28	27
IPd IgG	101	93	86	75	70	64	62	60	54	51	49	43	41	36
Pd Non-IgG	51	46	41	39	36	35	33	32	27	24	21	19	18	16
IPd Non-IgG	50	41	38	33	33	31	28	28	24	22	20	19	18	17

SOC are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12soc_type_s_f_x.rtf (17NOV2020 14:45)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.9 Treatment emergent not severe adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Insomnia (days)					
Number (%) of events	12 (12.4)	8 (7.9)	1 (2.0)	7 (14.0)	0.0290
Number (%) of patients censored	85 (87.6)	93 (92.1)	50 (98.0)	43 (86.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.8337 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2201		0.1117	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.5744 (0.2341 to 1.4090)		4.9174 (0.5699 to 42.4308)	
P-value	-	0.2259		0.1475	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.9 Treatment emergent not severe adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]					
2 Months	0.9061 (0.8272 to 0.9500)	0.9601 (0.8972 to 0.9848)	1.0000 (1.0000 to 1.0000)	0.9600 (0.8494 to 0.9898)	
4 Months	0.8950 (0.8136 to 0.9421)	0.9601 (0.8972 to 0.9848)	1.0000 (1.0000 to 1.0000)	0.9377 (0.8187 to 0.9795)	
6 Months	0.8826 (0.7977 to 0.9333)	0.9267 (0.8522 to 0.9644)	1.0000 (1.0000 to 1.0000)	0.9136 (0.7851 to 0.9668)	
8 Months	0.8826 (0.7977 to 0.9333)	0.9267 (0.8522 to 0.9644)	1.0000 (1.0000 to 1.0000)	0.8629 (0.7183 to 0.9364)	
10 Months	0.8826 (0.7977 to 0.9333)	0.9267 (0.8522 to 0.9644)	1.0000 (1.0000 to 1.0000)	0.8367 (0.6859 to 0.9192)	
12 Months	0.8656 (0.7733 to 0.9222)	0.9267 (0.8522 to 0.9644)	1.0000 (1.0000 to 1.0000)	0.8367 (0.6859 to 0.9192)	
14 Months	0.8656 (0.7733 to 0.9222)	0.9127 (0.8319 to 0.9556)	1.0000 (1.0000 to 1.0000)	0.8367 (0.6859 to 0.9192)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_type_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.9 Treatment emergent not severe adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.8656 (0.7733 to 0.9222)	0.9127 (0.8319 to 0.9556)	0.9667 (0.7861 to 0.9952)	0.8367 (0.6859 to 0.9192)	
18 Months	0.8656 (0.7733 to 0.9222)	0.9127 (0.8319 to 0.9556)	0.9667 (0.7861 to 0.9952)	0.8367 (0.6859 to 0.9192)	
20 Months	0.8656 (0.7733 to 0.9222)	0.9127 (0.8319 to 0.9556)	0.9667 (0.7861 to 0.9952)	0.8367 (0.6859 to 0.9192)	
22 Months	0.8656 (0.7733 to 0.9222)	0.9127 (0.8319 to 0.9556)	0.9667 (0.7861 to 0.9952)	0.8367 (0.6859 to 0.9192)	
24 Months	0.8656 (0.7733 to 0.9222)	0.9127 (0.8319 to 0.9556)	0.9667 (0.7861 to 0.9952)	0.8367 (0.6859 to 0.9192)	
26 Months	0.8656 (0.7733 to 0.9222)	0.9127 (0.8319 to 0.9556)	0.9667 (0.7861 to 0.9952)	0.8367 (0.6859 to 0.9192)	
Number of patients at risk[c]					
2 Months	84	96	48	46	
4 Months	80	91	43	42	
6 Months	65	80	41	36	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.9 Treatment emergent not severe adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	59	75	37	34	
10 Months	57	69	35	32	
12 Months	49	66	33	29	
14 Months	43	64	33	29	
16 Months	40	59	28	25	
18 Months	36	55	25	23	
20 Months	35	53	22	21	
22 Months	35	47	20	20	
24 Months	35	45	19	19	
26 Months	34	40	17	18	
Upper respiratory tract infection (days)					
Number (%) of events	23 (23.7)	27 (26.7)	4 (7.8)	23 (46.0)	0.0013
Number (%) of patients censored	74 (76.3)	74 (73.3)	47 (92.2)	27 (54.0)	
Kaplan-Meier estimates of event in months					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.9 Treatment emergent not severe adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
25% quantile (95% CI)	13.9302 (4.4353 to NC)	12.5832 (5.9138 to NC)	NC (NC to NC)	4.5339 (2.5955 to 11.8275)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	16.0657 (8.1807 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (17.5441 to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.9855		<.0001	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.9949 (0.5699 to 1.7367)		6.7143 (2.2855 to 19.7254)	
P-value	-	0.9855		0.0005	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.1489 (0.0507 to 0.4375)		
Events probability (95% CI)[c]					
2 Months	0.8725 (0.7864 to 0.9255)	0.9200 (0.8464 to 0.9592)	0.9796 (0.8638 to 0.9971)	0.9000 (0.7763 to 0.9571)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.9 Treatment emergent not severe adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	0.8506 (0.7607 to 0.9087)	0.8992 (0.8207 to 0.9445)	0.9379 (0.8197 to 0.9795)	0.7693 (0.6214 to 0.8654)	
6 Months	0.8253 (0.7302 to 0.8894)	0.8193 (0.7249 to 0.8838)	0.9379 (0.8197 to 0.9795)	0.7218 (0.5681 to 0.8287)	
8 Months	0.7964 (0.6948 to 0.8673)	0.7818 (0.6815 to 0.8539)	0.9379 (0.8197 to 0.9795)	0.6683 (0.5083 to 0.7867)	
10 Months	0.7811 (0.6763 to 0.8555)	0.7681 (0.6655 to 0.8429)	0.9095 (0.7738 to 0.9655)	0.6416 (0.4797 to 0.7648)	
12 Months	0.7811 (0.6763 to 0.8555)	0.7536 (0.6485 to 0.8313)	0.9095 (0.7738 to 0.9655)	0.6111 (0.4461 to 0.7404)	
14 Months	0.7451 (0.6319 to 0.8282)	0.7391 (0.6318 to 0.8195)	0.9095 (0.7738 to 0.9655)	0.5194 (0.3522 to 0.6629)	
16 Months	0.7451 (0.6319 to 0.8282)	0.7070 (0.5945 to 0.7936)	0.9095 (0.7738 to 0.9655)	0.5194 (0.3522 to 0.6629)	
18 Months	0.7451 (0.6319 to 0.8282)	0.6902 (0.5751 to 0.7799)	0.9095 (0.7738 to 0.9655)	0.4102 (0.2451 to 0.5684)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.9 Treatment emergent not severe adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
20 Months	0.7226 (0.6027 to 0.8118)	0.6725 (0.5548 to 0.7654)	0.9095 (0.7738 to 0.9655)	0.4102 (0.2451 to 0.5684)	
22 Months	0.7226 (0.6027 to 0.8118)	0.6725 (0.5548 to 0.7654)	0.9095 (0.7738 to 0.9655)	0.4102 (0.2451 to 0.5684)	
24 Months	0.6993 (0.5734 to 0.7944)	0.6725 (0.5548 to 0.7654)	0.9095 (0.7738 to 0.9655)	0.4102 (0.2451 to 0.5684)	
26 Months	0.6993 (0.5734 to 0.7944)	0.6725 (0.5548 to 0.7654)	0.9095 (0.7738 to 0.9655)	0.4102 (0.2451 to 0.5684)	
Number of patients at risk[c]					
2 Months	81	92	47	43	
4 Months	76	85	40	34	
6 Months	60	70	38	27	
8 Months	53	62	35	25	
10 Months	51	56	32	23	
12 Months	46	52	31	20	
14 Months	40	51	31	17	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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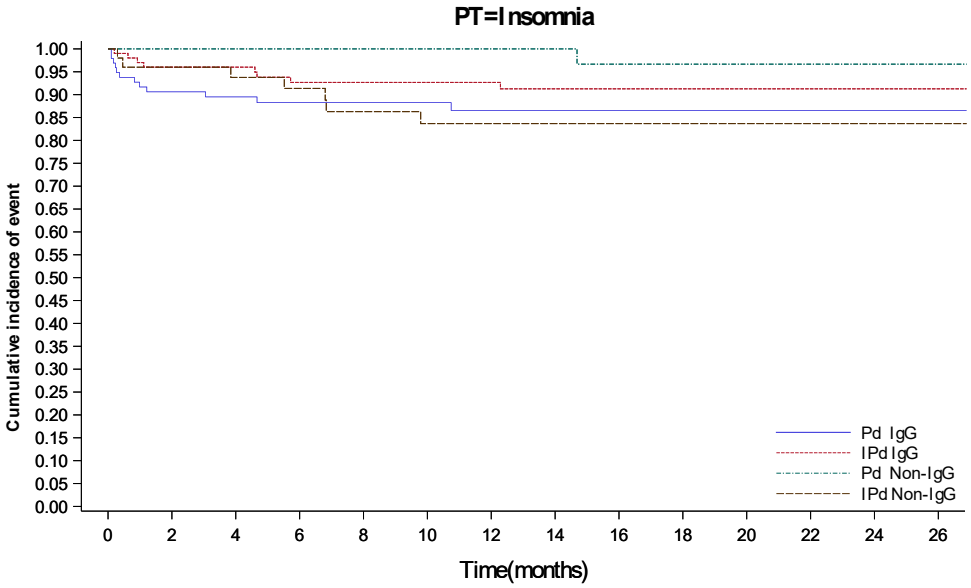
16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.9 Treatment emergent not severe adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Pd (N=97)	**IPd (N=101)**	**Pd (N=51)**	**IPd (N=50)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	38	44	27	15	
18 Months	33	39	24	9	
20 Months	31	37	21	8	
22 Months	31	32	19	7	
24 Months	30	32	18	7	
26 Months	30	29	16	6	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_type_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.10 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per PT by treatment group according to MM type - Safety population

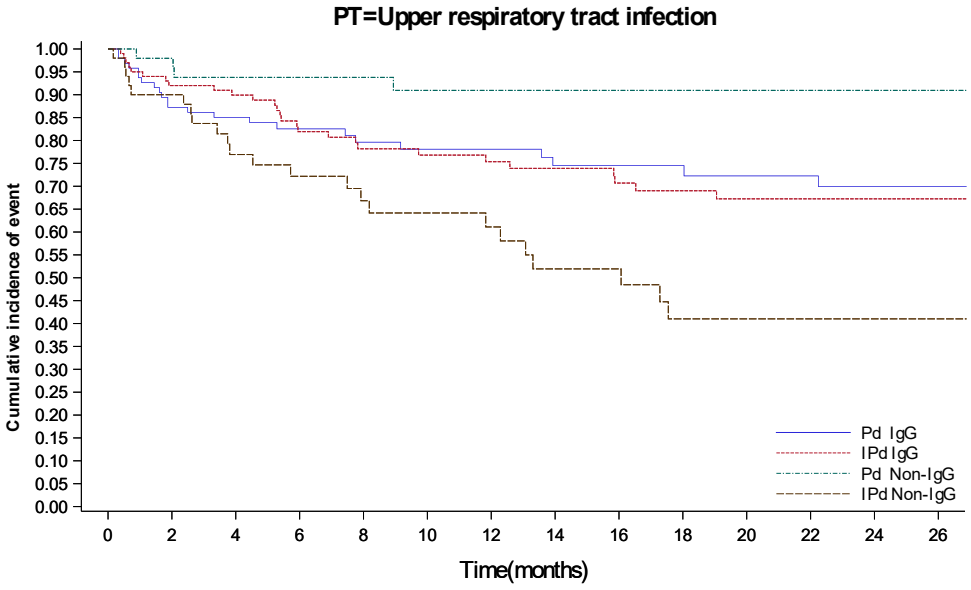


Number at Risk

Pd IgG	97	84	80	65	59	57	49	43	40	36	35	35	35	34
IPd IgG	101	96	91	80	75	69	66	64	59	55	53	47	45	40
Pd Non-IgG	51	48	43	41	37	35	33	33	28	25	22	20	19	17
IPd Non-IgG	50	46	42	36	34	32	29	29	25	23	21	20	19	18

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_type_s_f_x.rtf (17NOV2020 14:45)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by MM type
16.2.7.1.53.10 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per PT by treatment group according to MM type - Safety population



Number at Risk

Pd IgG	97	81	76	60	53	51	46	40	38	33	31	31	30	30
IPd IgG	101	92	85	70	62	56	52	51	44	39	37	32	32	29
Pd Non-IgG	51	47	40	38	35	32	31	31	27	24	21	19	18	16
IPd Non-IgG	50	43	34	27	25	23	20	17	15	9	8	7	7	6

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_type_s_f_x.rtf (17NOV2020 14:45)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.1 Treatment emergent adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
Respiratory, thoracic and mediastinal disorders (days)					
Number (%) of events	28 (29.8)	44 (51.2)	20 (42.6)	21 (38.9)	0.0463
Number (%) of patients censored	66 (70.2)	42 (48.8)	27 (57.4)	33 (61.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	6.9322 (1.0185 to NC)	4.1068 (1.8398 to 5.0267)	1.6756 (0.5585 to 7.2279)	3.7454 (0.6571 to 7.6879)	
Median (95% CI)	NC (NC to NC)	13.2402 (7.3922 to NC)	22.3737 (5.6181 to NC)	NC (7.6879 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (22.3737 to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0354		0.4037	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.6658 (1.0307 to 2.6924)		0.7634 (0.4043 to 1.4413)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_crcl_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.1 Treatment emergent adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
P-value	-	0.0372		0.4050	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.6003 (0.3714 to 0.9702)				
Events probability (95% CI)[c]					
2 Months	0.8068 (0.7110 to 0.8737)	0.8130 (0.7130 to 0.8810)	0.7133 (0.5578 to 0.8224)	0.7593 (0.6218 to 0.8524)	
4 Months	0.7623 (0.6617 to 0.8366)	0.7539 (0.6479 to 0.8321)	0.6895 (0.5324 to 0.8032)	0.6993 (0.5565 to 0.8039)	
6 Months	0.7502 (0.6482 to 0.8265)	0.6427 (0.5300 to 0.7351)	0.6338 (0.4709 to 0.7587)	0.6793 (0.5353 to 0.7872)	
8 Months	0.7377 (0.6342 to 0.8161)	0.5894 (0.4749 to 0.6871)	0.6021 (0.4359 to 0.7335)	0.6308 (0.4818 to 0.7477)	
10 Months	0.7120 (0.6058 to 0.7944)	0.5476 (0.4323 to 0.6489)	0.5667 (0.3967 to 0.7055)	0.5771 (0.4235 to 0.7034)	
12 Months	0.6986 (0.5910 to 0.7830)	0.5188 (0.4033 to 0.6223)	0.5667 (0.3967 to 0.7055)	0.5771 (0.4235 to 0.7034)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_crcl_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.1 Treatment emergent adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.6849 (0.5759 to 0.7713)	0.4730 (0.3577 to 0.5797)	0.5231 (0.3469 to 0.6726)	0.5771 (0.4235 to 0.7034)	
16 Months	0.6849 (0.5759 to 0.7713)	0.4730 (0.3577 to 0.5797)	0.5231 (0.3469 to 0.6726)	0.5771 (0.4235 to 0.7034)	
18 Months	0.6849 (0.5759 to 0.7713)	0.4730 (0.3577 to 0.5797)	0.5231 (0.3469 to 0.6726)	0.5771 (0.4235 to 0.7034)	
20 Months	0.6849 (0.5759 to 0.7713)	0.4730 (0.3577 to 0.5797)	0.5231 (0.3469 to 0.6726)	0.5771 (0.4235 to 0.7034)	
22 Months	0.6849 (0.5759 to 0.7713)	0.4730 (0.3577 to 0.5797)	0.5231 (0.3469 to 0.6726)	0.5771 (0.4235 to 0.7034)	
24 Months	0.6849 (0.5759 to 0.7713)	0.4730 (0.3577 to 0.5797)	0.4484 (0.2500 to 0.6287)	0.5771 (0.4235 to 0.7034)	
26 Months	0.6849 (0.5759 to 0.7713)	0.4493 (0.3315 to 0.5601)	0.4484 (0.2500 to 0.6287)	0.5771 (0.4235 to 0.7034)	
Number of patients at risk[c]					
2 Months	74	69	31	41	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.1 Treatment emergent adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	67	62	27	35	
6 Months	62	49	20	30	
8 Months	58	44	18	25	
10 Months	54	39	16	19	
12 Months	51	34	13	18	
14 Months	48	31	11	17	
16 Months	44	29	10	14	
18 Months	40	26	9	13	
20 Months	38	25	8	13	
22 Months	37	22	7	11	
24 Months	37	20	5	11	
26 Months	35	18	5	10	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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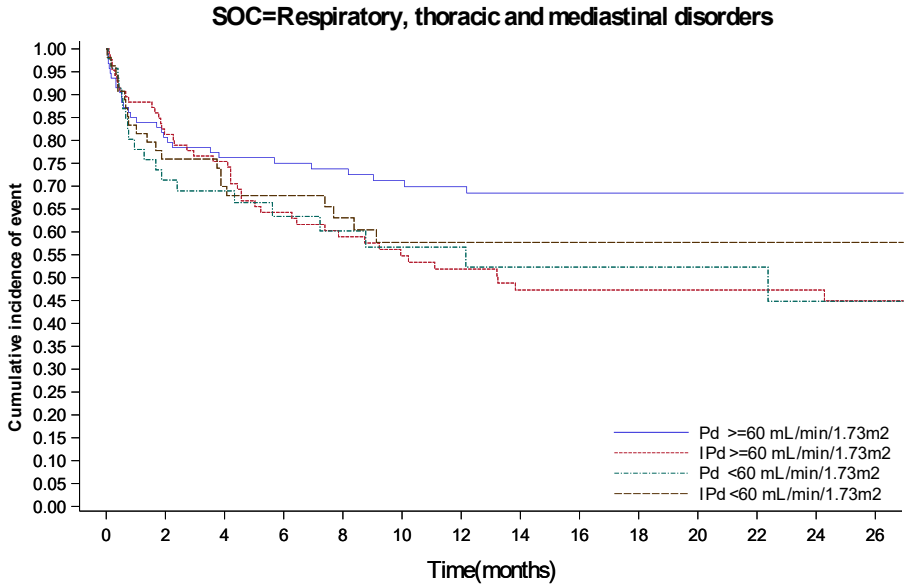
16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population



Number at Risk

Pd >=60 mL/min/1.73m2	94	74	67	62	58	54	51	48	44	40	38	37	37	35
IPd >=60 mL/min/1.73m2	86	69	62	49	44	39	34	31	29	26	25	22	20	18
Pd <60 mL/min/1.73m2	47	31	27	20	18	16	13	11	10	9	8	7	5	5
IPd <60 mL/min/1.73m2	54	41	35	30	25	19	18	17	14	13	13	11	11	10

SOC are presented if at least 10 events in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.3 Treatment emergent serious adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
General disorders and administration site conditions (days)					
Number (%) of events	12 (12.8)	5 (5.8)	2 (4.3)	13 (24.1)	0.0062
Number (%) of patients censored	82 (87.2)	81 (94.2)	45 (95.7)	41 (75.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (31.3758 to NC)	NC (NC to NC)	NC (NC to NC)	19.1211 (6.8337 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0802		0.0081	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.4037 (0.1413 to 1.1536)		6.3446 (1.3733 to 29.3117)	
P-value	-	0.0904		0.0180	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.3 Treatment emergent serious adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.1576 (0.0341 to 0.7282)		
Events probability (95% CI)[c]					
2 Months	0.9572 (0.8900 to 0.9837)	0.9884 (0.9203 to 0.9984)	1.0000 (1.0000 to 1.0000)	0.9815 (0.8757 to 0.9974)	
4 Months	0.9239 (0.8470 to 0.9630)	0.9765 (0.9091 to 0.9941)	0.9756 (0.8392 to 0.9965)	0.9441 (0.8365 to 0.9816)	
6 Months	0.8887 (0.8027 to 0.9386)	0.9646 (0.8941 to 0.9884)	0.9499 (0.8142 to 0.9873)	0.9047 (0.7859 to 0.9592)	
8 Months	0.8887 (0.8027 to 0.9386)	0.9646 (0.8941 to 0.9884)	0.9499 (0.8142 to 0.9873)	0.8626 (0.7327 to 0.9322)	
10 Months	0.8887 (0.8027 to 0.9386)	0.9646 (0.8941 to 0.9884)	0.9499 (0.8142 to 0.9873)	0.8166 (0.6758 to 0.9006)	
12 Months	0.8887 (0.8027 to 0.9386)	0.9646 (0.8941 to 0.9884)	0.9499 (0.8142 to 0.9873)	0.8166 (0.6758 to 0.9006)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.3 Treatment emergent serious adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.8887 (0.8027 to 0.9386)	0.9646 (0.8941 to 0.9884)	0.9499 (0.8142 to 0.9873)	0.8166 (0.6758 to 0.9006)	
16 Months	0.8887 (0.8027 to 0.9386)	0.9646 (0.8941 to 0.9884)	0.9499 (0.8142 to 0.9873)	0.7601 (0.6044 to 0.8612)	
18 Months	0.8887 (0.8027 to 0.9386)	0.9646 (0.8941 to 0.9884)	0.9499 (0.8142 to 0.9873)	0.7601 (0.6044 to 0.8612)	
20 Months	0.8887 (0.8027 to 0.9386)	0.9646 (0.8941 to 0.9884)	0.9499 (0.8142 to 0.9873)	0.7285 (0.5653 to 0.8387)	
22 Months	0.8887 (0.8027 to 0.9386)	0.9646 (0.8941 to 0.9884)	0.9499 (0.8142 to 0.9873)	0.7285 (0.5653 to 0.8387)	
24 Months	0.8887 (0.8027 to 0.9386)	0.9295 (0.8358 to 0.9706)	0.9499 (0.8142 to 0.9873)	0.7285 (0.5653 to 0.8387)	
26 Months	0.8713 (0.7775 to 0.9273)	0.9295 (0.8358 to 0.9706)	0.9499 (0.8142 to 0.9873)	0.7285 (0.5653 to 0.8387)	
Number of patients at risk[c]					
2 Months	89	85	44	53	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.3 Treatment emergent serious adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	82	82	40	49	
6 Months	74	78	34	43	
8 Months	69	76	29	40	
10 Months	66	73	28	35	
12 Months	63	69	24	33	
14 Months	61	69	22	33	
16 Months	57	65	19	26	
18 Months	54	62	17	24	
20 Months	52	59	15	23	
22 Months	51	55	14	20	
24 Months	51	51	13	19	
26 Months	48	47	12	17	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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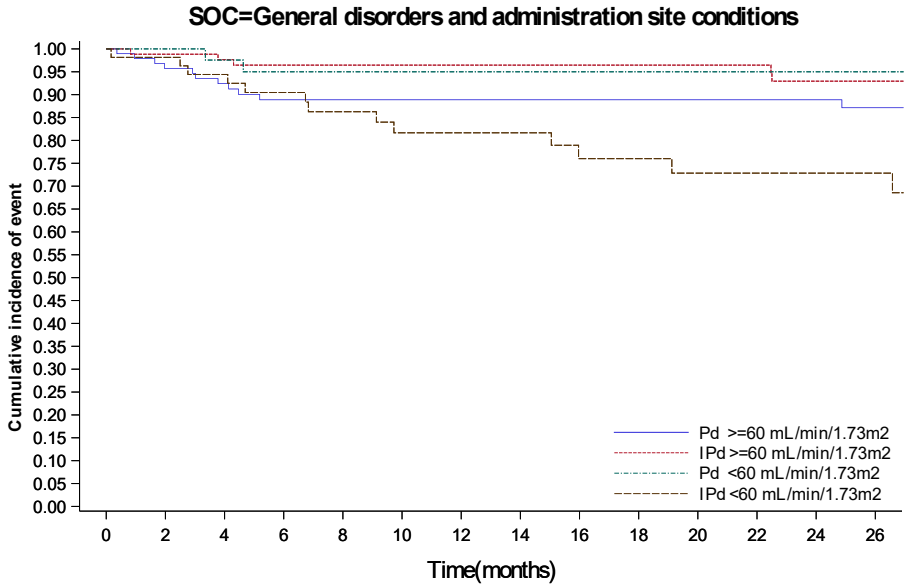
16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.4 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population



Number at Risk

Pd >=60 mL/min/1.73m2	94	89	82	74	69	66	63	61	57	54	52	51	51	48
IPd >=60 mL/min/1.73m2	86	85	82	78	76	73	69	69	65	62	59	55	51	47
Pd <60 mL/min/1.73m2	47	44	40	34	29	28	24	22	19	17	15	14	13	12
IPd <60 mL/min/1.73m2	54	53	49	43	40	35	33	33	26	24	23	20	19	17

SOC are presented if at least 5% of patients in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.5 Treatment emergent serious adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
Disease progression (days)					
Number (%) of events	6 (6.4)	1 (1.2)	1 (2.1)	5 (9.3)	0.0415
Number (%) of patients censored	88 (93.6)	85 (98.8)	46 (97.9)	49 (90.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.1211 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0502		0.1154	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.1571 (0.0188 to 1.3119)		4.8745 (0.5573 to 42.6348)	
P-value	-	0.0874		0.1523	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.5 Treatment emergent serious adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]					
2 Months	0.9784 (0.9163 to 0.9945)	0.9884 (0.9203 to 0.9984)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9561 (0.8873 to 0.9833)	0.9884 (0.9203 to 0.9984)	0.9756 (0.8392 to 0.9965)	0.9815 (0.8757 to 0.9974)	
6 Months	0.9445 (0.8717 to 0.9765)	0.9884 (0.9203 to 0.9984)	0.9756 (0.8392 to 0.9965)	0.9414 (0.8289 to 0.9807)	
8 Months	0.9445 (0.8717 to 0.9765)	0.9884 (0.9203 to 0.9984)	0.9756 (0.8392 to 0.9965)	0.9200 (0.8003 to 0.9693)	
10 Months	0.9445 (0.8717 to 0.9765)	0.9884 (0.9203 to 0.9984)	0.9756 (0.8392 to 0.9965)	0.9200 (0.8003 to 0.9693)	
12 Months	0.9445 (0.8717 to 0.9765)	0.9884 (0.9203 to 0.9984)	0.9756 (0.8392 to 0.9965)	0.9200 (0.8003 to 0.9693)	
14 Months	0.9445 (0.8717 to 0.9765)	0.9884 (0.9203 to 0.9984)	0.9756 (0.8392 to 0.9965)	0.9200 (0.8003 to 0.9693)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.5 Treatment emergent serious adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.9445 (0.8717 to 0.9765)	0.9884 (0.9203 to 0.9984)	0.9756 (0.8392 to 0.9965)	0.9200 (0.8003 to 0.9693)	
18 Months	0.9445 (0.8717 to 0.9765)	0.9884 (0.9203 to 0.9984)	0.9756 (0.8392 to 0.9965)	0.9200 (0.8003 to 0.9693)	
20 Months	0.9445 (0.8717 to 0.9765)	0.9884 (0.9203 to 0.9984)	0.9756 (0.8392 to 0.9965)	0.8846 (0.7360 to 0.9521)	
22 Months	0.9445 (0.8717 to 0.9765)	0.9884 (0.9203 to 0.9984)	0.9756 (0.8392 to 0.9965)	0.8846 (0.7360 to 0.9521)	
24 Months	0.9445 (0.8717 to 0.9765)	0.9884 (0.9203 to 0.9984)	0.9756 (0.8392 to 0.9965)	0.8846 (0.7360 to 0.9521)	
26 Months	0.9263 (0.8402 to 0.9669)	0.9884 (0.9203 to 0.9984)	0.9756 (0.8392 to 0.9965)	0.8846 (0.7360 to 0.9521)	
Number of patients at risk[c]					
2 Months	90	85	44	54	
4 Months	84	83	40	50	
6 Months	77	78	34	44	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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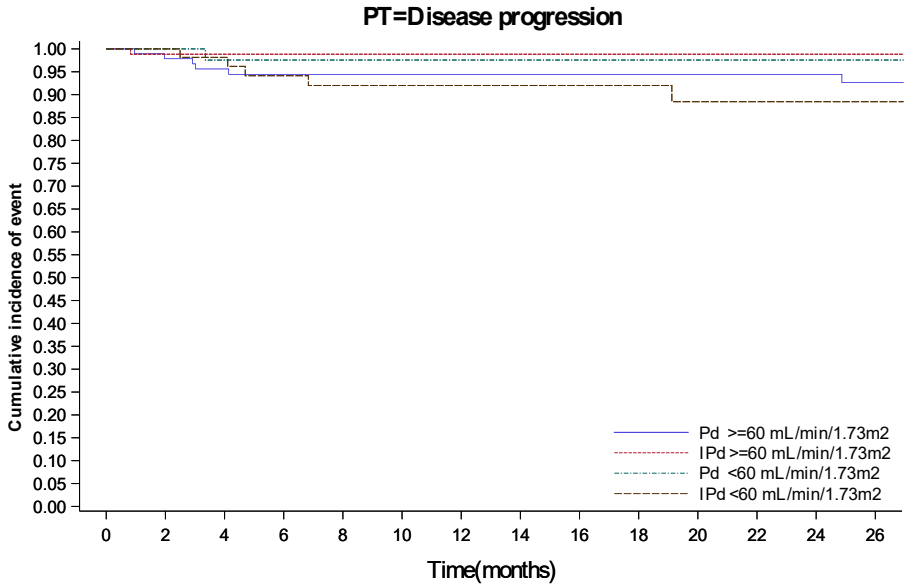
16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.5 Treatment emergent serious adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	71	76	29	42	
10 Months	68	73	28	38	
12 Months	65	69	24	35	
14 Months	63	69	22	34	
16 Months	59	65	19	29	
18 Months	55	62	17	26	
20 Months	53	59	15	25	
22 Months	52	55	14	20	
24 Months	52	53	13	19	
26 Months	49	49	12	17	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_seraept_crcl_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population



Number at Risk

Pd >=60 mL/min/1.73m2	94	90	84	77	71	68	65	63	59	55	53	52	52	49
IPd >=60 mL/min/1.73m2	86	85	83	78	76	73	69	69	65	62	59	55	53	49
Pd <60 mL/min/1.73m2	47	44	40	34	29	28	24	22	19	17	15	14	13	12
IPd <60 mL/min/1.73m2	54	54	50	44	42	38	35	34	29	26	25	20	19	17

PT are presented if at least 5% of patients in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_seraept_crcl_s_f_x.rtf (17NOV2020 14:45)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.7 Treatment emergent not severe adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
Arthralgia (days)					
Number (%) of events	8 (8.5)	11 (12.8)	7 (14.9)	2 (3.7)	0.0360
Number (%) of patients censored	86 (91.5)	75 (87.2)	40 (85.1)	52 (96.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.6037 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3554		0.0243	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.5341 (0.6149 to 3.8275)		0.1911 (0.0388 to 0.9404)	
P-value	-	0.3590		0.0418	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.7 Treatment emergent not severe adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]					
2 Months	0.9785 (0.9167 to 0.9946)	0.9535 (0.8808 to 0.9823)	0.9342 (0.8097 to 0.9783)	0.9815 (0.8757 to 0.9974)	
4 Months	0.9338 (0.8584 to 0.9697)	0.9177 (0.8351 to 0.9599)	0.9342 (0.8097 to 0.9783)	0.9815 (0.8757 to 0.9974)	
6 Months	0.9338 (0.8584 to 0.9697)	0.9177 (0.8351 to 0.9599)	0.9075 (0.7709 to 0.9645)	0.9815 (0.8757 to 0.9974)	
8 Months	0.9204 (0.8398 to 0.9614)	0.8911 (0.8009 to 0.9419)	0.8438 (0.6802 to 0.9279)	0.9815 (0.8757 to 0.9974)	
10 Months	0.9204 (0.8398 to 0.9614)	0.8911 (0.8009 to 0.9419)	0.8438 (0.6802 to 0.9279)	0.9815 (0.8757 to 0.9974)	
12 Months	0.9204 (0.8398 to 0.9614)	0.8770 (0.7828 to 0.9320)	0.8438 (0.6802 to 0.9279)	0.9815 (0.8757 to 0.9974)	
14 Months	0.9204 (0.8398 to 0.9614)	0.8770 (0.7828 to 0.9320)	0.7969 (0.6073 to 0.9018)	0.9526 (0.8177 to 0.9884)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.7 Treatment emergent not severe adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.9204 (0.8398 to 0.9614)	0.8770 (0.7828 to 0.9320)	0.7969 (0.6073 to 0.9018)	0.9526 (0.8177 to 0.9884)	
18 Months	0.9030 (0.8131 to 0.9510)	0.8770 (0.7828 to 0.9320)	0.7969 (0.6073 to 0.9018)	0.9526 (0.8177 to 0.9884)	
20 Months	0.9030 (0.8131 to 0.9510)	0.8770 (0.7828 to 0.9320)	0.7969 (0.6073 to 0.9018)	0.9526 (0.8177 to 0.9884)	
22 Months	0.9030 (0.8131 to 0.9510)	0.8770 (0.7828 to 0.9320)	0.7969 (0.6073 to 0.9018)	0.9526 (0.8177 to 0.9884)	
24 Months	0.9030 (0.8131 to 0.9510)	0.8770 (0.7828 to 0.9320)	0.7969 (0.6073 to 0.9018)	0.9526 (0.8177 to 0.9884)	
26 Months	0.9030 (0.8131 to 0.9510)	0.8770 (0.7828 to 0.9320)	0.7969 (0.6073 to 0.9018)	0.9526 (0.8177 to 0.9884)	
Number of patients at risk[c]					
2 Months	89	81	41	53	
4 Months	81	76	38	49	
6 Months	73	71	30	44	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.7 Treatment emergent not severe adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	66	67	24	41	
10 Months	64	64	23	37	
12 Months	61	60	19	34	
14 Months	57	60	16	32	
16 Months	53	57	14	27	
18 Months	49	54	12	24	
20 Months	47	53	11	23	
22 Months	47	49	10	19	
24 Months	47	47	9	18	
26 Months	45	43	8	16	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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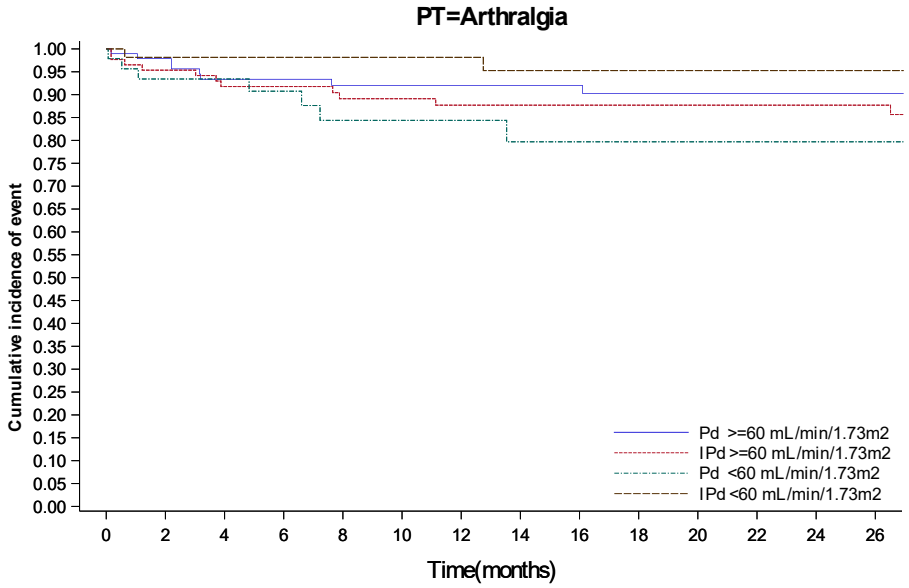
16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.8 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population



Number at Risk

Pd >=60 mL/min/1.73m2	94	89	81	73	66	64	61	57	53	49	47	47	47	45
IPd >=60 mL/min/1.73m2	86	81	76	71	67	64	60	60	57	54	53	49	47	43
Pd <60 mL/min/1.73m2	47	41	38	30	24	23	19	16	14	12	11	10	9	8
IPd <60 mL/min/1.73m2	54	53	49	44	41	37	34	32	27	24	23	19	18	16

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_crcl_s_f_x.rtf (17NOV2020 14:45)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.9 Treatment emergent severe adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
Respiratory, thoracic and mediastinal disorders (days)					
Number (%) of events	4 (4.3)	9 (10.5)	7 (14.9)	4 (7.4)	0.0464
Number (%) of patients censored	90 (95.7)	77 (89.5)	40 (85.1)	50 (92.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	26.4805 (7.2279 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1227		0.1249	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.4617 (0.7546 to 8.0306)		0.3833 (0.1082 to 1.3578)	
P-value	-	0.1354		0.1373	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.9 Treatment emergent severe adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]					
2 Months	0.9894 (0.9269 to 0.9985)	0.9535 (0.8808 to 0.9823)	0.9565 (0.8369 to 0.9889)	0.9815 (0.8757 to 0.9974)	
4 Months	0.9894 (0.9269 to 0.9985)	0.9416 (0.8653 to 0.9753)	0.9565 (0.8369 to 0.9889)	0.9622 (0.8573 to 0.9904)	
6 Months	0.9768 (0.9101 to 0.9942)	0.9292 (0.8491 to 0.9676)	0.9320 (0.8031 to 0.9776)	0.9622 (0.8573 to 0.9904)	
8 Months	0.9768 (0.9101 to 0.9942)	0.9032 (0.8154 to 0.9504)	0.8987 (0.7473 to 0.9616)	0.9388 (0.8207 to 0.9800)	
10 Months	0.9633 (0.8898 to 0.9881)	0.8897 (0.7984 to 0.9412)	0.8627 (0.6940 to 0.9421)	0.9388 (0.8207 to 0.9800)	
12 Months	0.9633 (0.8898 to 0.9881)	0.8897 (0.7984 to 0.9412)	0.8627 (0.6940 to 0.9421)	0.9103 (0.7746 to 0.9660)	
14 Months	0.9485 (0.8674 to 0.9805)	0.8897 (0.7984 to 0.9412)	0.8196 (0.6305 to 0.9178)	0.9103 (0.7746 to 0.9660)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.9 Treatment emergent severe adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.9485 (0.8674 to 0.9805)	0.8897 (0.7984 to 0.9412)	0.8196 (0.6305 to 0.9178)	0.9103 (0.7746 to 0.9660)	
18 Months	0.9485 (0.8674 to 0.9805)	0.8897 (0.7984 to 0.9412)	0.8196 (0.6305 to 0.9178)	0.9103 (0.7746 to 0.9660)	
20 Months	0.9485 (0.8674 to 0.9805)	0.8897 (0.7984 to 0.9412)	0.8196 (0.6305 to 0.9178)	0.9103 (0.7746 to 0.9660)	
22 Months	0.9485 (0.8674 to 0.9805)	0.8897 (0.7984 to 0.9412)	0.8196 (0.6305 to 0.9178)	0.9103 (0.7746 to 0.9660)	
24 Months	0.9485 (0.8674 to 0.9805)	0.8897 (0.7984 to 0.9412)	0.8196 (0.6305 to 0.9178)	0.9103 (0.7746 to 0.9660)	
26 Months	0.9485 (0.8674 to 0.9805)	0.8897 (0.7984 to 0.9412)	0.8196 (0.6305 to 0.9178)	0.9103 (0.7746 to 0.9660)	
Number of patients at risk[c]					
2 Months	91	81	42	53	
4 Months	87	78	39	48	
6 Months	78	73	31	43	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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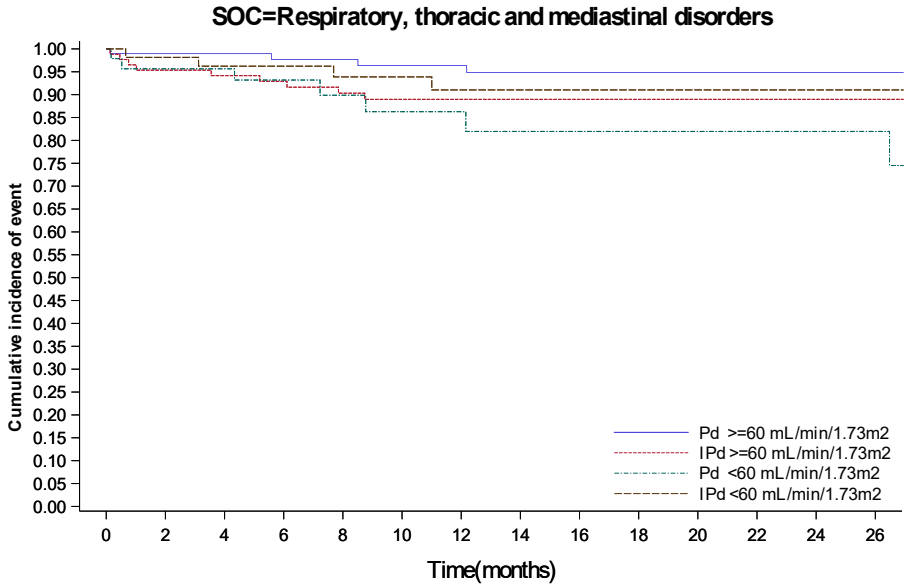
16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.9 Treatment emergent severe adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	72	69	26	39	
10 Months	68	65	24	35	
12 Months	65	61	20	31	
14 Months	60	61	18	30	
16 Months	56	57	16	26	
18 Months	52	54	15	23	
20 Months	50	51	13	22	
22 Months	49	48	12	18	
24 Months	49	46	11	17	
26 Months	47	43	11	15	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae34soc_crcl_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.10 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population



Number at Risk

Pd >=60 mL/min/1.73m2	94	91	87	78	72	68	65	60	56	52	50	49	49	47
IPd >=60 mL/min/1.73m2	86	81	78	73	69	65	61	61	57	54	51	48	46	43
Pd <60 mL/min/1.73m2	47	42	39	31	26	24	20	18	16	15	13	12	11	11
IPd <60 mL/min/1.73m2	54	53	48	43	39	35	31	30	26	23	22	18	17	15

SOC are presented if at least 5% of patients in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae34soc_crcl_s_f_x.rtf (17NOV2020 14:45)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.11 Treatment emergent severe adverse event including death per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
Respiratory, thoracic and mediastinal disorders (days)					
Number (%) of events	4 (4.3)	9 (10.5)	7 (14.9)	4 (7.4)	0.0464
Number (%) of patients censored	90 (95.7)	77 (89.5)	40 (85.1)	50 (92.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	26.4805 (7.2279 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.1227		0.1249	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.4617 (0.7546 to 8.0306)		0.3833 (0.1082 to 1.3578)	
P-value	-	0.1354		0.1373	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae345soc_crcl_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.11 Treatment emergent severe adverse event including death per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]					
2 Months	0.9894 (0.9269 to 0.9985)	0.9535 (0.8808 to 0.9823)	0.9565 (0.8369 to 0.9889)	0.9815 (0.8757 to 0.9974)	
4 Months	0.9894 (0.9269 to 0.9985)	0.9416 (0.8653 to 0.9753)	0.9565 (0.8369 to 0.9889)	0.9622 (0.8573 to 0.9904)	
6 Months	0.9768 (0.9101 to 0.9942)	0.9292 (0.8491 to 0.9676)	0.9320 (0.8031 to 0.9776)	0.9622 (0.8573 to 0.9904)	
8 Months	0.9768 (0.9101 to 0.9942)	0.9032 (0.8154 to 0.9504)	0.8987 (0.7473 to 0.9616)	0.9388 (0.8207 to 0.9800)	
10 Months	0.9633 (0.8898 to 0.9881)	0.8897 (0.7984 to 0.9412)	0.8627 (0.6940 to 0.9421)	0.9388 (0.8207 to 0.9800)	
12 Months	0.9633 (0.8898 to 0.9881)	0.8897 (0.7984 to 0.9412)	0.8627 (0.6940 to 0.9421)	0.9103 (0.7746 to 0.9660)	
14 Months	0.9485 (0.8674 to 0.9805)	0.8897 (0.7984 to 0.9412)	0.8196 (0.6305 to 0.9178)	0.9103 (0.7746 to 0.9660)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.11 Treatment emergent severe adverse event including death per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.9485 (0.8674 to 0.9805)	0.8897 (0.7984 to 0.9412)	0.8196 (0.6305 to 0.9178)	0.9103 (0.7746 to 0.9660)	
18 Months	0.9485 (0.8674 to 0.9805)	0.8897 (0.7984 to 0.9412)	0.8196 (0.6305 to 0.9178)	0.9103 (0.7746 to 0.9660)	
20 Months	0.9485 (0.8674 to 0.9805)	0.8897 (0.7984 to 0.9412)	0.8196 (0.6305 to 0.9178)	0.9103 (0.7746 to 0.9660)	
22 Months	0.9485 (0.8674 to 0.9805)	0.8897 (0.7984 to 0.9412)	0.8196 (0.6305 to 0.9178)	0.9103 (0.7746 to 0.9660)	
24 Months	0.9485 (0.8674 to 0.9805)	0.8897 (0.7984 to 0.9412)	0.8196 (0.6305 to 0.9178)	0.9103 (0.7746 to 0.9660)	
26 Months	0.9485 (0.8674 to 0.9805)	0.8897 (0.7984 to 0.9412)	0.8196 (0.6305 to 0.9178)	0.9103 (0.7746 to 0.9660)	
Number of patients at risk[c]					
2 Months	91	81	42	53	
4 Months	87	78	39	48	
6 Months	78	73	31	43	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.11 Treatment emergent severe adverse event including death per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Pd (N=94)	**IPd (N=86)**	**Pd (N=47)**	**IPd (N=54)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	72	69	26	39	
10 Months	68	65	24	35	
12 Months	65	61	20	31	
14 Months	60	61	18	30	
16 Months	56	57	16	26	
18 Months	52	54	15	23	
20 Months	50	51	13	22	
22 Months	49	48	12	18	
24 Months	49	46	11	17	
26 Months	47	43	11	15	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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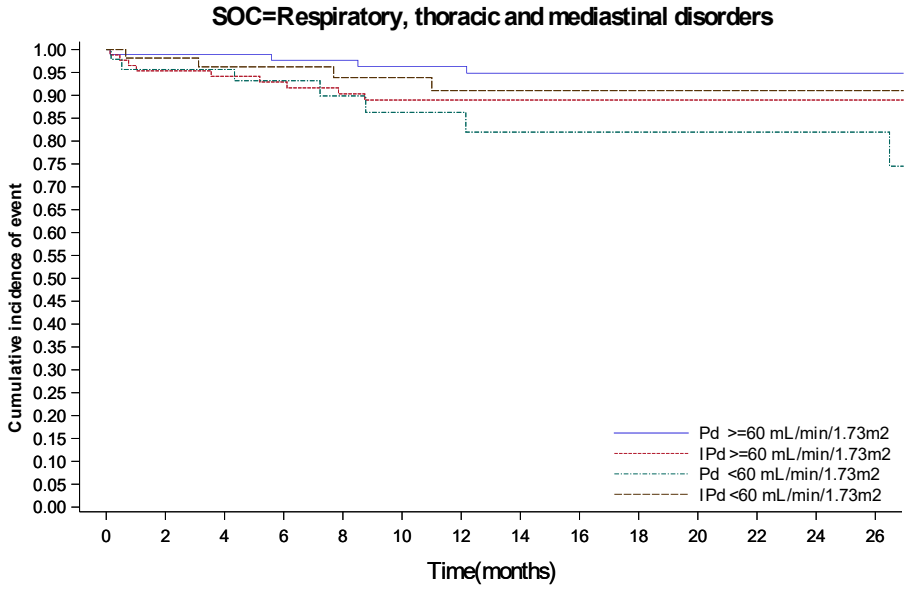
16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.54.12 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population



Number at Risk

Pd >=60 mL/min/1.73m2	94	91	87	78	72	68	65	60	56	52	50	49	49	47
IPd >=60 mL/min/1.73m2	86	81	78	73	69	65	61	61	57	54	51	48	46	43
Pd <60 mL/min/1.73m2	47	42	39	31	26	24	20	18	16	15	13	12	11	11
IPd <60 mL/min/1.73m2	54	53	48	43	39	35	31	30	26	23	22	18	17	15

SOC are presented if at least 5% of patients in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.1 Treatment emergent adverse event per SOC by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
Infections and infestations (days)					
Number (%) of events	78 (70.3)	93 (79.5)	23 (60.5)	33 (94.3)	0.0239
Number (%) of patients censored	33 (29.7)	24 (20.5)	15 (39.5)	2 (5.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	1.3142 (0.8214 to 1.5441)	0.7228 (0.4928 to 0.9856)	0.9856 (0.2628 to 2.3655)	0.4600 (0.2628 to 0.7228)	
Median (95% CI)	2.0370 (1.8070 to 3.6140)	2.6612 (1.8070 to 3.6797)	7.1622 (2.2998 to NC)	1.3142 (0.6571 to 2.2341)	
75% quantile (95% CI)	27.1704 (6.5051 to NC)	6.6694 (4.4353 to 12.5832)	NC (9.3306 to NC)	4.1725 (2.1684 to 9.1663)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2916		0.0028	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.1 Treatment emergent adverse event per SOC by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.1780 (0.8680 to 1.5987)		2.2753 (1.3094 to 3.9537)	
P-value	-	0.2931		0.0035	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.4395 (0.2529 to 0.7637)		
Events probability (95% CI)[c]					
2 Months	0.5205 (0.4225 to 0.6096)	0.5649 (0.4693 to 0.6498)	0.6791 (0.5044 to 0.8035)	0.4571 (0.2890 to 0.6105)	
4 Months	0.3828 (0.2904 to 0.4744)	0.3681 (0.2800 to 0.4562)	0.5419 (0.3699 to 0.6856)	0.2571 (0.1280 to 0.4077)	
6 Months	0.3503 (0.2598 to 0.4419)	0.2737 (0.1942 to 0.3590)	0.5419 (0.3699 to 0.6856)	0.1714 (0.0696 to 0.3113)	
8 Months	0.3144 (0.2262 to 0.4063)	0.2230 (0.1497 to 0.3056)	0.4496 (0.2832 to 0.6026)	0.1429 (0.0522 to 0.2774)	
10 Months	0.3018 (0.2144 to 0.3938)	0.2119 (0.1400 to 0.2939)	0.3804 (0.2206 to 0.5390)	0.1143 (0.0362 to 0.2423)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.1 Treatment emergent adverse event per SOC by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	0.3018 (0.2144 to 0.3938)	0.1883 (0.1195 to 0.2692)	0.3424 (0.1872 to 0.5038)	0.1143 (0.0362 to 0.2423)	
14 Months	0.2887 (0.2022 to 0.3807)	0.1648 (0.0998 to 0.2440)	0.3424 (0.1872 to 0.5038)	0.1143 (0.0362 to 0.2423)	
16 Months	0.2887 (0.2022 to 0.3807)	0.1648 (0.0998 to 0.2440)	0.3424 (0.1872 to 0.5038)	0.0857 (0.0220 to 0.2057)	
18 Months	0.2717 (0.1855 to 0.3651)	0.1648 (0.0998 to 0.2440)	0.3424 (0.1872 to 0.5038)	0.0571 (0.0103 to 0.1672)	
20 Months	0.2536 (0.1678 to 0.3484)	0.1648 (0.0998 to 0.2440)	0.3424 (0.1872 to 0.5038)	0.0571 (0.0103 to 0.1672)	
22 Months	0.2536 (0.1678 to 0.3484)	0.1648 (0.0998 to 0.2440)	0.3424 (0.1872 to 0.5038)	0.0571 (0.0103 to 0.1672)	
24 Months	0.2536 (0.1678 to 0.3484)	0.1648 (0.0998 to 0.2440)	0.3424 (0.1872 to 0.5038)	0.0571 (0.0103 to 0.1672)	
26 Months	0.2536 (0.1678 to 0.3484)	0.1648 (0.0998 to 0.2440)	0.3424 (0.1872 to 0.5038)	0.0571 (0.0103 to 0.1672)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.1 Treatment emergent adverse event per SOC by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
Number of patients at risk[c]					
2 Months	55	64	25	16	
4 Months	38	40	19	9	
6 Months	31	27	18	6	
8 Months	26	22	13	5	
10 Months	24	19	11	4	
12 Months	23	16	9	4	
14 Months	20	14	9	4	
16 Months	17	13	9	3	
18 Months	15	11	9	2	
20 Months	13	10	8	2	
22 Months	13	9	6	2	
24 Months	12	9	6	2	
26 Months	11	7	5	2	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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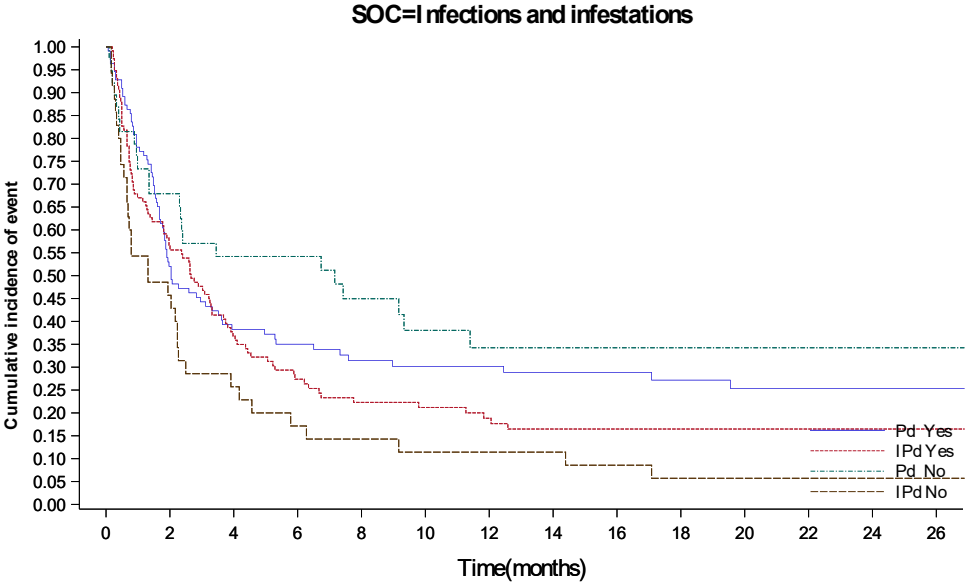
16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per SOC by treatment group according to refractory to PI - Safety population



Number at Risk

Pd Yes	111	55	38	31	26	24	23	20	17	15	13	13	12	11
IPd Yes	116	64	40	27	22	19	16	14	13	11	10	9	9	7
Pd No	38	25	19	18	13	11	9	9	9	9	8	6	6	5
IPd No	35	16	9	6	5	4	4	4	3	2	2	2	2	2

SOC are presented if at least 10 events in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.3 Treatment emergent adverse event per PT by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
Urinary tract infection (days)					
Number (%) of events	13 (11.7)	12 (10.3)	1 (2.6)	7 (20.0)	0.0425
Number (%) of patients censored	98 (88.3)	105 (89.7)	37 (97.4)	28 (80.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	32.7556 (2.0370 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.5492		0.0377	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.7867 (0.3582 to 1.7278)		6.9133 (0.8306 to 57.5425)	
P-value	-	0.5501		0.0737	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.3 Treatment emergent adverse event per PT by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]					
2 Months	0.9533 (0.8915 to 0.9803)	0.9655 (0.9107 to 0.9869)	0.9730 (0.8232 to 0.9961)	0.9143 (0.7573 to 0.9715)	
4 Months	0.9133 (0.8398 to 0.9540)	0.9219 (0.8552 to 0.9586)	0.9730 (0.8232 to 0.9961)	0.8857 (0.7236 to 0.9555)	
6 Months	0.9023 (0.8257 to 0.9463)	0.9219 (0.8552 to 0.9586)	0.9730 (0.8232 to 0.9961)	0.8857 (0.7236 to 0.9555)	
8 Months	0.8647 (0.7771 to 0.9196)	0.9219 (0.8552 to 0.9586)	0.9730 (0.8232 to 0.9961)	0.8857 (0.7236 to 0.9555)	
10 Months	0.8647 (0.7771 to 0.9196)	0.9219 (0.8552 to 0.9586)	0.9730 (0.8232 to 0.9961)	0.8857 (0.7236 to 0.9555)	
12 Months	0.8647 (0.7771 to 0.9196)	0.9103 (0.8392 to 0.9509)	0.9730 (0.8232 to 0.9961)	0.8857 (0.7236 to 0.9555)	
14 Months	0.8647 (0.7771 to 0.9196)	0.9103 (0.8392 to 0.9509)	0.9730 (0.8232 to 0.9961)	0.8857 (0.7236 to 0.9555)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.3 Treatment emergent adverse event per PT by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.8647 (0.7771 to 0.9196)	0.9103 (0.8392 to 0.9509)	0.9730 (0.8232 to 0.9961)	0.8472 (0.6679 to 0.9341)	
18 Months	0.8647 (0.7771 to 0.9196)	0.8965 (0.8191 to 0.9420)	0.9730 (0.8232 to 0.9961)	0.8472 (0.6679 to 0.9341)	
20 Months	0.8647 (0.7771 to 0.9196)	0.8965 (0.8191 to 0.9420)	0.9730 (0.8232 to 0.9961)	0.8472 (0.6679 to 0.9341)	
22 Months	0.8647 (0.7771 to 0.9196)	0.8965 (0.8191 to 0.9420)	0.9730 (0.8232 to 0.9961)	0.8001 (0.5995 to 0.9074)	
24 Months	0.8647 (0.7771 to 0.9196)	0.8796 (0.7935 to 0.9314)	0.9730 (0.8232 to 0.9961)	0.8001 (0.5995 to 0.9074)	
26 Months	0.8647 (0.7771 to 0.9196)	0.8796 (0.7935 to 0.9314)	0.9730 (0.8232 to 0.9961)	0.8001 (0.5995 to 0.9074)	
Number of patients at risk[c]					
2 Months	100	111	36	32	
4 Months	90	102	35	28	
6 Months	77	93	31	26	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.3 Treatment emergent adverse event per PT by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	66	89	28	26	
10 Months	62	82	28	26	
12 Months	58	76	26	24	
14 Months	52	75	26	24	
16 Months	47	67	25	21	
18 Months	44	62	24	19	
20 Months	41	59	23	19	
22 Months	41	53	21	16	
24 Months	40	49	21	16	
26 Months	38	44	20	15	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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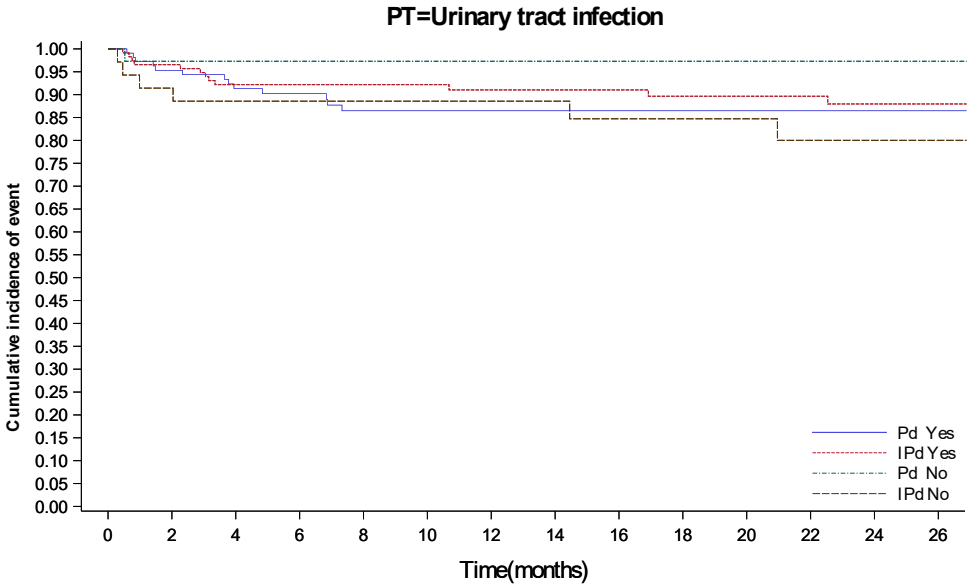
16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to refractory to PI - Safety population



Number at Risk

Pd Yes	111	100	90	77	66	62	58	52	47	44	41	41	40	38
IPd Yes	117	111	102	93	89	82	76	75	67	62	59	53	49	44
Pd No	38	36	35	31	28	28	26	26	25	24	23	21	21	20
IPd No	35	32	28	26	26	26	24	24	21	19	19	16	16	15

PT are presented if at least 10 events in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.5 Treatment emergent serious adverse event per SOC by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
Infections and infestations (days)					
Number (%) of events	43 (38.7)	53 (45.3)	11 (28.9)	23 (65.7)	0.0211
Number (%) of patients censored	68 (61.3)	64 (54.7)	27 (71.1)	12 (34.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	3.5154 (1.9384 to 9.0021)	5.6181 (2.7269 to 8.8049)	13.7988 (2.2998 to NC)	2.2998 (0.7228 to 6.2752)	
Median (95% CI)	NC (17.0842 to NC)	24.8706 (14.4887 to NC)	NC (24.2136 to NC)	9.9548 (4.1725 to 25.9220)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	35.7782 (15.1458 to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.8180		0.0048	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.5 Treatment emergent serious adverse event per SOC by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio (95% CI) vs Pd	-	1.0487 (0.6991 to 1.5732)		2.7535 (1.3238 to 5.7271)	
P-value	-	0.8183		0.0067	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.3632 (0.1746 to 0.7554)		
Events probability (95% CI)[c]					
2 Months	0.8255 (0.7402 to 0.8850)	0.8436 (0.7632 to 0.8984)	0.9196 (0.7710 to 0.9733)	0.8000 (0.6258 to 0.8992)	
4 Months	0.7393 (0.6451 to 0.8122)	0.7994 (0.7137 to 0.8619)	0.7834 (0.6131 to 0.8853)	0.7119 (0.5304 to 0.8335)	
6 Months	0.6982 (0.6006 to 0.7763)	0.7253 (0.6327 to 0.7983)	0.7834 (0.6131 to 0.8853)	0.6190 (0.4349 to 0.7586)	
8 Months	0.6758 (0.5763 to 0.7568)	0.6861 (0.5906 to 0.7638)	0.7834 (0.6131 to 0.8853)	0.5865 (0.4024 to 0.7314)	
10 Months	0.6635 (0.5628 to 0.7462)	0.6561 (0.5588 to 0.7370)	0.7834 (0.6131 to 0.8853)	0.4887 (0.3102 to 0.6454)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.5 Treatment emergent serious adverse event per SOC by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	0.6380 (0.5348 to 0.7241)	0.6032 (0.5033 to 0.6892)	0.7834 (0.6131 to 0.8853)	0.4887 (0.3102 to 0.6454)	
14 Months	0.6380 (0.5348 to 0.7241)	0.6032 (0.5033 to 0.6892)	0.7494 (0.5718 to 0.8616)	0.4887 (0.3102 to 0.6454)	
16 Months	0.6224 (0.5171 to 0.7111)	0.5916 (0.4911 to 0.6787)	0.7137 (0.5299 to 0.8360)	0.4189 (0.2474 to 0.5816)	
18 Months	0.6056 (0.4978 to 0.6972)	0.5795 (0.4783 to 0.6679)	0.7137 (0.5299 to 0.8360)	0.4189 (0.2474 to 0.5816)	
20 Months	0.5872 (0.4766 to 0.6822)	0.5394 (0.4357 to 0.6321)	0.7137 (0.5299 to 0.8360)	0.3770 (0.2092 to 0.5443)	
22 Months	0.5872 (0.4766 to 0.6822)	0.5259 (0.4216 to 0.6199)	0.7137 (0.5299 to 0.8360)	0.3770 (0.2092 to 0.5443)	
24 Months	0.5683 (0.4550 to 0.6665)	0.5259 (0.4216 to 0.6199)	0.7137 (0.5299 to 0.8360)	0.3299 (0.1672 to 0.5028)	
26 Months	0.5683 (0.4550 to 0.6665)	0.4945 (0.3880 to 0.5922)	0.6717 (0.4794 to 0.8062)	0.2828 (0.1290 to 0.4588)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.5 Treatment emergent serious adverse event per SOC by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
Number of patients at risk[c]					
2 Months	88	96	34	28	
4 Months	76	89	28	23	
6 Months	65	75	27	19	
8 Months	56	70	25	18	
10 Months	54	64	25	15	
12 Months	49	55	23	15	
14 Months	44	54	22	15	
16 Months	39	49	20	11	
18 Months	33	44	20	10	
20 Months	31	40	19	9	
22 Months	31	36	17	8	
24 Months	29	34	17	7	
26 Months	28	28	15	6	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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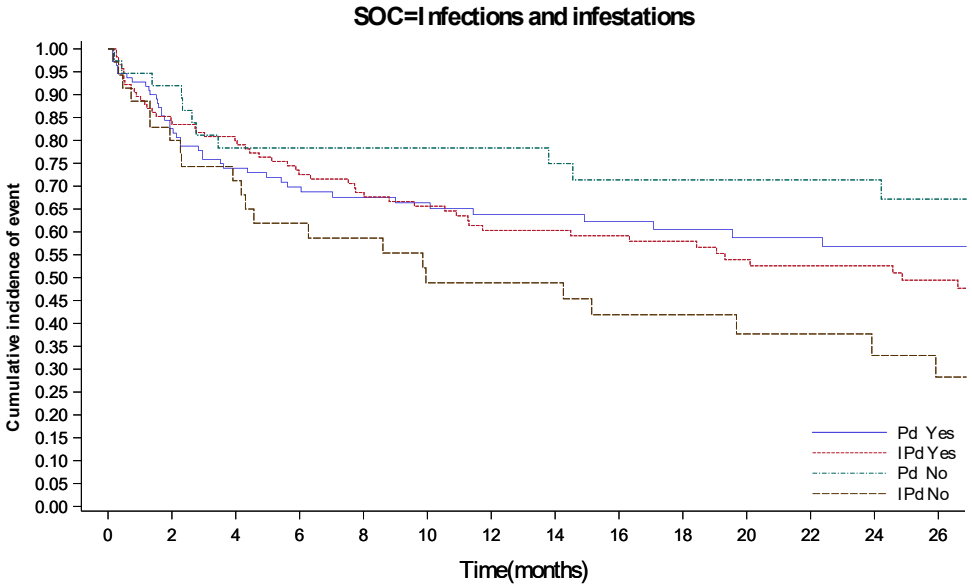
16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event per SOC by treatment group according to refractory to PI - Safety population



Number at Risk

Pd Yes	111	88	76	65	56	54	49	44	39	33	31	31	29	28
IPd Yes	116	96	89	75	70	64	55	54	49	44	40	36	34	28
Pd No	38	34	28	27	25	25	23	22	20	20	19	17	17	15
IPd No	35	28	23	19	18	15	15	15	11	10	9	8	7	6

SOC are presented if at least 5% of patients in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.7 Treatment emergent not severe adverse event per PT by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
Pyrexia (days)					
Number (%) of events	16 (14.4)	13 (11.1)	3 (7.9)	10 (28.6)	0.0270
Number (%) of patients censored	95 (85.6)	104 (88.9)	35 (92.1)	25 (71.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (10.9405 to NC)	NC (37.5195 to NC)	NC (NC to NC)	9.7248 (3.2526 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (34.9569 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.2587		0.0413	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.6559 (0.3138 to 1.3707)		3.5377 (0.9699 to 12.9030)	
P-value	-	0.2621		0.0557	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.7 Treatment emergent not severe adverse event per PT by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]					
2 Months	0.9255 (0.8565 to 0.9620)	0.9573 (0.9004 to 0.9820)	0.9196 (0.7710 to 0.9733)	0.9429 (0.7903 to 0.9854)	
4 Months	0.8955 (0.8192 to 0.9408)	0.9396 (0.8775 to 0.9708)	0.9196 (0.7710 to 0.9733)	0.8819 (0.7148 to 0.9540)	
6 Months	0.8740 (0.7925 to 0.9250)	0.9396 (0.8775 to 0.9708)	0.9196 (0.7710 to 0.9733)	0.8492 (0.6741 to 0.9345)	
8 Months	0.8624 (0.7780 to 0.9163)	0.9296 (0.8640 to 0.9642)	0.9196 (0.7710 to 0.9733)	0.7785 (0.5885 to 0.8884)	
10 Months	0.8497 (0.7621 to 0.9070)	0.9189 (0.8495 to 0.9571)	0.9196 (0.7710 to 0.9733)	0.7431 (0.5489 to 0.8633)	
12 Months	0.8360 (0.7447 to 0.8968)	0.8960 (0.8189 to 0.9414)	0.9196 (0.7710 to 0.9733)	0.7431 (0.5489 to 0.8633)	
14 Months	0.8360 (0.7447 to 0.8968)	0.8960 (0.8189 to 0.9414)	0.9196 (0.7710 to 0.9733)	0.7077 (0.5108 to 0.8370)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.7 Treatment emergent not severe adverse event per PT by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.8360 (0.7447 to 0.8968)	0.8824 (0.8003 to 0.9321)	0.9196 (0.7710 to 0.9733)	0.7077 (0.5108 to 0.8370)	
18 Months	0.8360 (0.7447 to 0.8968)	0.8824 (0.8003 to 0.9321)	0.9196 (0.7710 to 0.9733)	0.7077 (0.5108 to 0.8370)	
20 Months	0.8360 (0.7447 to 0.8968)	0.8824 (0.8003 to 0.9321)	0.9196 (0.7710 to 0.9733)	0.7077 (0.5108 to 0.8370)	
22 Months	0.8360 (0.7447 to 0.8968)	0.8824 (0.8003 to 0.9321)	0.9196 (0.7710 to 0.9733)	0.7077 (0.5108 to 0.8370)	
24 Months	0.8360 (0.7447 to 0.8968)	0.8824 (0.8003 to 0.9321)	0.9196 (0.7710 to 0.9733)	0.7077 (0.5108 to 0.8370)	
26 Months	0.8360 (0.7447 to 0.8968)	0.8824 (0.8003 to 0.9321)	0.9196 (0.7710 to 0.9733)	0.7077 (0.5108 to 0.8370)	
Number of patients at risk[c]					
2 Months	97	111	34	32	
4 Months	89	105	33	28	
6 Months	76	95	29	25	

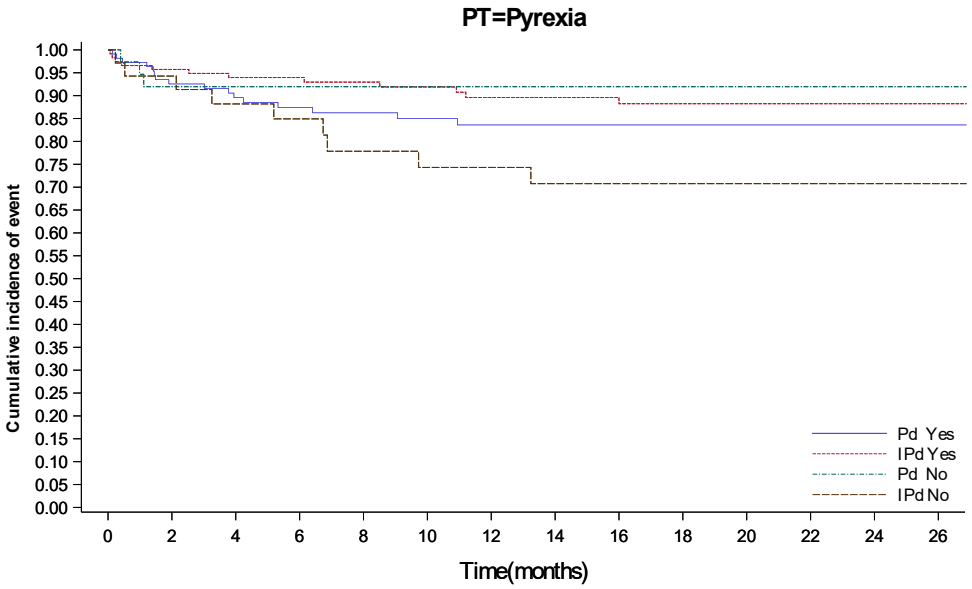
PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_pi_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.7 Treatment emergent not severe adverse event per PT by treatment group according to refractory to PI - Safety population

	Yes		No		
	Pd (N=111)	**IPd (N=117)**	**Pd (N=38)**	**IPd (N=35)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	71	90	26	22	
10 Months	66	82	26	21	
12 Months	58	75	24	21	
14 Months	53	74	24	20	
16 Months	47	66	23	18	
18 Months	42	61	22	16	
20 Months	40	59	21	15	
22 Months	40	52	19	14	
24 Months	39	49	19	14	
26 Months	37	46	18	13	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_pi_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by refractory to PI
16.2.7.1.55.8 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per PT by treatment group according to refractory to PI - Safety population



Number at Risk

Pd Yes	111	97	89	76	71	66	58	53	47	42	40	40	39	37
IPd Yes	117	111	105	95	90	82	75	74	66	61	59	52	49	46
Pd No	38	34	33	29	26	26	24	24	23	22	21	19	19	18
IPd No	35	32	28	25	22	21	21	20	18	16	15	14	14	13

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_pi_s_f_x.rtf (17NOV2020 14:45)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.1 Treatment emergent adverse event per SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
Injury, poisoning and procedural complications (days)					
Number (%) of events	8 (9.2)	52 (57.1)	10 (16.1)	23 (37.7)	0.0279
Number (%) of patients censored	79 (90.8)	39 (42.9)	52 (83.9)	38 (62.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (31.3101 to NC)	0.0986 (0.0657 to 0.1314)	NC (6.6037 to NC)	5.2238 (0.1314 to 15.4415)	
Median (95% CI)	NC (NC to NC)	0.5585 (0.1643 to NC)	NC (NC to NC)	NC (15.4415 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	<.0001		0.0111	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	9.0724 (4.2857 to 19.2052)		2.6599 (1.2156 to 5.8202)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.1 Treatment emergent adverse event per SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
P-value	-	<.0001		0.0143	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.1102 (0.0521 to 0.2333)		0.3759 (0.1718 to 0.8226)		
Events probability (95% CI)[c]					
2 Months	0.9767 (0.9102 to 0.9941)	0.4940 (0.3878 to 0.5916)	0.9318 (0.8284 to 0.9739)	0.7705 (0.6435 to 0.8571)	
4 Months	0.9520 (0.8771 to 0.9817)	0.4825 (0.3767 to 0.5805)	0.9143 (0.8061 to 0.9634)	0.7541 (0.6257 to 0.8438)	
6 Months	0.9520 (0.8771 to 0.9817)	0.4698 (0.3642 to 0.5684)	0.8956 (0.7820 to 0.9518)	0.7370 (0.6070 to 0.8298)	
8 Months	0.9374 (0.8554 to 0.9736)	0.4275 (0.3222 to 0.5286)	0.8310 (0.6986 to 0.9089)	0.7190 (0.5873 to 0.8151)	
10 Months	0.9056 (0.8106 to 0.9542)	0.4275 (0.3222 to 0.5286)	0.8310 (0.6986 to 0.9089)	0.6996 (0.5657 to 0.7992)	
12 Months	0.9056 (0.8106 to 0.9542)	0.4275 (0.3222 to 0.5286)	0.8310 (0.6986 to 0.9089)	0.6770 (0.5397 to 0.7813)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.1 Treatment emergent adverse event per SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.9056 (0.8106 to 0.9542)	0.4275 (0.3222 to 0.5286)	0.8310 (0.6986 to 0.9089)	0.6770 (0.5397 to 0.7813)	
16 Months	0.9056 (0.8106 to 0.9542)	0.4275 (0.3222 to 0.5286)	0.8310 (0.6986 to 0.9089)	0.6249 (0.4793 to 0.7404)	
18 Months	0.9056 (0.8106 to 0.9542)	0.4275 (0.3222 to 0.5286)	0.8310 (0.6986 to 0.9089)	0.6249 (0.4793 to 0.7404)	
20 Months	0.9056 (0.8106 to 0.9542)	0.4081 (0.3016 to 0.5116)	0.8310 (0.6986 to 0.9089)	0.6249 (0.4793 to 0.7404)	
22 Months	0.9056 (0.8106 to 0.9542)	0.4081 (0.3016 to 0.5116)	0.8310 (0.6986 to 0.9089)	0.6249 (0.4793 to 0.7404)	
24 Months	0.9056 (0.8106 to 0.9542)	0.4081 (0.3016 to 0.5116)	0.8310 (0.6986 to 0.9089)	0.6249 (0.4793 to 0.7404)	
26 Months	0.9056 (0.8106 to 0.9542)	0.4081 (0.3016 to 0.5116)	0.8310 (0.6986 to 0.9089)	0.6249 (0.4793 to 0.7404)	
Number of patients at risk[c]					
2 Months	81	44	54	47	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.1 Treatment emergent adverse event per SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	76	39	51	46	
6 Months	68	34	43	41	
8 Months	59	30	37	37	
10 Months	57	28	34	33	
12 Months	50	26	32	29	
14 Months	48	26	28	28	
16 Months	43	22	28	24	
18 Months	37	22	26	21	
20 Months	34	19	25	20	
22 Months	32	16	25	19	
24 Months	32	16	24	18	
26 Months	30	15	23	16	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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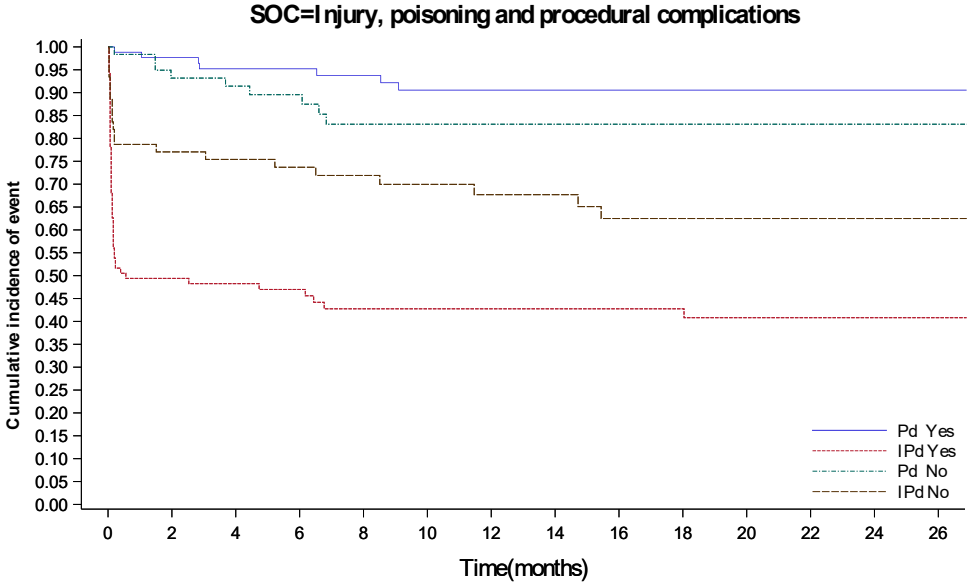
16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population



Number at Risk

Pd Yes	87	81	76	68	59	57	50	48	43	37	34	32	32	30
IPd Yes	91	44	39	34	30	28	26	26	22	22	19	16	16	15
Pd No	61	54	51	43	37	34	32	28	28	26	25	25	24	23
IPd No	61	47	46	41	37	33	29	28	24	21	20	19	18	16

SOC are presented if at least 10 events in a arm
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.3 Treatment emergent adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
Diarrhoea (days)					
Number (%) of events	12 (13.8)	28 (30.8)	21 (33.9)	18 (29.5)	0.0130
Number (%) of patients censored	75 (86.2)	63 (69.2)	41 (66.1)	43 (70.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (14.8501 to NC)	8.3778 (2.2341 to 31.0801)	3.2854 (0.8871 to 33.9384)	14.9487 (3.8439 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (26.9076 to NC)	NC (21.3224 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0147		0.4108	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.2828 (1.1549 to 4.5122)		0.7641 (0.4016 to 1.4537)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.3 Treatment emergent adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
P-value	-	0.0176		0.4122	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.4381 (0.2216 to 0.8659)				
Events probability (95% CI)[c]					
2 Months	0.9529 (0.8794 to 0.9821)	0.8450 (0.7523 to 0.9051)	0.8175 (0.6946 to 0.8945)	0.9016 (0.7941 to 0.9546)	
4 Months	0.9404 (0.8626 to 0.9748)	0.8095 (0.7114 to 0.8771)	0.6953 (0.5604 to 0.7961)	0.8515 (0.7341 to 0.9199)	
6 Months	0.9119 (0.8233 to 0.9572)	0.8095 (0.7114 to 0.8771)	0.6953 (0.5604 to 0.7961)	0.8175 (0.6945 to 0.8945)	
8 Months	0.8964 (0.8024 to 0.9471)	0.7542 (0.6470 to 0.8329)	0.6953 (0.5604 to 0.7961)	0.7997 (0.6740 to 0.8810)	
10 Months	0.8798 (0.7801 to 0.9361)	0.7397 (0.6304 to 0.8211)	0.6953 (0.5604 to 0.7961)	0.7811 (0.6526 to 0.8667)	
12 Months	0.8798 (0.7801 to 0.9361)	0.6947 (0.5800 to 0.7838)	0.6713 (0.5324 to 0.7773)	0.7594 (0.6264 to 0.8505)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.3 Treatment emergent adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.8607 (0.7536 to 0.9235)	0.6796 (0.5634 to 0.7710)	0.6713 (0.5324 to 0.7773)	0.7594 (0.6264 to 0.8505)	
16 Months	0.8402 (0.7258 to 0.9097)	0.6638 (0.5461 to 0.7576)	0.6713 (0.5324 to 0.7773)	0.7349 (0.5964 to 0.8323)	
18 Months	0.8402 (0.7258 to 0.9097)	0.6638 (0.5461 to 0.7576)	0.6713 (0.5324 to 0.7773)	0.7096 (0.5660 to 0.8131)	
20 Months	0.8147 (0.6894 to 0.8933)	0.6638 (0.5461 to 0.7576)	0.6713 (0.5324 to 0.7773)	0.6812 (0.5317 to 0.7919)	
22 Months	0.8147 (0.6894 to 0.8933)	0.6638 (0.5461 to 0.7576)	0.6713 (0.5324 to 0.7773)	0.6516 (0.4968 to 0.7693)	
24 Months	0.8147 (0.6894 to 0.8933)	0.6638 (0.5461 to 0.7576)	0.6713 (0.5324 to 0.7773)	0.6516 (0.4968 to 0.7693)	
26 Months	0.8147 (0.6894 to 0.8933)	0.6638 (0.5461 to 0.7576)	0.6713 (0.5324 to 0.7773)	0.6516 (0.4968 to 0.7693)	
Number of patients at risk[c]					
2 Months	79	75	48	54	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.3 Treatment emergent adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	74	67	39	51	
6 Months	63	60	33	46	
8 Months	54	54	31	43	
10 Months	53	50	29	38	
12 Months	48	46	28	34	
14 Months	45	45	26	33	
16 Months	39	39	25	30	
18 Months	33	37	23	26	
20 Months	29	35	22	24	
22 Months	28	31	22	22	
24 Months	28	30	21	22	
26 Months	26	27	20	20	
Muscular weakness (days)					
Number (%) of events	3 (3.4)	12 (13.2)	4 (6.5)	1 (1.6)	0.0272
Number (%) of patients censored	84 (96.6)	79 (86.8)	58 (93.5)	60 (98.4)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_llen_s_t_x.rtf (17NOV2020 9:35)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.3 Treatment emergent adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (22.5708 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0310		0.1742	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	3.6745 (1.0354 to 13.0407)		0.2460 (0.0275 to 2.2031)	
P-value	-	0.0440		0.2099	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.2721 (0.0767 to 0.9658)				
Events probability (95% CI)[c]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.3 Treatment emergent adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
2 Months	0.9885 (0.9212 to 0.9984)	0.9777 (0.9136 to 0.9944)	0.9836 (0.8893 to 0.9977)	1.0000 (1.0000 to 1.0000)	
4 Months	0.9763 (0.9085 to 0.9940)	0.9435 (0.8696 to 0.9761)	0.9475 (0.8457 to 0.9828)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9763 (0.9085 to 0.9940)	0.9313 (0.8533 to 0.9686)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
8 Months	0.9763 (0.9085 to 0.9940)	0.9176 (0.8344 to 0.9600)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
10 Months	0.9763 (0.9085 to 0.9940)	0.9176 (0.8344 to 0.9600)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
12 Months	0.9589 (0.8752 to 0.9869)	0.9030 (0.8145 to 0.9505)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
14 Months	0.9589 (0.8752 to 0.9869)	0.9030 (0.8145 to 0.9505)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
16 Months	0.9589 (0.8752 to 0.9869)	0.8548 (0.7508 to 0.9177)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.3 Treatment emergent adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
18 Months	0.9589 (0.8752 to 0.9869)	0.8548 (0.7508 to 0.9177)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
20 Months	0.9589 (0.8752 to 0.9869)	0.8548 (0.7508 to 0.9177)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
22 Months	0.9589 (0.8752 to 0.9869)	0.8548 (0.7508 to 0.9177)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
24 Months	0.9589 (0.8752 to 0.9869)	0.8329 (0.7197 to 0.9034)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
26 Months	0.9589 (0.8752 to 0.9869)	0.8329 (0.7197 to 0.9034)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
Number of patients at risk[c]					
2 Months	82	87	58	60	
4 Months	77	78	52	59	
6 Months	68	70	43	53	
8 Months	60	67	40	51	
10 Months	60	64	36	47	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.3 Treatment emergent adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
12 Months	52	60	34	43	
14 Months	50	60	30	42	
16 Months	45	51	28	40	
18 Months	39	48	26	36	
20 Months	36	45	25	35	
22 Months	35	39	25	32	
24 Months	35	37	24	31	
26 Months	33	34	23	28	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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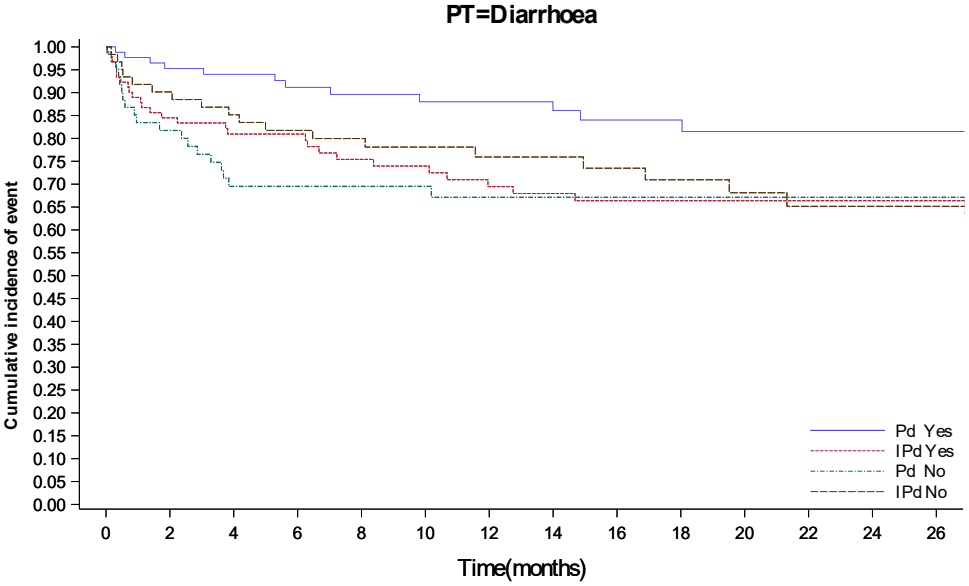
16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population



Number at Risk

Pd Yes	87	79	74	63	54	53	48	45	39	33	29	28	28	26
IPd Yes	91	75	67	60	54	50	46	45	39	37	35	31	30	27
Pd No	62	48	39	33	31	29	28	26	25	23	22	22	21	20
IPd No	61	54	51	46	43	38	34	33	30	26	24	22	22	20

PT are presented if at least 10 events in a arm
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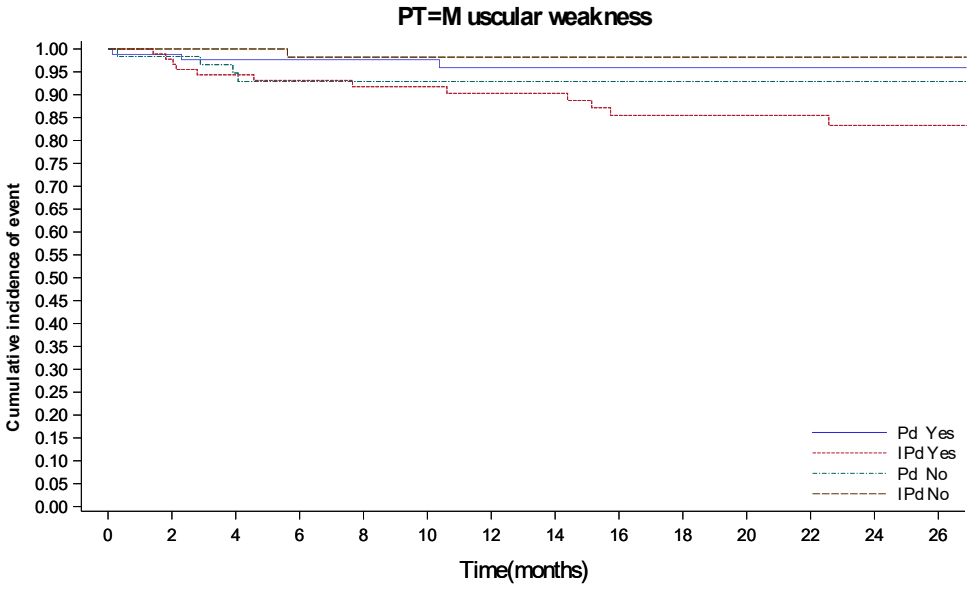
16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population



Number at Risk

Pd Yes	87	82	77	68	60	60	52	50	45	39	36	35	35	33
IPd Yes	91	87	78	70	67	64	60	60	51	48	45	39	37	34
Pd No	62	58	52	43	40	36	34	30	28	26	25	25	24	23
IPd No	61	60	59	53	51	47	43	42	40	36	35	32	31	28

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_teaept_llen_s_f_x.rtf (17NOV2020 14:46)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.5 Treatment emergent serious adverse event per SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
Metabolism and nutrition disorders (days)					
Number (%) of events	1 (1.1)	8 (8.8)	5 (8.1)	2 (3.3)	0.0263
Number (%) of patients censored	86 (98.9)	83 (91.2)	57 (91.9)	59 (96.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0199		0.1807	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	7.9874 (0.9983 to 63.9100)		0.3383 (0.0643 to 1.7791)	
P-value	-	0.0502		0.2007	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.5 Treatment emergent serious adverse event per SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
Events probability (95% CI)[c]					
2 Months	0.9885 (0.9212 to 0.9984)	0.9558 (0.8865 to 0.9832)	0.9335 (0.8325 to 0.9745)	0.9836 (0.8893 to 0.9977)	
4 Months	0.9885 (0.9212 to 0.9984)	0.9329 (0.8566 to 0.9693)	0.9335 (0.8325 to 0.9745)	0.9836 (0.8893 to 0.9977)	
6 Months	0.9885 (0.9212 to 0.9984)	0.9329 (0.8566 to 0.9693)	0.9156 (0.8088 to 0.9640)	0.9836 (0.8893 to 0.9977)	
8 Months	0.9885 (0.9212 to 0.9984)	0.9329 (0.8566 to 0.9693)	0.9156 (0.8088 to 0.9640)	0.9836 (0.8893 to 0.9977)	
10 Months	0.9885 (0.9212 to 0.9984)	0.9329 (0.8566 to 0.9693)	0.9156 (0.8088 to 0.9640)	0.9635 (0.8609 to 0.9908)	
12 Months	0.9885 (0.9212 to 0.9984)	0.9329 (0.8566 to 0.9693)	0.9156 (0.8088 to 0.9640)	0.9635 (0.8609 to 0.9908)	
14 Months	0.9885 (0.9212 to 0.9984)	0.9183 (0.8354 to 0.9604)	0.9156 (0.8088 to 0.9640)	0.9635 (0.8609 to 0.9908)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.5 Treatment emergent serious adverse event per SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	0.9885 (0.9212 to 0.9984)	0.9183 (0.8354 to 0.9604)	0.9156 (0.8088 to 0.9640)	0.9635 (0.8609 to 0.9908)	
18 Months	0.9885 (0.9212 to 0.9984)	0.9183 (0.8354 to 0.9604)	0.9156 (0.8088 to 0.9640)	0.9635 (0.8609 to 0.9908)	
20 Months	0.9885 (0.9212 to 0.9984)	0.8999 (0.8069 to 0.9495)	0.9156 (0.8088 to 0.9640)	0.9635 (0.8609 to 0.9908)	
22 Months	0.9885 (0.9212 to 0.9984)	0.8999 (0.8069 to 0.9495)	0.9156 (0.8088 to 0.9640)	0.9635 (0.8609 to 0.9908)	
24 Months	0.9885 (0.9212 to 0.9984)	0.8999 (0.8069 to 0.9495)	0.9156 (0.8088 to 0.9640)	0.9635 (0.8609 to 0.9908)	
26 Months	0.9885 (0.9212 to 0.9984)	0.8999 (0.8069 to 0.9495)	0.9156 (0.8088 to 0.9640)	0.9635 (0.8609 to 0.9908)	
Number of patients at risk[c]					
2 Months	82	85	55	59	
4 Months	78	77	53	58	
6 Months	69	71	44	53	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_seraesoc_llen_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.5 Treatment emergent serious adverse event per SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
8 Months	62	69	41	50	
10 Months	62	66	38	45	
12 Months	55	64	36	41	
14 Months	53	63	32	40	
16 Months	48	55	31	38	
18 Months	42	52	30	35	
20 Months	39	48	29	34	
22 Months	37	43	29	31	
24 Months	37	41	28	30	
26 Months	35	38	27	27	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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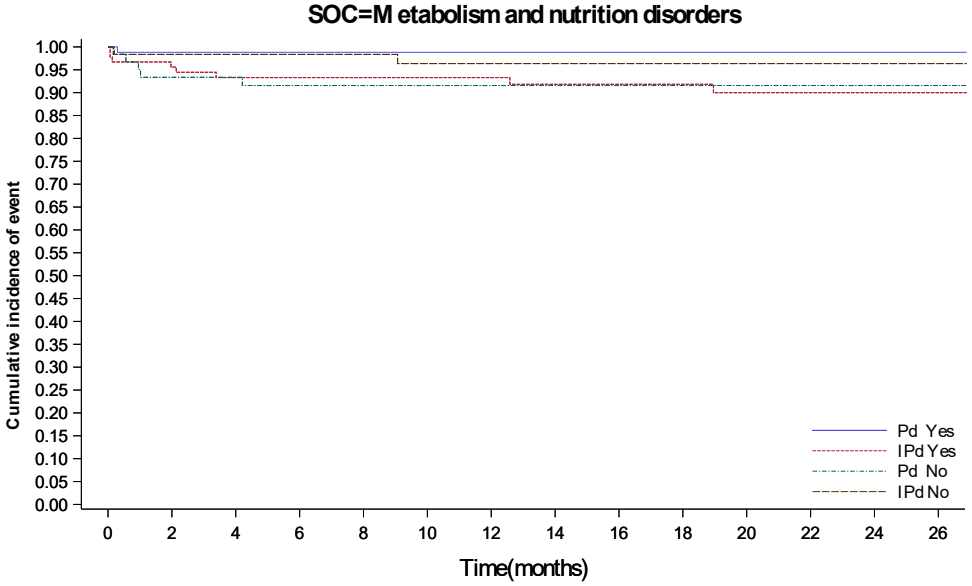
16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event per SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population



Number at Risk

Pd Yes	87	82	78	69	62	62	55	53	48	42	39	37	37	35
IPd Yes	91	85	77	71	69	66	64	63	55	52	48	43	41	38
Pd No	62	55	53	44	41	38	36	32	31	30	29	29	28	27
IPd No	61	59	58	53	50	45	41	40	38	35	34	31	30	27

SOC are presented if at least 5% of patients in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_seraesoc_llen_s_f_x.rtf (17NOV2020 14:46)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.7 Treatment emergent not severe adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
Diarrhoea (days)					
Number (%) of events	12 (13.8)	28 (30.8)	20 (32.3)	18 (29.5)	0.0190
Number (%) of patients censored	75 (86.2)	63 (69.2)	42 (67.7)	43 (70.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (14.8501 to NC)	8.3778 (2.2341 to 31.0801)	3.6140 (0.8871 to 33.9384)	14.9487 (3.8439 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (33.9384 to NC)	NC (21.3224 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0147		0.5145	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	2.2828 (1.1549 to 4.5122)		0.8061 (0.4207 to 1.5447)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.7 Treatment emergent not severe adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
P-value	-	0.0176		0.5160	
Stratified[a] Hazard ratio inverted (95% CI) vs IPd	0.4381 (0.2216 to 0.8659)				
Events probability (95% CI)[c]					
2 Months	0.9529 (0.8794 to 0.9821)	0.8450 (0.7523 to 0.9051)	0.8175 (0.6946 to 0.8945)	0.9016 (0.7941 to 0.9546)	
4 Months	0.9404 (0.8626 to 0.9748)	0.8095 (0.7114 to 0.8771)	0.7127 (0.5788 to 0.8108)	0.8515 (0.7341 to 0.9199)	
6 Months	0.9119 (0.8233 to 0.9572)	0.8095 (0.7114 to 0.8771)	0.7127 (0.5788 to 0.8108)	0.8175 (0.6945 to 0.8945)	
8 Months	0.8964 (0.8024 to 0.9471)	0.7542 (0.6470 to 0.8329)	0.7127 (0.5788 to 0.8108)	0.7997 (0.6740 to 0.8810)	
10 Months	0.8798 (0.7801 to 0.9361)	0.7397 (0.6304 to 0.8211)	0.7127 (0.5788 to 0.8108)	0.7811 (0.6526 to 0.8667)	
12 Months	0.8798 (0.7801 to 0.9361)	0.6947 (0.5800 to 0.7838)	0.6889 (0.5507 to 0.7924)	0.7594 (0.6264 to 0.8505)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_llen_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.7 Treatment emergent not severe adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.8607 (0.7536 to 0.9235)	0.6796 (0.5634 to 0.7710)	0.6889 (0.5507 to 0.7924)	0.7594 (0.6264 to 0.8505)	
16 Months	0.8402 (0.7258 to 0.9097)	0.6638 (0.5461 to 0.7576)	0.6889 (0.5507 to 0.7924)	0.7349 (0.5964 to 0.8323)	
18 Months	0.8402 (0.7258 to 0.9097)	0.6638 (0.5461 to 0.7576)	0.6889 (0.5507 to 0.7924)	0.7096 (0.5660 to 0.8131)	
20 Months	0.8147 (0.6894 to 0.8933)	0.6638 (0.5461 to 0.7576)	0.6889 (0.5507 to 0.7924)	0.6812 (0.5317 to 0.7919)	
22 Months	0.8147 (0.6894 to 0.8933)	0.6638 (0.5461 to 0.7576)	0.6889 (0.5507 to 0.7924)	0.6516 (0.4968 to 0.7693)	
24 Months	0.8147 (0.6894 to 0.8933)	0.6638 (0.5461 to 0.7576)	0.6889 (0.5507 to 0.7924)	0.6516 (0.4968 to 0.7693)	
26 Months	0.8147 (0.6894 to 0.8933)	0.6638 (0.5461 to 0.7576)	0.6889 (0.5507 to 0.7924)	0.6516 (0.4968 to 0.7693)	
Number of patients at risk[c]					
2 Months	79	75	48	54	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.7 Treatment emergent not severe adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	74	67	40	51	
6 Months	63	60	34	46	
8 Months	54	54	32	43	
10 Months	53	50	30	38	
12 Months	48	46	29	34	
14 Months	45	45	26	33	
16 Months	39	39	25	30	
18 Months	33	37	23	26	
20 Months	29	35	22	24	
22 Months	28	31	22	22	
24 Months	28	30	21	22	
26 Months	26	27	20	20	
Muscular weakness (days)					
Number (%) of events	3 (3.4)	11 (12.1)	4 (6.5)	1 (1.6)	0.0330
Number (%) of patients censored	84 (96.6)	80 (87.9)	58 (93.5)	60 (98.4)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.7 Treatment emergent not severe adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (22.5708 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.0502		0.1742	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	3.3330 (0.9283 to 11.9669)		0.2460 (0.0275 to 2.2031)	
P-value	-	0.0649		0.2099	
Events probability (95% CI)[c]					
2 Months	0.9885 (0.9212 to 0.9984)	0.9777 (0.9136 to 0.9944)	0.9836 (0.8893 to 0.9977)	1.0000 (1.0000 to 1.0000)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.7 Treatment emergent not severe adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	0.9763 (0.9085 to 0.9940)	0.9552 (0.8850 to 0.9829)	0.9475 (0.8457 to 0.9828)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9763 (0.9085 to 0.9940)	0.9429 (0.8682 to 0.9759)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
8 Months	0.9763 (0.9085 to 0.9940)	0.9293 (0.8488 to 0.9677)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
10 Months	0.9763 (0.9085 to 0.9940)	0.9293 (0.8488 to 0.9677)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
12 Months	0.9589 (0.8752 to 0.9869)	0.9147 (0.8285 to 0.9587)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
14 Months	0.9589 (0.8752 to 0.9869)	0.9147 (0.8285 to 0.9587)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
16 Months	0.9589 (0.8752 to 0.9869)	0.8662 (0.7631 to 0.9265)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
18 Months	0.9589 (0.8752 to 0.9869)	0.8662 (0.7631 to 0.9265)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.7 Treatment emergent not severe adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
20 Months	0.9589 (0.8752 to 0.9869)	0.8662 (0.7631 to 0.9265)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
22 Months	0.9589 (0.8752 to 0.9869)	0.8662 (0.7631 to 0.9265)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
24 Months	0.9589 (0.8752 to 0.9869)	0.8440 (0.7310 to 0.9123)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
26 Months	0.9589 (0.8752 to 0.9869)	0.8440 (0.7310 to 0.9123)	0.9289 (0.8213 to 0.9728)	0.9821 (0.8799 to 0.9975)	
Number of patients at risk[c]					
2 Months	82	87	58	60	
4 Months	77	79	52	59	
6 Months	68	71	43	53	
8 Months	60	68	40	51	
10 Months	60	65	36	47	
12 Months	52	61	34	43	
14 Months	50	61	30	42	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.7 Treatment emergent not severe adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
16 Months	45	51	28	40	
18 Months	39	48	26	36	
20 Months	36	45	25	35	
22 Months	35	39	25	32	
24 Months	35	37	24	31	
26 Months	33	34	23	28	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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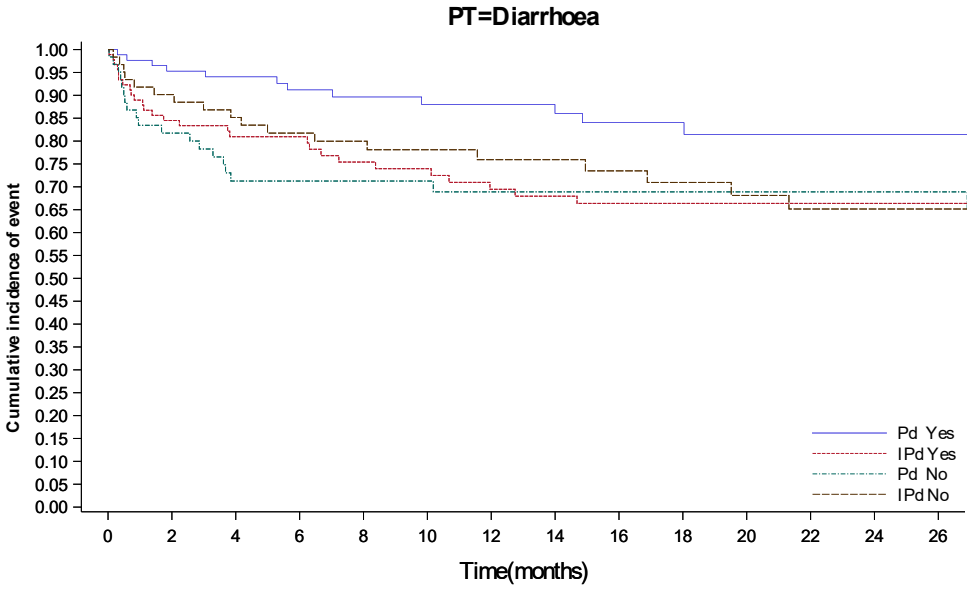
16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.8 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

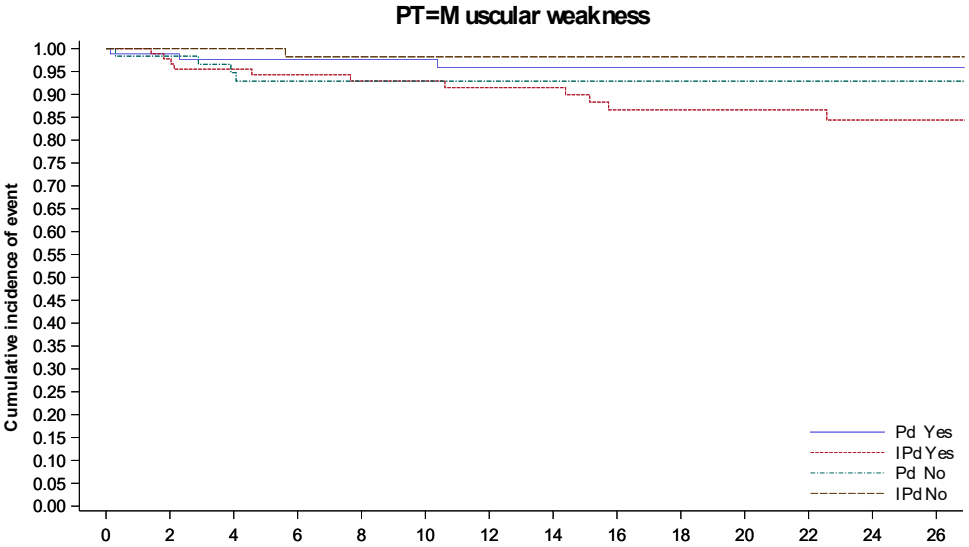


Number at Risk

Pd Yes	87	79	74	63	54	53	48	45	39	33	29	28	28	26
IPd Yes	91	75	67	60	54	50	46	45	39	37	35	31	30	27
Pd No	62	48	40	34	32	30	29	26	25	23	22	22	21	20
IPd No	61	54	51	46	43	38	34	33	30	26	24	22	22	20

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_llen_s_f_x.rtf (17NOV2020 14:46)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.8 Kaplan-Meier cumulative incidence curve of treatment emergent not severe adverse event per PT by treatment group according to refractory to lenalidomide in last previous regimen - Safety population



Number at Risk

Pd Yes	87	82	77	68	60	60	52	50	45	39	36	35	35	33
IPd Yes	91	87	79	71	68	65	61	61	51	48	45	39	37	34
Pd No	62	58	52	43	40	36	34	30	28	26	25	25	24	23
IPd No	61	60	59	53	51	47	43	42	40	36	35	32	31	28

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae12pt_llen_s_f_x.rtf (17NOV2020 14:46)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.9 Treatment emergent severe adverse event per SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
General disorders and administration site conditions (days)					
Number (%) of events	12 (13.8)	9 (9.9)	3 (4.8)	12 (19.7)	0.0227
Number (%) of patients censored	75 (86.2)	82 (90.1)	59 (95.2)	49 (80.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (31.3758 to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.0472 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd					
Stratified[a] Log-Rank test p-value[b] vs Pd	-	0.3064		0.0107	
Stratified[a] Hazard ratio (95% CI) vs Pd	-	0.6354 (0.2646 to 1.5259)		4.4981 (1.2678 to 15.9583)	
P-value	-	0.3103		0.0200	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.9 Treatment emergent severe adverse event per SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
Stratified[a] Hazard ratio inverted (95% CI) vs IPd			0.2223 (0.0627 to 0.7887)		
Events probability (95% CI)[c]					
2 Months	0.9295 (0.8497 to 0.9677)	0.9779 (0.9145 to 0.9944)	1.0000 (1.0000 to 1.0000)	0.9016 (0.7941 to 0.9546)	
4 Months	0.9173 (0.8342 to 0.9597)	0.9667 (0.9002 to 0.9891)	0.9649 (0.8668 to 0.9911)	0.8849 (0.7737 to 0.9434)	
6 Months	0.8910 (0.8008 to 0.9419)	0.9543 (0.8825 to 0.9826)	0.9649 (0.8668 to 0.9911)	0.8682 (0.7537 to 0.9318)	
8 Months	0.8767 (0.7823 to 0.9319)	0.9276 (0.8453 to 0.9669)	0.9649 (0.8668 to 0.9911)	0.8682 (0.7537 to 0.9318)	
10 Months	0.8616 (0.7630 to 0.9212)	0.9135 (0.8263 to 0.9580)	0.9649 (0.8668 to 0.9911)	0.8682 (0.7537 to 0.9318)	
12 Months	0.8616 (0.7630 to 0.9212)	0.9135 (0.8263 to 0.9580)	0.9649 (0.8668 to 0.9911)	0.8682 (0.7537 to 0.9318)	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.9 Treatment emergent severe adverse event per SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
14 Months	0.8616 (0.7630 to 0.9212)	0.9135 (0.8263 to 0.9580)	0.9649 (0.8668 to 0.9911)	0.8682 (0.7537 to 0.9318)	
16 Months	0.8616 (0.7630 to 0.9212)	0.9135 (0.8263 to 0.9580)	0.9649 (0.8668 to 0.9911)	0.8213 (0.6902 to 0.9008)	
18 Months	0.8616 (0.7630 to 0.9212)	0.9135 (0.8263 to 0.9580)	0.9649 (0.8668 to 0.9911)	0.8213 (0.6902 to 0.9008)	
20 Months	0.8616 (0.7630 to 0.9212)	0.8949 (0.7981 to 0.9468)	0.9649 (0.8668 to 0.9911)	0.8213 (0.6902 to 0.9008)	
22 Months	0.8616 (0.7630 to 0.9212)	0.8949 (0.7981 to 0.9468)	0.9649 (0.8668 to 0.9911)	0.8213 (0.6902 to 0.9008)	
24 Months	0.8616 (0.7630 to 0.9212)	0.8949 (0.7981 to 0.9468)	0.9649 (0.8668 to 0.9911)	0.7666 (0.6187 to 0.8631)	
26 Months	0.8616 (0.7630 to 0.9212)	0.8949 (0.7981 to 0.9468)	0.9304 (0.7864 to 0.9786)	0.7666 (0.6187 to 0.8631)	
Number of patients at risk[c]					
2 Months	78	87	59	55	

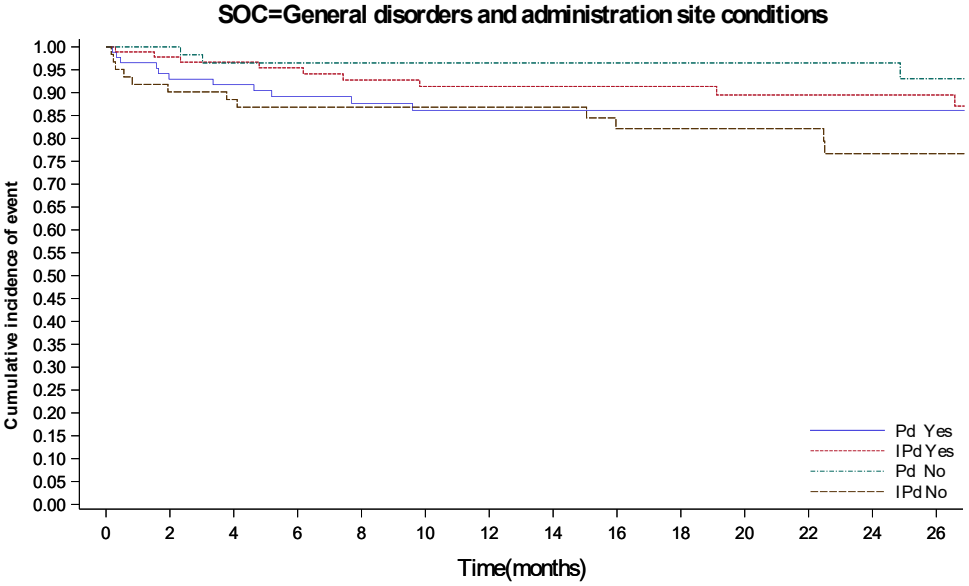
SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae34soc_llen_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.9 Treatment emergent severe adverse event per SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population

	Yes		No		
	Pd (N=87)	**IPd (N=91)**	**Pd (N=62)**	**IPd (N=61)**	**p-value of treatment-by-sub group interaction[d]**
4 Months	74	80	53	53	
6 Months	67	72	46	48	
8 Months	58	69	43	47	
10 Months	57	65	39	43	
12 Months	50	62	37	39	
14 Months	49	62	34	39	
16 Months	44	54	32	35	
18 Months	39	51	30	33	
20 Months	36	48	29	32	
22 Months	34	42	29	30	
24 Months	34	40	28	27	
26 Months	33	37	26	24	

SOC are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowle
[a] stratified on age (<75 years versus >=75 years) and Number of previous lines of therapy (2 or 3 versus > 3) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
[d] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae34soc_llen_s_t_x.rtf (17NOV2020 9:34)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by refractory to lenalidomide in last previous regimen
16.2.7.1.56.10 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event per SOC by treatment group according to refractory to lenalidomide in last previous regimen - Safety population



Number at Risk

Pd Yes	87	78	74	67	58	57	50	49	44	39	36	34	34	33
IPd Yes	91	87	80	72	69	65	62	62	54	51	48	42	40	37
Pd No	62	59	53	46	43	39	37	34	32	30	29	29	28	26
IPd No	61	55	53	48	47	43	39	39	35	33	32	30	27	24

SOC are presented if at least 5% of patients in a arm
PGM=DEVOPS/SAR650984/EFC14335/CIR_02_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_sevae34soc_llen_s_f_x.rtf (17NOV2020 14:46)